



Department of Vermont Health Access

Therapeutic Class Review Ophthalmic Antibiotics

Overview/Summary

Ophthalmic antibiotics are used to treat ocular infections including blepharitis, conjunctivitis, keratitis and several others. There are ophthalmic antibiotics available from the many drug classes including aminoglycosides, macrolides, polypeptides, quinolones and sulfonamides.¹ In addition, many are available as combination products with other antibiotics or corticosteroids. A list of available ophthalmic antibiotics is available in Table 1. Moreover, there is at least one generic product available for treating each of the conditions outlined in Table 2.¹

Blepharitis is a chronic inflammatory condition of the eyelids, often presenting with the symptoms of eye irritation and redness. Overgrowth of normal bacterial flora plays a role in the pathophysiology of blepharitis, with the most common causative organisms including *Staphylococcus* species, *Corynebacterium* species and *Propionibacterium acnes*. The mainstay of the treatment of blepharitis is patient education regarding eye lid hygiene as well as the use of ophthalmic antibiotics. Of note, blepharitis is a chronic condition without definitive cure; therefore, satisfactory results require a long-term commitment to treatment and appropriate expectations. Ophthalmic corticosteroids may also be used acutely to treat blepharitis exacerbations.^{2,3}

All ophthalmic antibiotics, with the exception of ophthalmic levofloxacin 1.5%, are approved by the Food and Drug Administration (FDA) to treat bacterial conjunctivitis.⁴⁻³⁷ Conjunctivitis occurs worldwide and affects all ages, social strata, and both genders. This infection rarely causes permanent visual loss or structural damage and mild cases may be self limited as many cases will resolve without treatment in immunocompetent individuals. The most common causative pathogens seen with bacterial conjunctivitis include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.³⁸ Use of ophthalmic antibiotics is associated with earlier clinical and microbiological remission when compared to placebo. The selection of an ophthalmic antibiotic is typically empirical, and the most convenient or least expensive ophthalmic antibiotic is typically effective for most cases of conjunctivitis.³⁹

Severe bacterial conjunctivitis is characterized by purulent discharge, pain and marked eye inflammation. In these cases cultures and slides for gram staining should be obtained and the results of these laboratory tests should guide the choice of the antibiotic. Methicillin-resistant *Staphylococcus aureus* (MRSA) has been isolated in patients with bacterial conjunctivitis with increasing frequency and may be resistant to many available ophthalmic antibiotics. In patients with conjunctivitis caused by *Neisseria gonorrhoea* and *Chlamydia trachomatis* systemic antibiotic therapy is necessary, and while not necessary ophthalmic antibiotics are also typically used.³⁹

Bacterial keratitis is characterized by an inflammation of the cornea and rarely occurs in the normal eye due to the cornea's natural resistance to infection. However several predisposing factors such as contact lens wear, trauma, corneal surgery, ocular surface disease, systemic disease and immunosuppression may alter the defense mechanisms of the ocular surface and allow for infection of the cornea.⁴⁰ Due to corneal scarring or topographic irregularity, many forms of this infection results in visual loss. Untreated or severe bacterial keratitis can result in corneal perforation and may develop into endophthalmitis and result in the loss of the eye. The most common causative organisms of bacterial keratitis include *Staphylococci* and gram-negative rods, of which the most frequent organisms identified are *Pseudomonas* species. Ophthalmic antibiotics are the preferred method of treatment in many cases, and

antibiotic ointments may be useful at bedtime in less severe cases or as adjunctive therapy. In addition, broad-spectrum ophthalmic antibiotics are used initially as empiric treatment. In severe cases, patients should be followed daily until stabilization or clinical improvement is documented.⁴⁰

Medications

Table 1. Medications Included Within Class Review

Generic Name (Trade name)	Medication Class	Generic Availability
Single Entity Products		
Azithromycin ophthalmic (Azasite [®])	Macrolide antibiotic	-
Bacitracin ophthalmic (Bacticin [®])	Polypeptide antibiotic	✓
Besifloxacin ophthalmic (Besivance [®])	Quinolone antibiotic	-
Ciprofloxacin ophthalmic (Ciloxan ^{®*})	Quinolone antibiotic	✓ (solution)
Erythromycin ophthalmic (Ilotycin [®] , Romycin [®])	Macrolide antibiotic	✓
Gatifloxacin ophthalmic (Zymaxid [®])	Quinolone antibiotic	-
Gentamicin sulfate ophthalmic (Genoptic ^{®*} , Gentak ^{®*})	Aminoglycoside antibiotic	✓
Levofloxacin ophthalmic (Iquix [®] , Quixin [®])	Quinolone antibiotic	-
Moxifloxacin hydrochloride ophthalmic (Moxeza [®] , Vigamox [®])	Quinolone antibiotic	-
Ofloxacin ophthalmic (Ocuflox [®])	Quinolone antibiotic	✓
Sulfacetamide sodium ophthalmic (AKSulf [®] , Bleph-10 ^{®*} , Ocusulf [®] , Sturzulf [®] , Sulster [®])	Miscellaneous anti-infective	✓
Tobramycin ophthalmic (AKTob ^{®*} , Tobrex [®])	Aminoglycoside antibiotic	✓
Combination Products		
Bacitracin zinc/polymyxin B sulfate ophthalmic (AK-Poly-Bac [®] , Polysporin [®])	Polypeptide antibiotic	✓
Gentamicin sulfate/prednisolone acetate ophthalmic (Pred G [®])	Aminoglycoside antibiotic/corticosteroid	-
Polymyxin B sulfate/trimethoprim ophthalmic (Polytrim [®])	Polypeptide antibiotic	✓
Sulfacetamide sodium/prednisolone acetate ophthalmic (Blephamide [®])	Miscellaneous anti-infective/corticosteroid	✓
Sulfacetamide sodium/prednisolone sodium phosphate ophthalmic (Vasocidin [®])	Miscellaneous anti-infective/corticosteroid	✓
Tobramycin/dexamethasone ophthalmic (Tobradex ^{®*} , Tobradex [®] ST)	Aminoglycoside antibiotic/corticosteroid	✓ (suspension)
Tobramycin/loteprednol etabonate ophthalmic (Zylet [®])	Aminoglycoside antibiotic/corticosteroid	-
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc ophthalmic (Neosporin [®])	Polypeptide antibiotic	✓
Neomycin sulfate/polymyxin B sulfate/dexamethasone ophthalmic (Maxitrol [®])	Polypeptide antibiotic/corticosteroid	✓
Neomycin sulfate/polymyxin B sulfate/gramicidin ophthalmic (Neosporin [®])	Polypeptide antibiotic	✓
Neomycin sulfate/polymyxin B sulfate/hydrocortisone ophthalmic	Polypeptide antibiotic/corticosteroid	✓
Neomycin sulfate/polymyxin B sulfate/prednisolone acetate sulfate ophthalmic (Poly-Pred [®])	Polypeptide antibiotic/corticosteroid	-
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc/hydrocortisone ophthalmic	Polypeptide antibiotic/corticosteroid	✓

*Generic available in at least one dosage form or strength.

