


## Arrow - Norfloxacin

Norfloxacin 400 mg Tablets

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### Presentation

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Arrow - Norfloxacin is a white, film-coated, convex, oval-shaped scored tablet, embossed with "N / F" on one side and '  ' on the other side.

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### Uses

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#### **Actions**

Norfloxacin has a broad spectrum of antibacterial activity against Gram-negative and some Gram-positive aerobic pathogens. The fluorine atom at the 6 position provides increased potency against Gram-negative organisms and the piperazine moiety at the 7 position is responsible for anti-pseudomonal activity.

#### **Microbiology**

Norfloxacin inhibits bacterial deoxyribonucleic acid synthesis and is bactericidal. At the molecular level, three specific events were attributed to norfloxacin in *Escherichia coli* cells:

1. inhibition of the ATP-dependent DNA supercoiling reaction catalysed by DNA gyrase;
2. inhibition of the relaxation of supercoiled DNA; and
3. promotion of double-stranded DNA breakage.

Resistance to norfloxacin due to spontaneous mutation is a rare occurrence (range from  $10^{-9}$  to  $10^{-12}$  cells). Resistance of the organism has developed during therapy with norfloxacin in less than 1% of patients being treated. Organisms in which development of resistance is greatest are *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter spp.*, *Enterococci* and *Methicillin-resistant Staphylococcus aureus*. For this reason, when there is a lack of satisfactory clinical response, culture and susceptibility testing should be repeated.

Because of its specific structure, norfloxacin is generally active against organisms that are resistant to other organic acids such as nalidixic, oxolinic, and pipemidic acids, cinoxacin and flumequine. Organisms resistant to norfloxacin *in vitro* are also resistant to these organic acids. Preliminary studies suggest that norfloxacin-resistant organisms are also generally resistant to pefloxacin, ofloxacin, ciprofloxacin and enoxacin. There is generally no cross resistance between norfloxacin and other classes of antibacterial agents. Therefore, norfloxacin often demonstrates activity against indicated organisms resistant to aminoglycosides (including

gentamicin), aminocyclitols (spectinomycin), penicillins, cephalosporins, tetracyclines, macrolides, sulfonamides (including combinations of sulfamethoxazole and trimethoprim), and 2,4-diaminopyrimidines.

Antagonism has been demonstrated *in vitro* between norfloxacin and nitrofurantoin.

Analysis of the overall clinical experience with norfloxacin revealed a high correlation between the results of susceptibility tests conducted *in vitro* and the bacteriological and clinical efficacy of the agent in humans. Norfloxacin is active *in vitro* against the following bacteria:

### **Bacteria found in urinary tract infections**

#### **Enterobacteriaceae**

Citrobacter spp.; Citrobacter koseri (formerly known as Citrobacter diversus); Citrobacter freundii; Edwardsiella tarda; Enterobacter spp.; Enterobacter aerogenes; Enterobacter agglomerans; Enterobacter cloacae; Escherichia coli; Hafnia alvei; Klebsiella spp.; Klebsiella oxytoca; Klebsiella pneumoniae; Morganella morganii; Proteus spp. (indole positive); Proteus mirabilis; Proteus vulgaris; Providencia spp.; Providencia rettgeri; Providencia stuartii; Serratia spp.; Serratia marcescens.

#### **Pseudomonadaceae**

Pseudomonas aeruginosa; Pseudomonas cepacia; Pseudomonas fluorescens; Pseudomonas stutzeri.

#### **Gram-positive cocci**

Enterococcus faecalis; Group G streptococci; Staphylococcus spp.; Staphylococcus Coag. Negative; Staphylococcus aureus (including penicillinase-producing and most methicillin-resistant strains); Staphylococcus epidermidis; Staphylococcus saprophyticus; Streptococcus agalactiae; Viridans group streptococci.

#### **Other**

Flavobacterium spp.

### **Bacteria associated with acute gastroenteritis**

Aeromonas hydrophila; Campylobacter foetus subsp. Jejuni; enterotoxigenic Escherichia coli; Plesiomonas shigelloides; Salmonella spp.; Salmonella typhi; Shigella spp.; Shigella boydii; Shigella dysenteriae; Shigella flexneri; Shigella sonnei; Vibrio cholerae; Vibrio parahaemolyticus; Yersinia enterocolitica.

#### **Other bacteria**

Norfloxacin is active against Bacillus cereus, Neisseria gonorrhoeae, Ureaplasma urealyticum, Haemophilus influenzae and Haemophilus ducreyi.

