

**DESCRIPTION**

Each ml contains

Gatifloxacin sesquihydrate equivalent to

Gatifloxacin	0.3% W/V
Benzalkonium chloride US - NF	0.01% W/V
Purified water I.P	q.s

**CLINICAL PHARMACOLOGY**

**Pharmacokinetics:** Gatifloxacin ophthalmic solution 0.3% or 0.5% 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 and these antibiotics may be active against pathogens that are resistant to gatifloxacin. 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



**ZYMAR**  
(gatifloxacin ophthalmic solution) 0.3%  
POWER TO PROTECT

gatifloxacin in vitro develops via multiple-step mutations. Resistance to gatifloxacin in vitro occurs at a general frequency of between  $1 \times 10^{-7}$  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 as described in the INDICATIONS AND USAGE section.

**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 ZYMAR™ 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  $2\mu\text{g/mL}$  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, E, G
- **Aerobes, Gram-Negative:**
- *Acinetobacter lwoffii*
- *Enterobacter aerogenes*
- *Enterobacter cloacae*
- *Escherichia coli*
- *Citrobacter freundii*
- *Citrobacter koseri*
- *Haemophilus parainfluenzae*
- *Klebsiella oxytoca*
- *Klebsiella pneumoniae*
- *Moraxella catarrhalis*
- *Morganella*

*morganii* • *Neisseria gonorrhoeae* • *Neisseria meningitides* • *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*

**Clinical Studies:** In a randomized, double-masked, multicenter clinical trial, where patients were dosed for 5 days, ZYMAR™ solution was superior to its vehicle on day 5-7 in patients with conjunctivitis and positive conjunctival cultures. Clinical outcomes for the trial demonstrated clinical cure of 77% (40/52) for the gatifloxacin treated group versus 58% (28/48) for the placebo treated group. Microbiological outcomes for the same clinical trial demonstrated a statistically superior eradication rate for causative pathogens of 92% (48/52) for gatifloxacin vs. 72% (34/48) for placebo. Please note that microbiological eradication does not always correlate with clinical outcome in anti-infective trials.

### INDICATIONS AND USAGE

ZYMAR™ solution is indicated for the treatment of external bacterial infections of the eye.

### CONTRAINDICATIONS

ZYMAR™ solution is contraindicated in patients with a history of hypersensitivity to gatifloxacin, to other quinolones, or to any of the components in this medication.

### WARNINGS

#### NOT FOR INJECTION

ZYMAR™ solution 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. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to gatifloxacin occurs, discontinue the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

### **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.

**Information for Patients:** Avoid contaminating the applicator tip with material from the eye, fingers or other source. Systemic quinolones, including gatifloxacin, have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

**Drug Interactions:** Specific drug interaction studies have not been conducted with ZYMAR™ ophthalmic solution. 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 its derivatives, and has been associated with transient elevations in serum creatinine in patients receiving systemic cyclosporine concomitantly.

### **Carcinogenesis, Mutagenesis, Impairment of Fertility:**

There was no increase in neoplasms among B6C3F1 mice given gatifloxacin in the diet for 18 months at doses averaging 81 mg/kg/day in males and 90 mg/kg/day in females. These

doses are approximately 2000-fold higher than the maximum recommended ophthalmic dose of 0.04 mg/kg/day in a 50 kg human.

There was no increase in neoplasms among Fischer 344 rats given gatifloxacin in the diet for 2 years at doses averaging 47 mg/kg/day in males and 139 mg/kg/day in females (1000 and 3000- fold higher, respectively, than the maximum recommended ophthalmic dose). A statistically significant increase in the incidence of large granular lymphocyte (LGL) leukemia was seen in males treated with a high dose of approximately 2000-fold higher than the maximum recommended ophthalmic dose. Fisher 344 rats have a high spontaneous background rate of LGL leukemia and the incidence in high-dose males only slightly exceeded the historical control range established for this strain. In genetic toxicity tests, gatifloxacin was positive in 1 of 5 strains used in bacterial reverse mutation assays; Salmonella strain TA102. Gatifloxacin was positive in in vitro mammalian cell mutation and chromosome aberration assays. Gatifloxacin was positive in in vitro unscheduled DNA synthesis in rat hepatocytes but not human leukocytes. Gatifloxacin was negative in in vivo micronucleus tests in mice, cytogenetics test in rats, and DNA repair test in rats. The findings may be due to the inhibitory effects of high concentrations on eukaryotic type II DNA topoisomerase. There were no adverse effects on fertility or reproduction in rats given gatifloxacin orally at doses up to 200 mg/kg/day (approximately 4500-fold higher than the maximum recommended ophthalmic dose for ZYMAR™).