Indications

Table 2. Food and Drug Administration Approved Indications^{1,4-37}

Generic Name	Acute Meibomianitis	Bacterial Conjunctivitis	Bacterial Blepharitis	Bacterial Blepharoconjunctivitis	Corneal Ulcer	Dacryocystitis	Keratitis	Keratoconjunctivitis	Prophylaxis of Ophthalmia Neonatorum*	Treatment of Trachoma (Adjunct Therapy)
Single Entity Products										
Azithromycin		✓								
Bacitracin	✓	✓	✓	✓	✓	✓	✓	✓		
Besifloxacin		✓								
Ciprofloxacin		✓			✓ (solution)					
Erythromycin		✓			✓ [†]				✓	
Gatifloxacin		✓								
Gentamicin sulfate	✓	✓	✓	✓	✓	✓	✓	✓		
Levofloxacin		✓ (Quixin [®])			✓ (Iquix [®])					
Moxifloxacin hydrochloride		✓								
Ofloxacin		✓			✓					
Sulfacetamide sodium		✓	✓ [‡]	✓ [‡]			✓ [‡]	✓ [‡]		✓ [‡]
Tobramycin		✓ [§]	✓ [§]	✓ [§]			✓ [§]	✓ [§]		
Combination Products										
Bacitracin zinc/polymyxin B sulfate		✓	✓	✓			✓	✓		
Gentamicin sulfate/prednisolone acetate		✓			✓					
Polymyxin B sulfate/trimethoprim		✓		✓						
Sulfacetamide sodium/prednisolone acetate		✓			✓					
Sulfacetamide sodium/prednisolone sodium phosphate		✓			✓					
Tobramycin/dexamethasone		✓			✓					

Generic Name	Acute Meibomianitis	Bacterial Conjunctivitis	Bacterial Blepharitis	Bacterial Blepharoconjunctivitis	Corneal Ulcer	Dacryocystitis	Keratitis	Keratoconjunctivitis	Prophylaxis of Ophthalmia Neonatorum*	Treatment of Trachoma (Adjunct Therapy)
Tobramycin/loteprednol etabonate		✓ †			✓ †					
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc		✓	✓	✓			✓	✓		
Neomycin sulfate/polymyxin B sulfate/dexamethasone		✓ ‖			✓ ‖					
Neomycin sulfate/polymyxin B sulfate/gramicidin		✓	✓	✓			✓	✓		
Neomycin sulfate/polymyxin B sulfate/hydrocortisone		✓ ‖			✓ ‖					
Neomycin sulfate/polymyxin B sulfate/prednisolone acetate sulfate		✓ ‖			✓ ‖					
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc/hydrocortisone		✓ ‖			✓ ‖					

* Due to Neisseria gonorrhoeae or Chlamydia trachomatis.

† Indicated for the treatment of superficial ocular infections involving the conjunctiva and/or cornea caused by organisms susceptible to erythromycin.

‡ Indicated for the treatment of conjunctivitis and other superficial ocular infections due to susceptible microorganisms, and as an adjunctive in systemic sulfonamide therapy of trachoma.

§ Indicated in the treatment of external infections of the eye and its adnexa caused by susceptible bacteria.

‖ Indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists, inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of corticosteroid use in certain infective conjunctivides is accepted to obtain diminution in edema and inflammation as well as use in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns or penetration of foreign bodies.

¶ Indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists, inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, and where the inherent risk of steroid use in certain infective conjunctivides is accepted to obtain a diminution in edema and inflammation, as well as use in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns or penetration of foreign bodies.

Pharmacokinetics⁴⁻³⁷

Limited pharmacokinetic data is available for the ophthalmic antibiotics. Although there is the potential for systemic absorption with the administration of these agents, the true clinical significance of this is not known. Specifically, for ophthalmic levofloxacin solution and ophthalmic moxifloxacin hydrochloride solution, post-administration, maximum mean concentrations were reported to be more than 1,000 times lower than those reported after standard oral doses of the respective oral medications.

Clinical Trials

Clinical trials have demonstrated that ophthalmic antibiotics are effective in treating and providing relief of conjunctivitis in pediatric and adult patients.⁴¹⁻⁶⁴ Several studies comparing ophthalmic antibiotics such as azithromycin, besifloxacin, levofloxacin, moxifloxacin and polymyxin B sulfate/bacitracin zinc to either placebo or vehicle have concluded that these medications resulted in significantly higher clinical resolution rates at days one through five. However, one trial with ophthalmic polymyxin B sulfate/bacitracin zinc did show that on days eight through ten the difference seen when compared to placebo was not significant.⁴⁴

Head-to-head trials evaluating the efficacy of ophthalmic antibiotics for the treatment of bacterial conjunctivitis have found that no one medication was inferior to another. In one trial, significantly more patients in the ophthalmic moxifloxacin group had complete resolution of ocular signs and symptoms at 48 hours when compared to patients treated with ophthalmic polymyxin B sulfate/trimethoprim ($P=0.001$).⁴⁹ In a seven day trial, a higher percentage of patients receiving levofloxacin had microbial eradication at the final visit compared to patients receiving ofloxacin ($P=0.034$); however, clinical cure rates were similar between the two treatments (P value not reported).⁶² In a small meta-analysis, moxifloxacin was found to be associated with fewer drop-outs for treatment failure ($P=0.002$) compared to ofloxacin.⁶⁴ Most other studies have shown no significant difference between ophthalmic antibiotic treatments with regard to bacterial eradication, clinical resolution, clinical response, efficacy, microbial eradication, physician's judgment of resolution, severity rating or symptom improvement. While no difference was found between ophthalmic formulations of azithromycin and tobramycin in regard to clinical resolution and bacterial eradication, azithromycin produced the same clinical outcome with 65% fewer drops.⁴⁶ In all studies, most adverse events were mild with no significant difference seen with regard to the rate of adverse events. Common adverse events included burning, ocular discomfort, stinging, and tearing.

