

GatitrustTM

Gatifloxacin Eye Drops 0.3% w/v

COMPOSITION:

Gatifloxacin IP	0.3% w/v.
(as Gatifloxacin Sesquihydrate)	
Benzalkonium Chloride	
Solution IP	0.01% w/v.
(as preservative)	
Sterile aqueous vehicle	q.s.

DESCRIPTION

Gatitrust Eye Drops 0.3% is a sterile solution for topical ophthalmic use.

CLINICAL PHARMACOLOGY

Pharmacokinetics : Gatifloxacin ophthalmic solution 0.3% was administered to one eye of 6 healthy male subjects each in an escalated dosing regimen starting with a single 2-drop dose, then 2 drops 4 times daily for 7 days and finally 2 drops 8 times daily for 3 days. At all time points, serum gatifloxacin levels were below the lower limit of quantification (5 ng/mL) in all subjects.

Microbiology : Gatifloxacin is an 8-methoxyfluoroquinolone with a 3-methylpiperazinyl substituent at C7. The antibacterial action of gatifloxacin results from inhibition of DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division.

The mechanism of action of fluoroquinolones including gatifloxacin is different from that of aminoglycoside, macrolide, and tetracycline antibiotics. Therefore, gatifloxacin may be active against pathogens that are resistant to these antibiotics. There is no cross-resistance between gatifloxacin and the aforementioned classes of antibiotics. Cross-resistance has been observed between systemic gatifloxacin and some other fluoroquinolones.

Resistance to gatifloxacin *in vitro* develops via multiple-step mutations. Resistance to gatifloxacin *in vitro* occurs at a general frequency of between 1×10^{-7} to 10^{-10} .

Gatifloxacin has been shown to be active against most strains of the following organisms both *in vitro* and clinically, in conjunctival infections:

Aerobes, Gram-Positive:

*Corynebacterium propinquum**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus mitis**, *Streptococcus pneumoniae*

Aerobes, Gram-Negative:

Haemophilus influenzae

* Efficacy for this organism was studied in fewer than 10 infections.

The following *in vitro* data are available, **but their clinical significance in ophthalmic infections is unknown**. The safety and effectiveness of Gatifloxacin in treating ophthalmic infections due to the following organisms have not been established in adequate and well-controlled clinical trials.

The following organisms are considered susceptible when evaluated using systemic breakpoints. However, a correlation between the *in vitro* systemic breakpoint and ophthalmological efficacy has not been established. The following list of organisms is provided as guidance only in assessing the potential treatment of conjunctival infections. Gatifloxacin exhibits *in vitro* minimal inhibitory concentrations (MICs) of 2mcg/mL or less (systemic susceptible breakpoint) against most ($\geq 90\%$) strains of the following ocular pathogens:

Aerobes, Gram-Positive:

Listeria monocytogenes, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Streptococcus pyogenes*, *Streptococcus viridans* Group, *Streptococcus* Groups C, F, G

Aerobes, Gram-Negative:

Acinetobacter Iwoffii, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Citrobacter freundii*, *Citrobacter koseri*, *Haemophilus parainfluenzae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Morganella morganii*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Proteus mirabilis*, *Proteus vulgaris*, *Serratia marcescens*, *Vibrio cholerae*, *Yersinia enterocolitica*

Other Microorganisms:

Chlamydia pneumoniae, *Legionella pneumophila*,
Mycobacterium marinum
Mycobacterium fortuitum, *Mycoplasma pneumoniae*

Anaerobic Microorganisms:

Bacteroides fragilis, *Clostridium perfringens*

INDICATIONS & USAGE

Gatitrust Eye Drops is indicated for the treatment of bacterial conjunctivitis caused by susceptible organisms.

DOSAGE & ADMINISTRATION

The recommended dosage regimen for the treatment of bacterial conjunctivitis is:

Days 1 & 2: Instill one drop every two hours in the affected eye(s) while awake, up to 8 times daily.

Days 3 through 7: Instill one drop up to four times daily while awake.

OVERDOSAGE

Topical overdose may be flushed with warm water.

CONTRAINDICATIONS

Gatitrust Eye Drops is contraindicated in patients with a history of hypersensitivity to gatifloxacin, to other quinolones, or to any of the components in this medication.

WARNINGS

Gatitrust Eye Drops is NOT FOR INJECTION

Gatitrust Eye Drops should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

In patients receiving systemic quinolones, including gatifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported. If an allergic reaction to gatifloxacin occurs, discontinue the drug and institute appropriate therapy immediately.

PRECAUTIONS

General: As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

DRUG INTERACTIONS

Specific drug interaction studies have not been conducted with **Gatitrust Eye Drops**. However, the systemic administration of some quinolones has been shown to elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine, and enhance the effects of the oral anticoagulant warfarin, and has been associated with transient elevations in serum creatinine in patients receiving systemic cyclosporine concomitantly.

Pregnancy**Pregnancy Category C:**

Because there are no adequate and well-controlled studies in pregnant women, **Gatitrust Eye Drops** solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Gatifloxacin is excreted in the breast milk of rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when gatifloxacin is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in infants below the age of one year have not been established.

Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Ophthalmic Use: The most frequently reported adverse events in the overall study population were conjunctival irritation, increased lacrimation, keratitis, and papillary conjunctivitis. Other reported reactions were chemosis, conjunctival hemorrhage, dry eye, eye discharge, eye irritation, eye pain, eyelid edema, headache, red eye, reduced visual acuity and taste disturbance.

PRESENTATION

Gatitrust Eye Drops (gatifloxacin ophthalmic solution) 0.3% is supplied sterile in a 5 mL sterile plastic bottle.

STORAGE

Store below 30°C, Protected from light, Do not freeze.



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