NORFLOXACIN (Ophthalmic)

Category

Antibacterial (ophthalmic) 2.

Indications

Accepted

Conjunctivitis, bacterial (treatment)¾Ophthalmic norfloxacin is indicated for the treatment of conjunctivitis caused by susceptible strains of: Acinetobacter calcoaceticus , Aeromonas hydrophila , Haemophilus influenzae , Proteus mirabilis , Pseudomonas aeruginosa 38 , Serratia marcescens , Staphylococcus aureus , S. epidermidis , S. warnerii , and Streptococcus pneumoniae. 1, 33, 34, 35, 38, 39, 40

Note: Not all species or strains of a particular organism may be susceptible to norfloxacin.

Pharmacology

Mechanism of action/Effect:

Norfloxacin is bactericidal and acts by inhibiting bacterial deoxyribonucleic acid (DNA) synthesis. Norfloxacin is a broad-spectrum anti-infective, active against a wide range of aerobic gram-positive and gram-negative organisms. The fluorine atom at the 6 position increases potency against gram-negative organisms, and the piperazine moiety at the 7 position is responsible for anti-pseudomonal activity. 1, 2, 4, 7, 10, 11

Precautions to Consider

Cross-sensitivity and/or related problems

Patients sensitive to systemic norfloxacin or to other quinolones (e.g., cinoxacin, ciprofloxacin, enoxacin, 41 lomefloxacin, 36, 41 nalidixic acid, ofloxacin), may be sensitive to ophthalmic norfloxacin also. 1, 4, 38

Carcinogenicity

In a study lasting up to 96 weeks, no increase in neoplastic changes was observed in rats administered doses 8 to 9 times the usual human oral dose of norfloxacin. 1, 2, 4

Mutagenicity

Norfloxacin had no mutagenic effect in the dominant lethal test in mice. In doses 30 to 60 times the usual human oral dose, norfloxacin did not cause chromosomal aberrations in hamsters or rats. Norfloxacin had no mutagenic activity in the Ames microbial mutagen test or in Chinese hamster

fibroblasts. Although norfloxacin was weakly positive in the Rec-assay for DNA repair, it had no mutagenic activity in the more sensitive V-79 mammalian cell assay. 1, 2, 4

Pregnancy/Reproduction

Fertility¾In male and female mice, oral doses of norfloxacin up to 33 times the usual human oral dose did not adversely affect fertility. 1, 2, 4

Pregnancy¾Since systemic norfloxacin has been shown to cause arthropathy in immature animals (see Pediatrics) and there is no information on ophthalmic norfloxacin, use of ophthalmic norfloxacin is not recommended during pregnancy. 1, 4, 19

Adequate and well controlled studies in humans have not been done. 1, 2 Systemic norfloxacin crosses the placenta. The umbilical cord serum concentration ranged from undetectable to 0.5 mg/mL and the amniotic fluid concentration ranged from undetectable to 0.92 mg/mL following the administration of a single 200 mg dose of norfloxacin. 2, 4, 19

At oral doses 6 to 50 times the human oral dose, there has been no evidence of a teratogenic effect in rats, rabbits, mice, or monkeys. However, in monkeys administered oral doses 10 times the maximum human oral dose (800 mg daily), norfloxacin has been shown to produce embryonic loss. Peak plasma levels reached 2 to 3 times those obtained in humans. 1, 2

FDA Pregnancy Category C. 1, 38

Breast-feeding

It is not known whether ophthalmic norfloxacin is distributed into breast milk. 1, 2 Systemic norfloxacin has not been detected in breast milk when it was given in low (200-mg) doses to nursing mothers. However, other systemic quinolone derivatives are distributed into breast milk, and systemic norfloxacin causes arthropathy in immature animals (see Pediatrics). Therefore, use of ophthalmic norfloxacin is not recommended in nursing mothers. 4, 7

Pediatrics

Appropriate studies on the relationship of age to the effects of ophthalmic norfloxacin have not been performed in infants up to 1 year of age. Safety and efficacy have not been established. 1, 38