In patients with a diagnosis of corneal ulcer, ophthalmic ciprofloxacin was shown to be an efficacious treatment option.^{65,66} Specifically, in one trial of patients with a diagnosis of infectious keratitis ophthalmic ciprofloxacin had a shorter average time to healing as compared to ophthalmic cefazolin sodium fortified with gentamicin sulfate, although this was not found to be significant (P value not reported).⁶⁶

A number of studies consisted of patients with multiple diagnoses such as blepharitis, blepharoconjunctivitis, bacterial conjunctivitis and blepharitis, keratoconjunctivitis, or symptoms of surface ocular infections. These studies found that the ophthalmic formulations of ciprofloxacin, gentamicin sulfate, ofloxacin, tobramycin solution, and polymyxin B sulfate/trimethoprim were efficacious in resolving or curing multiple ocular infections.⁶⁷⁻⁷⁸ No significant differences were observed in any study with regard to cure rates, decline in bacterial counts, bacterial eradication or reduction of bacteria, microbial improvement or overall improvement. In one study, ophthalmic ofloxacin was shown to significantly decrease the cumulative summary score on days three through five in patients with conjunctival hyperemia, eyelid crusting or discharge, and positive bacterial culture when compared to ophthalmic gentamicin sulfate ($P<0.05$); however, there were no significant differences between the two treatments with regard to clinical, microbial and overall improvement rates ($P=0.089$ for all outcomes).⁷³ In studies of patients with multiple diagnoses, the most commonly reported adverse events were not significantly different between treatment groups. The most common adverse events included burning, mild discomfort and stinging on instillation.

In one study evaluating the treatment of ophthalmia neonatorum, conjunctivitis in newborn babies principally caused by *Neisseria gonorrhoeae*, prophylaxis with ophthalmic erythromycin ointment was found to be most effective prior to the infant's second week of life. The efficacy of ophthalmic erythromycin prophylaxis from day zero to day 14 was found to be statistically significant when compared to no prophylaxis, however it was not found to be significant when compared from days 15 to 60 (14 vs 9%; $P=0.05$ and 7 vs 8%; $P=0.92$ respectively).⁷⁹ In another study, ophthalmic erythromycin prophylaxis resulted in significantly less reports of conjunctival redness and tearing, or serious or purulent discharge during the first 24 hours to two weeks of birth when compared to no prophylaxis (18.4 vs 22.4%; $P=0.03$).⁸⁰

Ophthalmic gentamicin sulfate was compared to ophthalmic neomycin sulfate/polymyxin B sulfate/dexamethasone in patients undergoing cataract and posterior chamber lens implant surgery. It was found that the bacterial colony count was significantly less in the ophthalmic gentamicin sulfate group at day six and eight ($P=0.033$), although there was no significant difference between the two groups with regard to the degree of intra-ocular inflammation or the global assessment of the success of therapy and local tolerance by the study patients and physicians (P value not reported).⁸¹ A separate study evaluated ophthalmic preparations of tobramycin/dexamethasone, neomycin sulfate/polymyxin B sulfate/dexamethasone and neomycin sulfate/polymyxin B sulfate/gramicidin in patients undergoing cataract extraction by either manual extraction or phacoemulsification with intraocular lens implantation. Ophthalmic tobramycin/dexamethasone was non-inferior to ophthalmic neomycin sulfate/polymyxin B sulfate/dexamethasone concerning inflammation scores at days three, eight, 14 and 21. Inflammation scores in the ophthalmic tobramycin/dexamethasone group were significantly lower than score seen in the ophthalmic neomycin sulfate/polymyxin B sulfate/gramicidin group at days 8, 14 and 21 ($P<0.05$ for all) and scores in the ophthalmic neomycin sulfate/polymyxin B sulfate/dexamethasone group were significantly lower than those seen in the ophthalmic neomycin sulfate/polymyxin B sulfate/gramicidin group at day 8 ($P<0.05$).⁸²

Ophthalmic tobramycin/dexamethasone has also been compared to ophthalmic tobramycin/loteprednol etabonate in patients with moderate blepharokeratoconjunctivitis with results showing significantly greater reductions in symptom scores in the ophthalmic tobramycin/dexamethasone group with regard to signs of blepharitis, conjunctivitis, and ocular discharge ($P=0.017$, $P=0.013$, $P=0.025$ respectively). However the reduction in keratitis score was not found to be statistically significant between the two treatment groups ($P=0.065$).⁸³