#### **Pregnancy: Teratogenic Effects. Pregnancy Category C:**

There were no teratogenic effects observed in rats or rabbits following oral gatifloxacin doses up to 50 mg/kg/day (approximately 1000-fold higher than the maximum recommended ophthalmic dose). However, skeletal/craniofacial malformations or delayed ossification, atrial enlargement, and reduced fetal weight were observed in fetuses from rats given  $\geq 150$  mg/kg/day (approximately 3000-fold higher than the maximum recommended ophthalmic

dose). In a perinatal/postnatal study, increased late post-implantation loss and neonatal/perinatal mortalities were observed at 200 mg/kg/day (approximately 4500 times the maximum recommended ophthalmic dose). Because there are no adequate and well-controlled studies in pregnant women, ZYMAR™ solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers:** 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. These events occurred in approximately 5-10% of patients. Other reported reactions occurring in 1-4% of patients were chemosis, conjunctival hemorrhage, dry eye, eye discharge, eye irritation, eye pain, eyelid edema, headache, red eye, reduced visual acuity and taste disturbance.

### DOSAGE AND ADMINISTRATION

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

Days 1 and 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.

**Storage:** Store in a cool dark place

## DESCRIPTION

Each ml contains:

Ofloxacin USP	3 mg
Beozalkonium chloride USP	0.05 mg

## ACTIONS

EXOCIN™ is fluorinated 4 — quinolone antibiotic. It is bactericidal in action. It is thought to exert a bactericidal effect on susceptible bacterial cells by inhibiting DNA gyrase, an essential bacterial enzyme which is a critical catalyst in the duplication, transcription and repair of bacterial DNA.

Ofloxacin has been shown to be active against most strains of the following organisms both in vitro and clinically, in conjunctival and / or corneal ulcer infections.

**AEROBES, GRAM POSITIVE:** *Staphylococcus aureus*.  
*Staphylococcus epidermidis*. *Staphyl coccus pneurnoniae*.

**AEROBES, GRAM NEGATIVE:** *Enterobacter cloacae*.  
*Haemophilus influenzae*. *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Serratia marcescens*.

**Anaerobic Species.**

*Propionibacterium acnes*.

**AEROBES, GRAM POSITIVE:** *Exterococcus faecalis*,  
*Listeria monocytogenes*.  
*Staphylococcus capitis*,  
*Staphylococcus hominus*,  
*Staphylococcus simulans*,  
*Staphylococcus pyogenes*.

**AEROBES. GRAM NEGATIVE:**  
*Acinetobacter calcoaceticus* var.  
*anitratu*s. *Acinetobacter*  
*calcoaceticus* var. *Iwoffii* *Citrobacter*  
*diversus*. *Citrobacter freundii*,  
*Enterobacter aerogenes*.  
*Enterobacter agglomerans*,



**Exocin™**  
(ofloxacin ophthalmic solution) 0.3%

Escherichia coli.  
Haemophilus parainfluenzae. Klebsiella oxytoca, Klebsiella pneumoniae, Moraxella (Branhamella) catarrhatis, Moraxella lacunata. Morganella morganii, Neisseria gonorrhoeae. Pseudomonas aeruginosa, Pseudomonas fluorescens, Shigella sonnei.

OTHER: Chlamydia trachomatis.

### INDICATIONS & USAGE

EXOCIN™ is indicated for the treatment of conjunctivitis, corneal ulcers, external infections of the eye and ocular surface caused by various gram-negative and gram-positive bacteria and anaerobic species.

### CONTRAINDICATIONS

EXOCIN™ is contraindicated in patients with a history of hypersensitivity to Ofloxacin, to other quinolones. or to any of the components in this medication.

### WARNINGS

NOT FOR INJECTION- EXOCIN™ should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

Use the solution within one month after opening the container. Do not touch the nozzle tip to any surface since this may contaminate solution. If irritation persists or increases, discontinue use and consult physician.

### PRECAUTIONS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolones including Ofloxacin. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioneurotic edema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria and itching.

If an allergic reaction to Ofloxacin occurs, discontinue the

drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management, including intubation should be administered as clinically indicated.

**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.

**PREGNANCY:** There are no established control studies to date on safety of using Ofloxacin TOPICAL, in pregnant women. Hence discretion on the part of the physician is called for in prescribing to pregnant women.