Norfloxacin is not active against anaerobes, including Actinomyces spp., Fusobacterium spp. Bacteroides spp. and Clostridium spp. other than C. perfringens.

## **Susceptibility testing**

The FDA standardised disc (formerly, Kirby-Bauer) technique of antibiotic susceptibility testing is recommended using a 10 mcg disc of 6 mm diameter.

<b>Category</b>	<b>Zone Diameter (mm)</b>	<b>MIC (mcg/mL)</b>
Susceptible	> 17	< 4
Intermediate	13 - 16	8
Resistant	< 12	> 16

MIC = Minimum inhibitory concentration

These susceptibility criteria apply only to organisms isolated from urine (urinary tract) and faeces (gastrointestinal tract).

*Neisseria gonorrhoeae* and organisms isolated from tissues are considered susceptible to norfloxacin if the zone diameter is > 21 mm or minimum inhibitory concentration (MIC) < 1 mcg/mL.

Norfloxacin susceptibility test results should not be used to predict susceptibility to other less potent quinolone antibacterial agents such as nalidixic acid.

## **Pharmacokinetics**

### **Absorption**

Norfloxacin is rapidly absorbed following oral administration. In healthy volunteers, at least 30 to 40% of an oral dose of norfloxacin is absorbed. This results in a serum concentration of 1.5 mcg/mL being attained approximately 1 hour after administration of a 400 mg dose. Peak serum levels of norfloxacin are slightly lower when administered with food than when given fasting. Mean serum half-life is 3 to 4 hours and is independent of dose. Steady-state concentrations of norfloxacin will be attained within 2 days of dosing.

### **Distribution**

The following are the mean concentrations of norfloxacin in various fluids and tissues measured 1 to 4 hours after two 400 mg doses, unless otherwise indicated:

Renal parenchyma 7.3 mcg/g

Prostate 2.5 mcg/g

Seminal fluid 2.7 mcg/mL

Testicle 1.6 mcg/g

Uterus/cervix 3.0 mcg/g

Vagina 4.3 mcg/g

Fallopian tube 1.9 mcg/g

Gallbladder tissue 1.8 mcg/g (measured 4 to 6 hours after one 400 mg dose)

Bile 6.9 mcg/mL (after two 200 mg doses).

The serum protein binding of norfloxacin is between 10 and 15%.

Two to three hours after a single 400 mg dose, urinary concentrations reach a value of 200 or more mcg/mL in healthy volunteers and remain above 30 mcg/mL for at least 12 hours. While the bactericidal potency of norfloxacin is not affected by the pH of urine, the urinary pH may affect its solubility. Norfloxacin is least soluble at urinary pH of 7.5 with solubility increasing at pHs above and below this value.

### **Metabolism and Elimination**

Norfloxacin is eliminated mainly through renal excretion. Renal excretion occurs by both glomerular filtration and net tubular secretion, as evidenced by the high rate of renal clearance (approximately 275 mL/minute). In the first 24 hours, 33 to 48% is recovered in the urine as norfloxacin. Six active metabolites of norfloxacin (5 to 8%) of lesser antimicrobial potency are also recovered in the urine. The parent compound accounts for over 70% of total excretion.

Following a single 400 mg dose of norfloxacin, the disposition of the drug in patients with creatinine clearance greater than 30 mL/minute/1.73 m<sup>2</sup> is similar to that of healthy volunteers. In patients with creatinine clearance less than 30 mL/minute/1.73 m<sup>2</sup>, the renal elimination of norfloxacin decreases significantly. The effective serum half-life in these patients is approximately 8 hours. Thus, alteration of dosage is necessary (see **Dosage and Administration**). Norfloxacin absorption appears, however, unaffected by decreasing renal function.

In healthy elderly volunteers (65 to 75 years of age with normal renal function for their age), norfloxacin is eliminated more slowly because of their slightly decreased renal function. The effective half-life of norfloxacin in these elderly subjects is 4 hours.

Faecal recovery accounts for another 30% of the administered dose. This represents the unabsorbed drug along with a small contribution through biliary excretion. After a single 400 mg dose of norfloxacin, mean antimicrobial activities equivalent to 278, 773 and 82 mcg norfloxacin/g faeces were obtained at 12, 24 and 48 hours, respectively.