Table 3. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Conjunctivitis				
<p>Abelson et al⁴¹</p> <p>Azithromycin 1% 1 drop into the affected eye(s) BID on days 1 and 2 and once daily on days 3 through 5</p> <p>vs</p> <p>vehicle 1 drop into the affected eye(s) BID on days 1 and 2 and once daily on days 3 through 5</p>	<p>Phase 3 DB, MC, PC, PG, RCT</p> <p>Male and female patients, ages 1 year and older, with a positive clinical diagnosis of bacterial conjunctivitis with signs and symptoms present for <3 days, and a best-corrected visual acuity score of 20/100 or better in each eye</p>	<p>N=685</p> <p>5 days</p>	<p>Primary: Clinical resolution at the test-of-cure visit (visit 3 on day 6 or 7)</p> <p>Secondary: Bacterial eradication at visit 3, as indicated by the absence of bacterial growth and incidence of adverse events</p>	<p>Primary: Clinical resolution rates at visit three were significantly higher in the azithromycin group when compared to the vehicle group (63.1 vs 49.7%, respectively; $P=0.03$).</p> <p>Secondary: Bacterial eradication rates measured at visit three were significantly higher in the azithromycin group when compared to the vehicle group (88.5 vs 66.4%; $P<0.001$).</p> <p>The rate of overall adverse events seen in the azithromycin group was 12.3% compared to 12.0% seen in the vehicle group with the most common adverse effects seen including conjunctival chemosis, lid swelling, and other lid events (P value not reported).</p>
<p>Karpecki et al⁴²</p> <p>Besifloxacin 0.6% 1 drop into the affected eye(s) TID for 5 days</p> <p>vs</p> <p>vehicle 1 drop into the affected eye(s) TID for 5 days</p>	<p>DB, MC, PC, PG, PRO, RCT</p> <p>Patients ages 1 year and older, in good health, with a clinical diagnosis of acute bacterial conjunctivitis as evidenced by a minimum of grade 1 for purulent conjunctival discharge and a minimum of grade 1 for either bulbar or palpebral conjunctival injection in at least 1 eye on</p>	<p>N=269</p> <p>5 days</p>	<p>Primary: Clinical resolution defined as the absence of conjunctival discharge and bulbar conjunctival injection at visit 3</p> <p>Secondary: Eradication of baseline bacterial infection, defined as the absence at visit 3 of bacterial species that were present at or above the threshold on day 1, clinical resolution of</p>	<p>Primary: Clinical resolution of baseline conjunctivitis at visit three was significantly higher in the besifloxacin group when compared to the vehicle group (73.3 vs 43.1% respectively; $P<0.001$).</p> <p>Secondary: Clinical resolution of conjunctivitis at visit two did not show significant differences between besifloxacin and vehicle (33.3 vs 17.2% respectively; P value not reported), while eradication of bacterial infection at visit two was significantly greater with besifloxacin (90.0 vs 46.6% respectively; $P<0.0001$). Investigators' ratings of individual signs and symptoms were significantly higher in the treatment group when compared to the vehicle group at visit two (ocular discharge; $P=0.008$, bulbar conjunctival injection; $P=0.004$, visit two overall; $P=0.003$) as well as at visit two ($P=0.013$). Ratings of global changes in signs and symptoms were also found to be significantly greater in the treatment group at visit two and visit three ($P=0.004$ and $P<0.001$).</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	ocular examination, with pinhole visual acuity of 20/200 or better in each eye, and females of childbearing potential using a reliable method of contraception		baseline conjunctivitis at visit 2, eradication of the baseline bacterial infection at visit 2, improvements in investigators' ratings of global change in clinical signs and symptoms	respectively).
<p>Tepedino et al⁶⁰</p> <p>Besifloxacin 0.6% 1 drop into the affected eye(s) TID for 5 days</p> <p>vs</p> <p>vehicle 1 drop into the affected eye(s) TID for 5 days</p>	<p>DB, MC, VC</p> <p>Patients ≥1 year of age with clinical manifestations of acute bacterial conjunctivitis in at least one eye</p>	<p>N=957</p> <p>9 days</p>	<p>Primary: Clinical resolution and microbial eradication of baseline bacterial infection at visit 2 (day 5)</p> <p>Secondary: Clinical resolution and microbial eradication at visit 3 (day 8 or 9), individual clinical outcomes at follow-up visits and safety</p>	<p>Primary: Clinical resolution rates were significantly higher in the besifloxacin treatment group compared to the vehicle group at the second visit (45.2 vs 33.0%; $P=0.0084$). By the second visit, microbial eradication rates were 91.5% and 59.7% for besifloxacin and vehicle, respectively; $P<0.0001$.</p> <p>Secondary: At visit three there was a significantly higher percentage of patients who had clinical resolution compared to the vehicle group (84.4 vs 69.1%; $P=0.0011$). By visit three, the microbial eradication rate continued to be significantly higher with besifloxacin treatment compared to vehicle alone (88.4 vs 71.7%; $P<0.0001$).</p> <p>The percentage of patients treated with besifloxacin who had a resolution of ocular discharge was significantly greater at visit two (73.9 vs 57.6%; $P=0.0012$) and three (93.0 vs 79.1%; $P=0.0002$) compared with those treated with vehicle.</p> <p>A significantly higher percentage of patients treated with besifloxacin had normal bulbar conjunctival injection than those treated with vehicle both at visit two (52.3 vs 36.1%; $P=0.0007$) and visit three (84.9% vs 70.7%; $P=0.0011$).</p> <p>The investigators assessment of cure increased in both the</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				<p>besifloxacin and vehicle groups between visits two and three. At visit two, 39.2% and 29.3% of patients treated with besifloxacin or vehicle, respectively, were considered cured by the investigator ($P=0.02$), while at visit three, the rates were 83.9% and 66.0% ($P=0.0002$).</p> <p>A significantly greater percentage of eyes treated with vehicle experienced at least one ocular adverse event compared with those treated with besifloxacin (13.9 vs 9.2%; $P=0.0047$).</p>
<p>Silverstein et al⁶¹</p> <p>Besifloxacin 0.6% 1 drop into the affected eye(s) BID for 3 days</p> <p>vs</p> <p>vehicle 1 drop into the affected eye(s) BID for 3 days</p>	<p>DB, MC, PG, PRO, RCT, VC</p> <p>Patients ≥ 1 year of age with a clinical diagnosis of acute bacterial conjunctivitis with purulent discharge, crusty or sticky eyelids, and ocular surface redness, and a minimum of grade 1 severity for both discharge and bulbar conjunctival injection in at least one eye</p>	<p>N=202</p> <p>7 days</p>	<p>Primary: Clinical resolution and bacterial eradication of the baseline bacterial infection at visit 2</p> <p>Secondary: Clinical resolution and bacterial eradication of the baseline bacterial infection at visit 3, individual clinical outcomes at the follow-up visits</p>	<p>Primary: At visit two, clinical resolution of conjunctivitis in the study eye was significantly higher in the besifloxacin group compared to vehicle (69.8 vs 37.5%; respectively; $P<0.001$).</p> <p>The eradication of bacterial infection at visit two occurred in significantly more patients in the besifloxacin group compared with the vehicle group (86.8 vs 57.1%; $P<0.001$).</p> <p>Secondary: Rates of eradication of bacterial infection in the study eye at visit three were significantly greater in the besifloxacin group compared to the vehicle group (86.8 vs 69.6%, respectively; $P=0.038$).</p> <p>Rates of clinical resolution of bacterial conjunctivitis at visit three did not differ significantly between the besifloxacin and vehicle treatment groups (73.6 vs 66.1%; $P=0.717$).</p> <p>At visit two, the percentage of patients treated with besifloxacin who had resolution of ocular discharge was significantly greater compared to those who received vehicle (83.0 vs 55.4%, respectively; $P=0.002$) but not at visit three (86.8 vs 76.8%; P value not reported).</p> <p>The proportion of patients treated with besifloxacin who had resolution of bulbar conjunctival injection was significantly greater compared to patients receiving vehicle at visit two (77.4 vs 44.6%;</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
<p>Hwang et al⁴³</p> <p>Levofloxacin 0.5% 1 to 2 drops into the affected eye(s) while awake on days 1 and 2 then every 4 hours while awake on days 3 through 5</p> <p>vs</p> <p>placebo 1 to 2 drops into the affected eye(s) while awake on days 1 and 2 then every 4 hours while awake on days 3 through 5</p>	<p>Phase 3, DB, MC, PC, RCT</p> <p>Male and female patients, ages 2 years and older, with a clinical diagnosis of bacterial conjunctivitis characterized by purulent ocular discharge and redness in at least one eye</p>	<p>N=249</p> <p>5 days</p>	<p>Primary: Antimicrobial efficacy, clinical efficacy, resolution of ocular signs and symptoms, safety</p> <p>Secondary: Not reported</p>	<p><i>P</i><0.001), but not at visit three (83.0 vs 73.2%; <i>P</i> value not reported).</p> <p>Primary: Microbial eradication rates were significantly higher in the levofloxacin group at study visits one, two and three when compared to placebo (95 vs 49%; <i>P</i><0.001, 92 vs 53%; <i>P</i><0.001, and 90 vs 53%; <i>P</i><0.001 respectively). Approximately twice as many patients in the treatment group achieved microbial eradication as those in the placebo group (<i>P</i><0.001).</p> <p>Clinical cure rates were significantly greater in the levofloxacin group when compared to placebo at both the final visit and the last observation made for patients who did not attend all visits (<i>P</i>=0.020 and <i>P</i>=0.026 respectively).</p> <p>Resolution of ocular signs and symptoms were consistently higher in the treatment group than with placebo at all study visits (<i>P</i> value not reported). Statistically significant differences were seen favoring the levofloxacin group with regard to resolution of the ocular signs of conjunctival discharge (<i>P</i>=0.027), bulbar conjunctival injection (<i>P</i>=0.018), and for the ocular symptoms of burning and stinging (<i>P</i>=0.008), itching (<i>P</i>=0.037), and photophobia (<i>P</i>=0.023)</p> <p>With regard to safety, a total of 91 adverse events were reported by 75 patients, 31% of the safety population. No significant differences were seen between the levofloxacin group and the placebo group with regard to the incidence of overall adverse events or treatment related events (<i>P</i> value not reported). Of the most common adverse events, only erythema and swelling was reported in significantly more patients in the levofloxacin group (<i>P</i>=0.672), while there was no statistically significant difference in the rate of conjunctival discharge, photophobia, and burning or stinging (<i>P</i>=0.027, <i>P</i>=0.023 and <i>P</i>=0.008 respectively).</p> <p>Secondary:</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Kodjikian et al (abstract) ⁶² Moxifloxacin vs ofloxacin vs levofloxacin	MA (5 RCT) Patients with a clinical diagnosis of acute bacterial conjunctivitis in one or more eyes	N=not reported Duration not reported	Primary: Clinical efficacy and drop-out rates for all reasons including lack of efficacy Secondary: Not reported	Not reported Primary: Patients treated with moxifloxacin were more likely to achieve a clinical cure (OR, 1.59; 95% CI, 1.21 to 2.04; $P<0.001$) and were less likely to experience a treatment failure compared to treatment with placebo (OR, 3.61; 95% CI, 2.30 to 5.65; $P<0.001$). Moxifloxacin treatment was associated with less risk of discontinuing therapy compared to placebo (OR, 2.22; 95% CI, 1.62 to 3.03; $P<0.001$). In comparison to ofloxacin, patients treated with moxifloxacin had fewer drop-outs for reasons other than treatment failure (OR, 1.92; 95% CI, 1.28 to 2.89; $P=0.02$) and fewer drop-outs for treatment failure (OR, 2.53; 95% CI, 1.41 to 4.56; $P=0.002$).
Tauber et al ⁶³ Moxifloxacin 0.5% 1 drop into the affected eye(s) BID for 3 days vs placebo 1 drop into the affected eye(s) BID for 3 days	DB, MC, PG, RCT, VC Patients ≥ 28 days old with a diagnosis of bacterial conjunctivitis in one or both eyes based on bulbar conjunctival injection and discharge (minimum score of 1 on a 4-point scale for each sign) and matting	N=1,180 6 days	Primary: Clinical cure rate, eradication rates by species Secondary: Not reported	Primary: Patients treated with moxifloxacin twice-daily for three days had a microbiological success rate of 74.5% compared to 56.0% of patients treated with vehicle ($P<0.0001$). Moxifloxacin administered twice-daily was significantly more effective than vehicle in eradicating the three principle conjunctivitis pathogens, <i>H. influenzae</i> (98.5 vs 59.6%; $P<0.001$), <i>S. pneumoniae</i> (86.4 vs 50.0%; $P<0.001$), and <i>S. aureus</i> (94.1 vs 80.0%; $P<0.001$).
Gigliotti et al ⁴⁴ Polymyxin/bacitracin applied to affected eye(s) QID for 7 days vs	DB, RCT Patients ages 1 month to 18 years, with acute conjunctivitis	N=102 10 days	Primary: Clinical cure rate, bacterial pathogen eradication Secondary: Not reported	Primary: During days three through five significantly more patients in the polymyxin/bacitracin group were clinically cured as compared to the placebo group (62 vs 28% respectively; $P<0.02$). However, on days eight through 10 the difference between the treatment group and placebo group was not significant (91 vs 72%; P value not reported). It was found that the bacterial pathogen was eradicated in