Although there is no information on ophthalmic norfloxacin, other ophthalmic quinolones have not been shown to cause arthropathy in immature animals. In addition, there is no evidence that these ophthalmic quinolones have any effects on the weight-bearing joints. 1, 2, 4, 7, 8, 9, 13, 38

Geriatrics

Appropriate studies on the relationship of age to the effects of ophthalmic norfloxacin have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date.
When systemic norfloxacin was administered to 6 patients, 67 to 74 years old, with normal renal function (creatinine clearance 91 mL/min/1.73 m 2), the plasma half-life was slightly prolonged (3.9 vs

3.2 hours) and there was a small increase in the plasma concentration (2.0 vs 1.5 hours). 2, 19 Alterations in dosage have not been recommended unless the patient has severe renal function impairment (creatinine clearance £ 30 mL/min/1.73 m 2). 19

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]), serum and

Alkaline phosphatase, serum and

Aspartate aminotransferase (AST [SGOT]), serum and

Blood urea nitrogen (BUN) and

Creatinine, serum and

Lactate dehydrogenase (LDH) serum

(although there is no information on ophthalmic norfloxacin, increased values have been observed with systemic norfloxacin 1, 4, 9)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used when the following medical problem exists

>> Hypersensitivity to norfloxacin or other quinolones 38

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence rare

Skin rash or other sign of hypersensitivity 1 (allergic reaction)
Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Burning or other eye discomfort 1
Incidence less frequent

Bitter taste following instillation 1; chemosis 1 (swelling of the membrane covering the white part of the eye); hyperemia, conjunctival 1 (redness of the lining of the eyelids); photophobia 1 (increased sensitivity of eye to light)

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Norfloxacin (Ophthalmic).
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Sensitivity to norfloxacin or other quinolone derivatives
Pregnancy¾Ophthalmic norfloxacin is not recommended during pregnancy, because it is not known whether it can cause arthropathy in immature animals as can systemic norfloxacin
Breast-feeding¾Ophthalmic norfloxacin is not recommended, because it is not known whether it can cause arthropathy in immature animals as can systemic norfloxacin
Use in children¾Ophthalmic norfloxacin is not recommended in infants, because it is not known whether it can cause arthropathy in immature animals as can systemic norfloxacin
Proper use of this medication

Proper administration technique

>> Proper dosage
>> Compliance with full course of therapy

Missed dose: Applying as soon as possible; not applying if almost time for next dose
>> Proper storage
Precautions while using this medication

Checking with physician if no improvement within a few days

Possible photophobic reactions; wearing sunglasses and avoiding prolonged exposure to bright light

Side/adverse effects

Signs of potential side effects, especially skin rash or other sign of hypersensitivity

General Dosing Information

For treatment of adverse effects 1, 38

Recommended treatment consists of the following
· For mild hypersensitivity reaction¾Administering antihistamines and, if necessary, glucocorticoids.

· For severe hypersensitivity or anaphylactic reaction¾Administering epinephrine. Antihistamines and/or glucocorticoids may also be administered as required.

Ophthalmic Dosage Forms

NORFLOXACIN OPHTHALMIC SOLUTION

Usual adult and adolescent dose

Topical, to the conjunctiva, 1 drop four times a day for up to 7 days. 1, 38, 39

Note: For severe infections, the dosage may be increased to 1 drop every two hours while awake. 1, 38, 39

Usual pediatric dose

Infants up to 1 year of age¾Safety and efficacy have not been established. 1, 38

Children 1 year of age and over¾See Usual adult and adolescent dose. 1

Strength(s) usually available

U.S.¾0.3% (Rx)[Chibroxin 1, 38 (benzalkonium chloride 0.0025%)]

Canada¾0.3% (Rx)[Noroxin 32, 37, 39 (benzalkonium chloride 0.0025%)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), 1, 2 unless otherwise specified by manufacturer. Protect from freezing and light. 1, 2, 38, 39

Stability:

Norfloxacin ophthalmic solution is a clear, colorless to light yellow solution. 1, 38, 39 The solution should not be used if it is discolored or contains a precipitate.
The solution is stable for at least 2 years if stored at room temperature and protected from light. 2

Norfloxacin solution is stable at a pH of 5.0 to 5.4. 2

Auxiliary labeling:

· For the eye.