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### **Indications**

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Norfloxacin is a broad-spectrum bactericidal agent indicated for the treatment of:

- upper and lower, complicated and uncomplicated acute urinary tract infections including cystitis, pyelitis, cystopyelitis, pyelonephritis, chronic prostatitis, epididymitis, and those urinary infections associated with urologic surgery, neurogenic bladder or nephrolithiasis caused by bacteria susceptible to norfloxacin;
- acute bacterial gastroenteritis caused by susceptible organisms;

- gonococcal urethritis pharyngitis, proctitis or cervicitis caused by both penicillinase and non-penicillinase producing *Neisseria gonorrhoeae*.

Infections caused by multiply-resistant organisms have been successfully treated with the usual doses of norfloxacin.

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## Dosage and Administration

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Arrow - Norfloxacin should be taken with a glass of water at least one hour before or two hours after a meal or milk ingestion. Patients receiving norfloxacin should drink fluids liberally to be well hydrated. Multivitamins, products containing iron or zinc, antacids containing magnesium and aluminium, sucralfate, or didanosine (tablets and solution) should not be taken concomitantly or within 2 hours after dosing norfloxacin.

Susceptibility of the causative organism to norfloxacin should be tested prior to and during treatment if clinical response warrants. However, therapy may be initiated before obtaining the results of these tests. Maximum total daily dosage should not exceed 800 mg/day.

Diagnosis	Dosage	Therapy Duration
Urinary tract infections	400 mg twice daily	7 - 10 days
Uncomplicated acute cystitis	400 mg twice daily	3 - 7 days
Chronic prostatitis	400 mg twice daily	4 weeks
Acute bacterial gastroenteritis (shigellosis, traveller's diarrhoea)	400 mg twice daily	5 days
Acute gonococcal urethritis, pharyngitis, proctitis or cervicitis	800 mg	single dose

### Renal impairment

Arrow - Norfloxacin is suitable for the treatment of patients with renal insufficiency. In studies involving patients whose creatinine clearance was less than 30 mL/minute/1.73 m<sup>2</sup>, but who did not require haemodialysis, the plasma half-life of norfloxacin was approximately 8 hours. Clinical studies showed that there was no difference in the mean half-life of norfloxacin in patients with creatinine clearance of less than 10 mL/minute/1.73 m<sup>2</sup>, compared to patients with creatinine clearance of 10 to 30 mL/minute/1.73 m<sup>2</sup>. Hence, for these patients, the recommended dose is one 400 mg tablet once daily. At this dosage, concentrations in appropriate body tissues or fluids exceed the MICs for most urinary pathogens sensitive to norfloxacin.

There are insufficient data on which to have a dosage recommendation for the treatment of gonorrhoea in patients with a creatinine clearance of 30 mL/minute/1.73 m<sup>2</sup> or less.

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## Contraindications

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Arrow - Norfloxacin should not be used in:

- patients with known hypersensitivity to norfloxacin, any chemically related quinoline antibacterials or any component of this product (see **Further Information**);
  - patients with a history of fluoroquinolone associated tendonopathy (see **Warnings and Precautions**);
  - pre-pubertal children;
  - pregnant women.
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## Warnings and Precautions

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### ***Crystalluria***

Needle-shaped crystals were found in the urine of some volunteers who received either placebo, norfloxacin 800 mg or norfloxacin 1,600 mg (at or twice the recommended daily dose, respectively) while participating in a double blind, crossover study comparing single doses of norfloxacin with placebo. While crystalluria is not expected to occur under usual conditions with a dosage regimen of 400 mg twice daily, as a precaution, the daily recommended dosage should not be exceeded. Patient should drink sufficient fluids to ensure a proper state of hydration and adequate urinary output, and to avoid excessively alkaline urine with the use of urinary alkaliniser (e.g. *Ural*).

### ***Pseudomembranous colitis***

Antibiotic-associated pseudomembranous colitis has been reported with many antibiotics including norfloxacin. A toxin produced with *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life-threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases, appropriate therapy with a suitable oral antibacterial agent effective against *Cl. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (*Lomotil*), may prolong and/or worsen the condition and should not be used.

### ***Tendonitis and tendon rupture***

Fluoroquinolones, including norfloxacin, may cause tendonitis, Achilles and other tendon ruptures. The risk of these adverse effects is present during use and for 6 months following use of fluoroquinolone. Also, the risk is increased in patients over the age of 60 years, on concomitant systemic steroid therapy, or who have a kidney, heart or lung transplant. Fluoroquinolones should not be used in patients with a history of fluoroquinolone associated tendonopathy.