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<p>placebo applied to affected eye(s) QID for 7 days</p>				<p>significantly more patients in the treatment group than the placebo group by day three to five, as well as in days eight to 10 (72 vs 19% and 79 vs 31% respectively; $P < 0.001$ for both).</p> <p>Secondary: Not reported</p>
<p>Cochereau et al⁴⁵</p> <p>Azithromycin 1.5% 1 drop into the affected eye(s) BID for 3 days</p> <p>vs</p> <p>tobramycin 0.3% 1 drop into the affected eye(s) every 2 hours up to 8 times a day for 2 days, then QID for 5 days</p>	<p>IB, MC, NI, PG, RCT</p> <p>Patients ages 1 day and older, with a diagnosis of purulent bacterial conjunctivitis defined as bulbar injection and purulent discharge</p>	<p>N=1,043</p> <p>9 days</p>	<p>Primary: Clinical efficacy, microbiological assessment, safety</p> <p>Secondary: Not reported</p>	<p>Primary: Clinical efficacy, measured as the number of patients cured on day nine, showed that azithromycin was NI to tobramycin (87.8 vs 89.4%, respectively; 95% CI -7.5 to 4.4). Noninferiority was also found for all efficacy criteria at assessment days three and nine (95% CI, -5.3 to 8.3 and -6.6 to 3.0 respectively). Additionally, azithromycin showed a statistically higher cure rate than tobramycin (29.8 vs 18.6% respectively; P value not reported).</p> <p>The rate of bacteriological resolution for azithromycin was found to be NI to tobramycin at both day three (85.2 vs 83.8%; 95% CI, not reported) and day nine (92.8 vs 94.6%; 95% CI, not reported).</p> <p>Adverse events reported were mild to moderate. Four patients presented with treatment-related adverse events, three from the azithromycin group, two with burning and one with burning/foreign body sensation, and one from the tobramycin group for discharge.</p> <p>Secondary: Not reported</p>
<p>Abelson et al⁴⁶</p> <p>Azithromycin 1% 1 drop into the affected eye(s) BID on days 1 and 2 and once daily on days 3 through 5</p> <p>vs</p>	<p>Phase 3, AC, DB, MC, PRO, RCT</p> <p>Patients ages 1 year and older, with purulent conjunctival discharge, and conjunctival or</p>	<p>N=743</p> <p>5 days</p>	<p>Primary: Clinical resolution of signs and symptoms of infective bacterial conjunctivitis</p> <p>Secondary: Bacterial eradication,</p>	<p>Primary: Differences in clinical resolution between azithromycin and tobramycin were not found to be statistically significant (79.9 vs 78.3%, respectively; $P=0.783$).</p> <p>Secondary: Bacterial eradication was not found to be statistically significant between the azithromycin group and the tobramycin group (88.1 vs</p>