**NURSING MOTHERS** Because of the potential for adverse reactions from Ofloxacin in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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

### **ADVERSE REACTIONS**

The most frequently reported drug-related adverse reaction was transient ocular burning or discomfort. Other reported reactions include stinging, redness, itching, chemical conjunctivitis / keratitis, periocular / facial edema, foreign body sensation, photophobia, blurred vision, tearing, dryness and eye pain. Rare reports of dizziness have been received.

### **DOSAGE & ADMINISTRATION**

One or two drops of EXOCIN™ should be instilled in the infected eye four times a day. Alterations (increase and decrease) of dosage may be made based upon the clinical response as judged by the physician. Therapy may be continued for 24 to 48 hours after targets are achieved.

**OVERDOSAGE**

Clinically apparent symptoms of overdosage may be seen as punctate keratitis, erythema, lid edema etc. The drug should be withheld and appropriate change in therapy instituted.

**HOW SUPPLIED**

**EXOCIN™** is available in a 5 ml plastic dropper bottle.

NOTE: Store in a cool place

KEEP MEDICAMENT OUT OF REACH OF CHILDREN.

DESCRIPTION:

Each ml contains:

- Ciprofloxacin Hydrochloride USP (equivalent to 3mg Ciprofloxacin)
- Benzalkonium Chloride solution IP 0.2 mg

ACTIONS:

Ciprofloxacin is a fluoroquinolone antibiotic active against a broad spectrum of pathogenic gram-positive and gram-negative bacteria. The gram-positive bacteria against which Ciprofloxacin is active include **Staphylococcus aureus** (including methicillin susceptible and methicillin-resistant strains), **Staphylococcus epidermidis**, **Streptococcus pneumoniae**, **Streptococcus** - (Viridans group). The gram-negative bacteria against which Ciprofloxacin is active include **Pseudomonas aeruginosa**, **Serratia marcescens**.

Ciprofloxacin does not cross react with other antimicrobial agents such as beta-lactams or aminoglycosides and hence organisms resistant to these drugs may be susceptible to Ciprofloxacin.

INDICATIONS AND USAGE:

For the topical treatment of infections of the external eye and its adnexa caused by susceptible bacteria. Such infections include conjunctivitis, keratitis and kerato conjunctivitis, corneal ulcers, blepharo-conjunctivitis, acute meibomianitis and dacryocystitis. QUINOBACT™ is also useful for surgical prophylaxis.

CONTRAINDICATION:

QUINOBACT™ is contraindicated

In patients sensitive to Ciprofloxacin.



**QUINOBACT™**

**WARNINGS:**

NOT FOR INJECTION. Use the solution within one month after opening the container. Do not touch the nozzle tip to any surface since this may contaminate solution. If irritation persists or increases, discontinue use and consult physician.

**PRECAUTIONS:**

As with other anti-infectives, prolonged use may result in overgrowth of non—susceptible organisms including fungi. If superinfection occurs or if clinical improvement is noticed within a reasonable period discontinue use and institute appropriate therapy. Use Ciprofloxacin with caution in patients who have exhibited sensitivity to other quinolones.

**Pregnancy** - There are no adequate and well-controlled studies in pregnant women. Ciprofloxacin should be used during pregnancy only if the potential benefit outweighs the potential risk to the foetus.

**Nursing mothers** - It is not known whether topical administration of Ciprofloxacin could result in sufficient systemic absorption to produce detectable quantities in breast milk. Hence Ciprofloxacin should be used with caution by nursing mothers.

**Paediatric use** - Safety and effectiveness in children has not been established.

**ADVERSE REACTIONS:**

The most frequently reported adverse reactions are transient ocular discomfort and irritation. These reactions resolve upon discontinuation of the medication.

Other reactions include lid margin crusting, foreign body sensation, itching and conjunctival hyperemia.

**DOSAGE & ADMINISTRATION:**

Bacterial conjunctivitis - One to two drops every two to four hours.

**Corneal ulcers** - Two drops every 15 minutes for the first 6 hours and then two drops every 30 minutes for the remainder of the first day. Two drops every hour during the second day. Two drops every four hours from 3rd through the 14th day.

**HOW SUPPLIED:**

QUINOACT™ is available in plastic bottles.

Note: Store in a cool place. Protect from light. On prescription only.

DESCRIPTION:

EYEBREX™ (Tobramycin 0.3%) is a sterile topical antibiotic formulation for ophthalmic use.