Prescribers should advise patients that at the first sign of tendon pain, inflammation or tendon rupture, to stop taking the fluoroquinolone, avoid exercise or use of the affected area, and immediately contact their doctors.

### ***Seizures***

As with other organic acids, norfloxacin should be used with caution in individuals with a history of convulsions or known factors that predispose to seizures. Convulsions have been reported rarely in patients receiving norfloxacin.

### ***Photosensitivity***

Photosensitivity reactions have been observed in patients who are exposed to excessive sunlight while receiving fluoroquinolones. Excessive sunlight should be avoided. Therapy should be discontinued if photosensitivity occurs.

### ***Haemolytic reactions***

Rarely, haemolytic reactions have been reported in patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity who take quinolone agents, including norfloxacin (see Adverse Effects).

### ***Myasthenia gravis***

Quinolones, including norfloxacin, may exacerbate the signs of myasthenia gravis and lead to life-threatening weakness of the respiratory muscles. Caution should be exercised when using quinolones, including norfloxacin, in patients with myasthenia gravis (see Adverse Effects).

### ***Arrhythmia***

Some quinolones have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. During post-marketing surveillance, extremely rare cases of torsades de pointes, have been reported in patients taking norfloxacin. These reports generally involve patients who had other concurrent medical conditions and the relationship to norfloxacin has not been established. Among drugs known to cause prolongation of the QT interval, the risk of arrhythmia may be reduced by avoiding use in the presence of hypokalaemia, significant bradycardia, or concurrent treatment with class IA or class III anti-arrhythmic agents. Quinolones should also be used with caution in patients using cisapride, erythromycin, antipsychotics, tricyclic antidepressants or have any personal or family history of QTc prolongation.

### ***Renal impairment***

Arrow - Norfloxacin is suitable for the treatment of patients with renal impairment. However, since norfloxacin is primarily excreted by the kidney, urinary levels may be significantly compromised by severe renal dysfunction (see **Dosage and Administration**).

### ***Carcinogenesis, mutagenesis and impairment of fertility***

No information is available on the carcinogenic potential of norfloxacin. For the mutagenic activity and fertility studies, refer to **Animal toxicology** in this section.

### ***Use in pregnancy (Category B3)***

The safe use of norfloxacin in pregnant women has not been established and, consequently, the benefits of treatment with norfloxacin should be weighed against potential risks. Since norfloxacin, like other fluoroquinolones, causes arthropathy in immature animals, it should not be used in pregnant women (see **Contraindications**).

Norfloxacin has been detected in cord blood and amniotic fluid. It has also been found to produce embryonic loss, embryoletality and slight maternotoxicity in animal studies (see **Animal toxicology** in this section).

### ***Use in lactation***

It is not known whether norfloxacin is excreted in human milk. When a 200 mg dose of norfloxacin was administered to breastfeeding mothers, norfloxacin was not detected in human milk. However, the dose studied was low. Also, there is a potential for serious adverse reactions from norfloxacin in breastfed infants, as other drugs in this class are secreted in human milk. A decision should be made to discontinue breastfeeding or to discontinue the drug at least 24 to 48 hours before re-starting breastfeeding, taking into account the importance of the drug to the mother.

### ***Use in children***

As with other quinolones, norfloxacin has been shown to cause arthropathy in immature animals. The safety of norfloxacin in children has not been adequately explored and, therefore, norfloxacin is not to be used in pre-pubertal children or growing adolescents (see **Contraindications** and **Animal toxicology** in this section).

### ***Effect on ability to drive or operate machinery***

Arrow - Norfloxacin may cause dizziness or light-headedness. Patients should know how they react to norfloxacin before they operate a vehicle or machinery, or engage in activities requiring mental alertness and coordination.

### ***Animal toxicology***

Norfloxacin and related medicines have been shown to cause arthropathy in immature animals of most species tested. The oral administration of single

doses of 100 mg/kg norfloxacin, six times the recommended human clinical dose, caused lameness in immature dogs. Histologic examination of the weight-bearing joints of these dogs revealed permanent lesions of the cartilage.

Related medicines (e.g. nalidixic acid and cinoxacin) also produced erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species. Dogs 6 months or older were not susceptible to these changes.

Crystalluria has occurred in laboratory animals tested with norfloxacin. In dogs, needle-shaped crystals were seen in the urine at doses of 50 mg/kg/day. In rats, crystals were reported following doses of 200 mg/kg/day.