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tobramycin 0.3% 1 drop into the affected eye(s) QID for 5 days	palpebral injection of no more than 3 days duration, with a best corrected visual acuity of 20/100 or better		and investigator ratings of clinical outcomes	94.3%, respectively; $P=0.073$ Clinical outcomes were based on the investigator severity ratings of ocular discharge and injection. At day three there was no significant difference ($P=0.949$), however equivalence with tobramycin was obtained with 65% fewer drops of azithromycin.
McDonald et al ⁴⁷ Besifloxacin 0.6% 1 drop into the affected eye(s) TID for 5 days vs moxifloxacin 0.5% 1 drop into the affected eye(s) TID for 5 days	DB, MC, NI, PG, RCT Patients ages 1 year and older, in good health, with a clinical diagnosis of bacterial conjunctivitis as evidenced by grade 1 or greater purulent conjunctival discharge and bulbar conjunctival injection in at least 1 eye, pinhole visual acuity of 20/200 or greater in both eyes, willing to discontinue contact lens use during the study, and females of childbearing potential using a reliable method of contraception	N=1,161 8 days	Primary: Clinical resolution on day 5, microbial eradication on day 5 of all accepted ocular bacterial species that were present at or above threshold at baseline Secondary: Clinical resolution on day 8, microbial eradication on day 8 of all accepted ocular bacterial species that were present at or above threshold at baseline, and safety	Primary: Findings on day five showed that there was no statistically significant difference in clinical resolution between the besifloxacin group and the moxifloxacin group (58.0 vs 59.4%, respectively; $P=0.652$). Besifloxacin was found to be NI to moxifloxacin (95% CI, -9.48 to 7.29). Besifloxacin was shown to be NI to moxifloxacin with regard to microbial eradication on day 5 (93.3 vs 91.1%, respectively; $P=0.124$). Secondary: On day eight there was no statistical difference seen with regard to clinical resolution between the besifloxacin and moxifloxacin groups (84.5 vs 84.0%, respectively; $P=0.501$). Besifloxacin was found to be NI to moxifloxacin on day eight (95% CI, -5.67 to 6.75). On day eight besifloxacin was shown to be NI to moxifloxacin with regard to microbial eradication (87.3 vs 84.7% respectively; $P=0.061$). No significant differences were seen with regard to adverse events between the besifloxacin group and the moxifloxacin group (12.0 vs 14.0% respectively; $P=0.224$). One eye irritation was statistically different between the besifloxacin group and the moxifloxacin group (0.3 vs 1.4%, respectively; $P=0.020$).
Gross et al ⁴⁸	DB, MC, RCT	N=257	Primary: Treatment efficacy	Primary: Microbiological eradication was shown to be higher in the

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<p>Ciprofloxacin 3 mg/mL 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4 hours on days 3 through 7</p> <p>vs</p> <p>tobramycin solution 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4 hours on days 3 through 7</p>	<p>Patients ages 12 years and younger, with bacterial conjunctivitis</p>	<p>7 days</p>	<p>assessed by microbiological culture and physicians' judgment of overall resolution</p> <p>Secondary: Safety</p>	<p>ciprofloxacin group when compared to the tobramycin group, however this difference was not significant ($P=0.29$).</p> <p>Physicians judgment of overall resolution was higher in the tobramycin group than in the ciprofloxacin group, however this difference was not significant (89.9 vs 87.0%; $P>0.5$).</p> <p>Secondary: No serious adverse events were attributed to either treatment.</p>
<p>Schwab et al⁶⁴</p> <p>Levofloxacin 0.5% 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4 hours on days 3 through 5</p> <p>vs</p> <p>ofloxacin 0.3% 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4 hours on days 3 through 5</p>	<p>AC, DB, MC, RCT</p> <p>Patients ≥ 1 year of age with a diagnosis of bacterial conjunctivitis, characteristic purulent conjunctival discharge (minimum score of 1 on a 4-point scale), and redness (minimum score of 1 on a 4-point scale for bulbar and/or palpebral injection) in at least one eye</p>	<p>N=423</p> <p>7 days</p>	<p>Primary: Microbial eradication and clinical cures</p> <p>Secondary: Evaluations of ocular signs and symptoms, safety</p>	<p>Primary: A significantly greater proportion of patients receiving 0.5% levofloxacin experienced microbial eradication compared to patients receiving 0.3% ofloxacin at both the final visit (89 vs 80%; $P=0.034$) and last available evaluation (90 vs 81%; $P=0.038$).</p> <p>Clinical cure rates were similar between the 0.5% levofloxacin and 0.3% ofloxacin treatment groups at all time points assessed. At the last evaluation period, clinical cure rates were 76% in each treatment group (P value not reported).</p> <p>Secondary: No significant differences were noted between the two treatment groups in resolution of baseline ocular signs at either the final visit or end point. In each treatment group, there was a trend toward resolution of the ocular signs of conjunctival discharge, bulbar and palpebral conjunctival injection and erythema/swelling, with most subjects ($>80\%$) showing resolution by the completion of the study. There was however, a significantly lower incidence of photophobia associated with ofloxacin compared to levofloxacin ($P=0.006$).</p>

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				<p>There were no significant differences between treatment groups in the overall incidence of adverse events. The most frequently reported nonocular adverse event was headache (3%). The most common ocular adverse events were conjunctivitis in the nonstudy eye or worsening conjunctivitis in the infected eye (8%), burning (2%), eye pain (2%) and decrease in visual acuity (2%).</p>
<p>Granet et al⁴⁹</p> <p>Polymyxin B sulfate/ trimethoprim 1 drop into the affected eye(s) QID for 7 days</p> <p>vs</p> <p>moxifloxacin 0.5% 1 drop into the affected eye(s) TID for 7 days</p>	<p>MC, RCT</p> <p>Patients ages 18 years and younger, with a clinical diagnosis of bacterial conjunctivitis</p>	<p>N=56</p> <p>7 days</p>	<p>Primary: Relief of all signs and symptoms of bacterial conjunctivitis</p> <p>Secondary: Safety</p>	<p>Primary: At the 48 hour visit complete resolution of ocular signs and symptoms were reported in significantly more patients in the moxifloxacin group when compared to the polymyxin B sulfate/trimethoprim group (81 vs 44%; $P=0.001$).</p> <p>Secondary: No adverse events were reported in either group.</p>
<p>Kernt et al⁵⁰</p> <p>Enhanced viscosity tobramycin 0.3% 1 drop into the affected eye(s) BID for 7 days</p> <p>vs</p> <p>tobramycin 0.3% 1 drop into the affected eye(s) QID for 7 days</p>	<p>IB, MC, PG, RCT</p> <p>Male and female patients with a negative pregnancy test prior to study entry who agreed to use birth control throughout the study, ages 1 year and older, with bacterial conjunctivitis based on clinical observation</p>	<p>N=276</p> <p>12 days</p>	<p>Primary: Percentage of patients with sustained cure/presumed bacterial eradication based on final clinical judgment at test-of-cure visit</p> <p>Secondary: Lid erythema/swelling, palpebral conjunctiva, bulbar conjunctiva, conjunctival discharge/exudates, tearing, and epithelial disease; microbiology,</p>	<p>Primary: At the test-of-cure visit no statistically significant differences were seen between the enhanced viscosity tobramycin group and the tobramycin group with regard to sustained cure/presumed eradication (98.0 vs 99.0% respectively; $P=0.604$).</p> <p>Secondary: No statistically significant differences were seen between the two groups with regard to lid erythema/swelling, palpebral conjunctiva, bulbar conjunctiva, conjunctival discharge/exudates, and tearing (P value not reported).</p> <p>Persistence of the original infecting organism was confirmed in two patients from the enhanced viscosity tobramycin group and in six patients from the tobramycin group (P value not reported).</p> <p>Adverse events reported were mild to moderate in severity and were</p>