**Each ml. contains:** Tobramycin sulphate USP equivalent to 3mg of Tobramycin, Benzalkonium Chloride USP - 0.04mg.

ACTIONS:

Tobramycin is an aminoglycoside antibiotic obtained from culture of *Streptomyces tenebrarius*. Tobramycin is usually bactericidal in action. Although the exact mechanism of action has not been fully elucidated, the drug appears to inhibit synthesis of susceptible bacteria by irreversible binding to 30 S ribosomal subunits.

*In Vitro Data:* In vitro studies have demonstrated that tobramycin is active against susceptible strains of the following micro-organisms: Staphylococci including *S. aureus* and *S. epidermidis* (coagulase-positive and coagulase-negative) including penicillin resistant strains. Streptococci including some of the Group A beta-hemolytic species, some non-hemolytic species, and some *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Proteus mirabilis* (indole-negative) and indole-positive *Proteus* species, *Haemophilus influenzae*, and *H. aegyptius*, *Moraxella lacumatta*, *Acinetobacter calcoaceticus* (*Herella vaginacola*), and some *Neisseria* species. Bacterial susceptibility studies demonstrate that in some cases micro-organisms resistant to gentamicin retain susceptibility to tobramycin. A significant bacterial population resistant to tobramycin has not yet emerged; however, bacterial resistance may develop upon prolonged use.



**EYEBREX™**  
(Tobramycin 0.3%) Eye Drops

**INDICATIONS AND USAGE:**

EYEBREX™ Ophthalmic Solution is a topical antibiotic formulation indicated in the treatment of external infections of the eye and its adnexa caused by susceptible bacteria. Appropriate monitoring of bacterial response to topical antibiotic therapy should accompany the use of EYEBREX™ Ophthalmic Solution. Clinical studies have shown tobramycin to be safe and effective for use in children.

**CONTRAINDICATIONS:**

EYEBREX™ Ophthalmic Solution is contraindicated in patients with known hypersensitivity to any ingredient in the formulation.

**WARNINGS/PRECAUTIONS:****GENERAL**

As with other antibiotic preparations, prolonged use may result in overgrowth of non-susceptible organisms including fungi. If superinfection occurs during tobramycin therapy, the drug should be discontinued and appropriate therapy should be initiated. If tobramycin is administered topically in conjunction with systemic aminoglycoside therapy, serum aminoglycoside concentrations should be monitored.

**Pregnancy:** CATEGORY B, Reproduction studies in animals using systemic tobramycin doses up to 33 times the normal human systemic dose have not revealed evidence of impaired fertility or harm to foetus. There are, however, no control studies to date using topical or systemic tobramycin in pregnant women and ophthalmic tobramycin should be used during pregnancy only when clearly needed.

**Nursing Mothers:** Because of the potential for serious adverse reactions from the drug in nursing infants, ophthalmic tobramycin should not normally be used in nursing women. A decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

**NOT FOR INJECTION INTO THE EYE**

**Adverse Reactions:** EYEBREX™ appears to have low order of toxicity when applied topically to the eye. However, sensitisation to the drug may occasionally result from topical application. If a sensitive reaction occurs during topical tobramycin therapy, the drug should be discontinued. The most frequent adverse reactions to tobramycin ophthalmic solution are: localized ocular toxicity and hypersensitivity, including increased lacrimation, itching and edema of the eyelid and conjunctival erythema. These reactions occur in less than 3% of patients receiving Ophthalmic tobramycin and usually disappear when the drug is discontinued. Punctate keratitis has also been reported following excessive application of tobramycin.

**DOSAGE & ADMINISTRATION:**

For mild to moderate infections, 1 or 2 drops of EYEBREX™ solution should be instilled into the infected eye(s) every 4 hours. In severe infections, including *Pseudomonas aeruginosa* infections, 2 drops of the solution should be instilled into the infected eye(s) every hour initially. When improvement occurs, frequency of application can be decreased. Therapy should be continued for at least 48 hours after the infection has been controlled.

**OVERDOSAGE:**

Clinically apparent signs and symptoms of an overdose of EYEBREX™ ophthalmic solution (Punctate keratitis, erythema, increased lacrimation, edema and lid itching) may be similar to adverse reactions seen in some patients.

**HOW SUPPLIED**

EYEBREX™ is available in 5 ml plastic dropper bottles.

**STORAGE:**

Store in a cool and dry place at normal room temperature.