Ocular toxicity, seen with some related drugs, was not observed in any norfloxacin treated animals.

Teratology studies in mice and rats and fertility studies in mice at oral doses of 30 to 50 times the usual dose for humans did not reveal teratogenic or foetal toxic effects. Embryotoxicity was observed in rabbits at doses of 100 mg/kg/day. This was secondary to maternal toxicity and it is a non-specific antimicrobial effect in the rabbit due to an unusual sensitivity to antibiotic induced changes in the gut microflora.

Norfloxacin has been shown to produce embryonic loss in cynomolgus monkeys when given in doses of 150 mg/kg/day with peak plasma levels that are two to three times those obtained in humans. There has been no evidence of a teratogenic effect in any of the animal species tested (rat, rabbit, mouse, monkey) at 100 to 800 mg/kg/day.

Embryolethality and slight maternotoxicity (vomiting and anorexia) were observed in cynomolgus monkeys at doses of 150 mg/kg/day or higher.

Norfloxacin was tested for mutagenic activity in a number of *in vivo* and *in vitro* tests. Norfloxacin had no mutagenic effect in the dominant lethal test in mice and did not cause chromosomal aberrations in hamsters or rats at 500 to 1,000 mg/kg/day. Norfloxacin had no mutagenic activity *in vitro* in the Ames microbial mutagen test and V-79 mammalian cell assay. Although norfloxacin was weakly positive in the Rec-assay for DNA repair, all other mutagenic assays were negative including a more sensitive test (V-79).

Norfloxacin did not adversely affect the fertility of male and female mice at oral doses up to 500 mg/kg/day.

No significant lethality was observed in male and female mice and rats at single oral doses up to 4 g/kg.

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## Adverse Effects

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In clinical trials, norfloxacin is generally well tolerated. Overall incidence of drug related adverse effects reported during worldwide clinical trials involving 2,346 patients was approximately 3%.

The most common adverse effects (less than 3% but occurring in > 0.1% of the patients) have been gastrointestinal, neuropsychiatric and skin reactions, which include nausea, headache, dizziness, rash, heartburn, abdominal pain or cramps, and diarrhoea.

In very rare instances (< 0.1%), other adverse effects such as anorexia, sleep disturbances, depression, anxiety or nervousness, irritability, euphoria, disorientation, hallucination, tinnitus and epiphora have been reported.

Abnormal laboratory adverse effects were rarely observed during clinical trials. However, the following have been reported with an incidence of < 0.3%: leucopenia, eosinophilia, neutropenia, thrombocytopenia, elevation of alanine transaminase and aspartate amino transferase.

The following additional adverse effects have been reported since the medicine was marketed:

**Hypersensitivity reactions:** anaphylaxis, angioedema, dyspnoea, vasculitis, urticaria, arthritis, myalgia and arthralgia, interstitial nephritis

**Skin:** photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, pruritus

**Gastrointestinal:** pseudomembranous colitis, pancreatitis (rare), hepatitis, jaundice (including cholestatic jaundice), elevated liver function tests

**Musculoskeletal:** tendonitis, tendon rupture, exacerbation of myasthenia gravis, elevated creatine kinase

**Nervous or psychiatric system:** polyneuropathy including Guillain-Barré syndrome, confusion, paraesthesia, hypoesthesia, psychic disturbances including psychotic reactions, convulsions, tremors, myoclonus

**Haematologic:** agranulocytosis, haemolytic anaemia, sometimes associated with glucose-6-phosphate dehydrogenase deficiency

**Genitourinary:** vaginal candidiasis

**Renal function:** renal failure

**Special senses:** dysgeusia, visual disturbances, hearing loss

### **Causal relationship unknown**

A definite causal relationship could not be established with regard to the following adverse effects: conjunctivitis, eye pain or irritation, asthenia or

fatigue, somnolence, constipation and flatulence. On very rare occasions, prolonged QTc interval and ventricular arrhythmia (including torsades de pointes), hypertonia, ataxia, dysarthria, dysphasia, haemophthalmia, nystagmus, periorbital erythema, fever, vomiting, dry mouth, and hypoglycaemia have been reported.

Without establishing a causal relationship, the following have also been reported: increased serum creatinine, proteinuria, increased BUN, and decreased haematocrit.

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## Interactions

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Co-administration of probenecid does not affect serum concentrations of norfloxacin, but urinary excretion of the drug diminishes.