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			and safety	reported in 5.8% of the total number of patients in both groups. The most frequent ocular adverse events in the enhanced viscosity tobramycin group were ocular pruritus (1.5%), ocular hyperemia (1.5%), and tearing (1.5%). Only ocular pruritus (0.7%) was reported in the tobramycin group (<i>P</i> value not reported).
<p>Behrens-Baumann et al⁵¹</p> <p>Trimethoprim/polymixin B sulfate 5 mg/g and 10,000 units/g applied QID to the lower conjunctival sac(s) for 7 days</p> <p>vs</p> <p>chloramphenicol 10 mg/g* applied QID to the lower conjunctival sac(s) for 7 days</p>	<p>DB, PG, RCT</p> <p>Patients with a clinical diagnosis of bacterial conjunctivitis</p>	<p>N=42</p> <p>10 days</p>	<p>Primary: Reduction in severity rating score</p> <p>Secondary: Safety</p>	<p>Primary: No significant difference was seen between the two groups with regard to reduction in severity rating score (<i>P</i>>0.1).</p> <p>Secondary: Three (7%) patients from the trimethoprim/polymixin B sulfate group experienced adverse events: one patient reported stinging/burning, one reported increases in transient grittiness and conjunctival hyperemia, and one reported periorbital edema (<i>P</i> value not reported).</p>
<p>Papa et al⁵²</p> <p>Gentamicin 0.3% 1 to 2 drops into the affected eye(s) QID until resolution and up to 10 days with gentamicin ointment applied to affected eye(s) HS</p> <p>vs</p> <p>netilmicin 0.3%* 1 to 2 drops into the affected eye(s) QID until resolution and up to 10 days with netilmicin ointment* applied to affected eye(s) HS</p>	<p>AC, DB, PG, PRO, RCT</p> <p>Male and female patients, ages 3 years and older, with suspected acute bacterial conjunctivitis</p>	<p>N=209</p> <p>10 days</p>	<p>Primary: Clinical resolution of ocular infection as assessed by either clinical or microbiologic parameters</p> <p>Secondary: Safety</p>	<p>Primary: Netilmicin was shown to be significantly more effective than gentamicin in increasing the percentage of infections eradication over time (<i>P</i>=0.001).</p> <p>Netilmicin was shown to be significantly more effective than gentamicin in ameliorating clinical symptoms as assessed by the cumulative score of several signs and symptoms of acute bacterial ocular infection at five and 10 days (<i>P</i>=0.001 for both five and 10 days).</p> <p>Secondary: Adverse events were reported in four (3.9%) patients in the gentamicin group and two (1.9%) patients in the netilmicin group (<i>P</i> value not reported). Treatment tolerance was rated slightly higher in the netilmicin group as compared to the gentamicin group, however</p>

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<p>Leibowitz et al⁵³</p> <p>Ciprofloxacin 0.3%</p> <p>vs</p> <p>tobramycin 0.3%</p> <p>vs</p> <p>placebo</p>	<p>2 MC, PRO, RCT</p> <p>Patients with bacterial conjunctivitis</p>	<p>N=288</p> <p>Duration not specified</p>	<p>Primary: Antibacterial efficacy, and eradication of bacterial pathogens</p> <p>Secondary: Not reported</p>	<p>this difference was not statistically significant (96.9 vs 70.9%; <i>P</i> value not reported)</p> <p>Primary: In one study ciprofloxacin was shown to be significantly more effective than placebo (<i>P</i><0.001), and eradicated or reduced the various bacterial pathogens in more patients when compared to placebo (93.6 vs 59.5%; <i>P</i> value not reported).</p> <p>In a second study ciprofloxacin and tobramycin were found to be equally effective in antibacterial efficacy (94.5 vs 91.9%; <i>P</i> value not reported).</p> <p>Secondary: Not reported</p>
<p>Lichtenstein et al⁵⁴</p> <p>Levofloxacin 0.5% 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4 hours on days 3 through 5</p> <p>vs</p> <p>ofloxacin 0.3% 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4 hours on days 3 through 5</p> <p>vs</p> <p>placebo 1 drop into the affected eye(s) every 2 hours on days 1 and 2 and every 4</p>	<p>DB, MC, PG, RCT</p> <p>Patients ages 1 to 16 years, with a diagnosis of bacterial conjunctivitis</p>	<p>N=167</p> <p>10 days</p>	<p>Primary: Rate of microbial eradication</p> <p>Secondary: Not reported</p>	<p>Primary: At the last observation the levofloxacin 0.5% group showed higher rates of microbial eradication when compared to ofloxacin 0.3% (<i>P</i> value not reported).</p> <p>In children ages two to 11 years this finding was statistically significant in favor of the levofloxacin 0.5% group when compared to both ofloxacin 0.3% and placebo (87 vs 62%; <i>P</i><0.032 and 88 vs 24%; <i>P</i><0.001).</p> <p>No statistically significant differences were observed between the three groups in the other age subgroups.</p> <p>Secondary: Not reported</p>