As with other organic acid antibacterials, antagonism has been demonstrated *in vitro* between norfloxacin and nitrofurantoin.

Quinolones, including norfloxacin, have been shown *in vitro* to inhibit CYP1A2. Concomitant use with drugs metabolised by CYP1A2 (e.g. caffeine, clozapine, ropinirole, tacrine, theophylline, tizanidine) may result in increased substrate drug concentrations when given in usual doses. Patients taking any of these drugs concomitantly with norfloxacin should be carefully monitored.

Elevated plasma levels of theophylline have been reported with concomitant quinolone use. There have been rare reports of theophylline-related adverse effects in patients on concomitant therapy with norfloxacin and theophylline. Monitoring of theophylline plasma levels should be considered and dosage of theophylline adjusted as required.

Some quinolones, including norfloxacin, have also been shown to interfere with the metabolism of caffeine. This may lead to reduced clearance of caffeine and a prolongation of its plasma half-life.

Elevated serum levels of cyclosporin have been reported with concomitant use with norfloxacin. Cyclosporin serum levels should be monitored and appropriate cyclosporin dosage adjustments made when these medicines are used concomitantly.

Quinolones, including norfloxacin, may enhance the effects of oral anticoagulants including warfarin or its derivatives and fludione or similar agents. When these products are administered concomitantly, prothrombin time or other suitable coagulation tests should be closely monitored.

The concomitant administration of quinolones including norfloxacin with glibenclamide (a sulfonylurea agent) has, on rare occasions, resulted in severe hypoglycaemia. Monitoring of blood glucose is recommended when these agents are co-administered.

Multivitamins, products containing iron or zinc, antacids or sucralfate should not be administered concomitantly with, or within 2 hours of, the

administration of norfloxacin because they may interfere with absorption, resulting in lower serum and urine levels of norfloxacin.

Didanosine (*Videx*) chewable buffered tablets or the paediatric powder for oral solution should not be administered concomitantly with, or within 2 hours of, the administration of norfloxacin, because these products may interfere with absorption, resulting in lower serum and urine levels of norfloxacin.

Concomitant administration of a non-steroidal anti-inflammatory drug (NSAID) with a quinolone, including norfloxacin, may increase the risk of stimulation of central nervous system and convulsive seizures. Norfloxacin should be used with caution in individuals receiving NSAIDs concomitantly.

Animal data have shown that quinolones in combination with fenbufen can lead to convulsions. Concomitant administration of quinolones and fenbufen should be avoided.

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## **Overdosage**

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### ***Overdosage***

The acute oral lethal dose 50% (LD<sub>50</sub>) values in male and female mice and rats were greater than 4 g/kg.

### ***Treatment***

No specific information is available on the treatment of overdosage with norfloxacin. Gastric lavage might be used. The patient should be carefully observed and given symptomatic and supportive treatment. Adequate hydration must be maintained.

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## **Pharmaceutical Precautions**

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### ***Storage***

Store in a cool, dry place where it stays below 30 °C.

### ***Shelf-life***

24 months

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## **Medicine Classification**

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Prescription only medicine

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## **Package Quantities**

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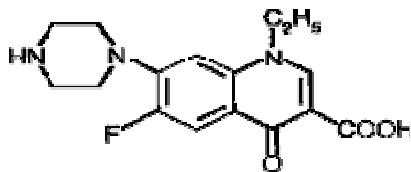
Arrow - Norfloxacin are available in blister packs of 6 tablets, and in bottles of 6 and 100 tablets.

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## Further Information

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The chemical name for 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid. Its structural formula is:



C<sub>16</sub>H<sub>18</sub>FN<sub>3</sub>O<sub>3</sub>      Molecular weight: 319.34      CAS: 70458-96-7

Norfloxacin is a synthetic fluoroquinolone, differs from quinolones by having a fluorine atom at the 6 position and a piperazine moiety at the 7 position. It is a white to pale yellow crystalline powder, freely soluble in glacial acetic acid, and very slightly soluble in ethanol, methanol and water.

Arrow - Norfloxacin tablets contains 400 mg of norfloxacin. The tablets also contain microcrystalline cellulose, croscarmellose sodium, magnesium stearate and Opadry AMB OY-B-28920. The tablets are gluten free.

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## Name and Address

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Arrow Pharmaceuticals (NZ) Limited  
Mount Eden Central Business Park  
33a Normanby Road, Mt. Eden  
Auckland, New Zealand

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## Date of Preparation

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18 August 2010