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hours on days 3 through 5 Lohr et al ⁵⁵ Trimethoprim/polymyxin B vs gentamicin sulfate vs sodium sulfacetamide	R Patients with culture-positive conjunctivitis	N=158 17 days	Primary: Patients cured and symptom improvement at days 3 to 6 after the start of treatment, patients cured and symptom improvement at days 2 to 7 after completion of therapy, and bacteriologic response at days 2 to 7 after completion of therapy Secondary: Not reported	Primary: Clinical response at days three to six after the start of treatment was similar for patients cured, as well as symptom improvement between the trimethoprim/polymyxin B, gentamicin sulfate, and sodium sulfacetamide groups (47 vs 49%, 41 and 45% vs 46 vs 48% respectively; <i>P</i> value not reported). Clinical response and symptom improvement at days two to seven after completion of therapy were also similar between all groups (84% vs 88% vs 89% and 9% vs 9% vs 4%; <i>P</i> value not reported). Bacteriologic response at days two to seven after completion of therapy was similar as well for all groups (83 vs 68%, 72; <i>P</i> value not reported). Secondary: Not reported
Gibson ⁵⁶ Trimethoprim/polymyxin B vs neomycin/polymyxin B/gramicidin vs chloramphenicol*	DB, MC, RCT Patients with a diagnosis of presumptive bacterial conjunctivitis	N=230 Duration not specified	Primary: Treatment efficacy, reduction of signs and symptoms of conjunctivitis Secondary: Not reported	Primary: All groups showed efficacy in the treatment of bacterial conjunctivitis with no statistically significant difference demonstrated between the trimethoprim/polymyxin B group and the neomycin/polymyxin B/gramicidin group (<i>P</i> value not reported). However, neomycin/polymyxin B/gramicidin was found to be significantly more efficacious than chloramphenicol in reducing signs and symptoms (<i>P</i> =0.03). Secondary: Not reported
Silver et al ⁵⁷ Moxifloxacin 0.5% 1 drop into the affected eye(s) TID for 4	MA Male and female patients of any race,	N=1,978 7 to 9 days	Primary: Safety Secondary:	Primary: The most frequent adverse events experienced by all patients were ocular discomfort, and transient burning and stinging, which were reported in more patients in the moxifloxacin group than the vehicle

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days vs ofloxacin 0.3% 1 drop into the affected eye(s) QID for 4 days vs ciprofloxacin 0.3% 1 drop into the affected eye(s) TID for 4 days vs vehicle	with a diagnosis of bacterial conjunctivitis		Not reported	<p>group (2.8 vs 2.1%; <i>P</i> value not reported).</p> <p>In pediatric patients similar results were found with ocular discomfort, transient burning and stinging reported as the most frequent adverse events experienced; these adverse events were reported in less patients the moxifloxacin group when compared to the vehicle group (1.9 vs 2.2%; <i>P</i> value not reported). The most common systemic adverse event reported in pediatric patients was increased cough which occurred in more patients in the moxifloxacin group than the vehicle group (3.2 vs 2.8%; <i>P</i> value not reported).</p> <p>Similar rates of adverse events were reported in a study comparing moxifloxacin to ofloxacin with regard to keratitis, corneal infiltrate, and ocular hyperemia (<i>P</i> value not reported).</p> <p>In a study comparing moxifloxacin to ciprofloxacin adverse events were also similar between the two groups with regard to tearing, ocular hyperemia, rash, and rhinitis (<i>P</i> value not reported).</p> <p>Secondary: Not reported</p>
Jauch et al ⁵⁸ Gentamicin 0.3% vs tobramycin 0.3% vs chloramphenicol 0.5%* vs	MA Patients with acute bacterial conjunctivitis, purulent discharge, and at least moderate conjunctival hyperemia	N=582 9 days	Primary: Decrease of cumulative sum score of key signs and symptoms of acute bacterial conjunctivitis Secondary: Safety	Primary: Within group comparisons of the sum score of key signs and symptoms statistically significant improvement in both groups was shown between any two visits (<i>P</i> value not reported). The between group comparison showed a statistically significant improvement in the sum score with lomefloxacin by assessment days seven to nine in both the intention to treat population and core population when compared to the other treatments (<i>P</i> =0.026 and <i>P</i> =0.016 respectively). <p>Secondary: When lomefloxacin was compared to all other medications, poor tolerance for the medication was reported less often in the</p>

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fusidic acid 1%* vs lomefloxacin 0.3%* vs norfloxacin 0.3%*				lomefloxacin group than with the other medications (1.5 vs 3.9%; <i>P</i> value not reported). Duration of any burning sensation was also significantly less in the lomefloxacin group when compared to all other medications (<i>P</i> =0.04).
Sheikh et al ⁵⁹ Bacitracin/polymyxin 500 units/g and 10,000 units/g vs ciprofloxacin 0.3% vs chloramphenicol 0.5%* vs fusidic acid gel 1%* vs norfloxacin 0.3%* vs vehicle	MA Patients ages one month and older, with acute bacterial conjunctivitis, and symptoms of less than four weeks duration	N=1,034 Duration not specified	Primary: Early clinical remission, early microbiological remission, late clinical remission, and late microbiological remission Secondary: Not reported	Primary: When bacitracin/polymyxin was compared to vehicle with regard to early clinical remission, bacitracin/polymyxin was favored at days three through five (RR, 2.20; 95% CI, 1.19 to 4.06). When bacitracin/polymyxin was compared to vehicle with regard to microbiological remission during days three through five it was found that bacitracin/polymyxin was favored (RR, 3.76; 95% CI, 1.77 to 8.00). Ciprofloxacin was also favored when compared to vehicle with regard to early microbiological remission, at day three (RR, 1.59; 95% CI, 1.21 to 2.08). Bacitracin/polymyxin was favored over vehicle with regard to late clinical remission at days eight to 10 (RR, 1.27; 95% CI, 1.00 to 1.61) as well as for late microbiological remission in days eight through 10 (RR, 2.54; 95% CI, 1.48 to 4.37). Secondary: Not reported

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Corneal Ulcer				
Booranapong et al ⁶⁵ Ciprofloxacin 0.3% vs lomefloxacin 0.3%*	DB, PRO, RCT Patients with suspected bacterial corneal ulcers	N=41 Duration not specified	Primary: Time to cure, treatment failure, and resolution of clinical signs and symptoms Secondary: Safety	Primary: No statistically significant differences were found with regard to time to cure, treatment failure, or the resolution of clinical signs and symptoms ($P>0.05$ for all). Secondary: No statistically significant difference was found between the two groups with regard to adverse events ($P>0.05$).
Kosirukvongs et al ⁶⁶ Ciprofloxacin 0.3% applied into the affected eye(s) every 15 minutes for the first 6 hours, then every 30 minutes on the first day, then every hour while awake till midnight until complete recovery without staining of fluorescein and no culture growth vs cefazolin 50 mg/mL fortified with gentamicin 14 mg/mL applied into the affected eye(s) every 15 minutes for the first 6 hours, then every 30 minutes on the first day, then every hour while awake till midnight until complete recovery without staining of fluorescein and no culture growth	RCT Patients with suspected corneal ulcers	N=41 16 days	Primary: Rate of therapeutically successful treatment, and mean duration for healing Secondary: Not reported	Primary: A higher number of patients in the ciprofloxacin group had therapeutically successful treatment when compared to the cefazolin fortified with gentamicin group; however this difference was not found to be statistically significant (70.6 vs 62.5%, respectively; P value not reported). The mean duration for healing after treatment was found to be less in the ciprofloxacin group but was not found to be statistically significant (14.6 vs 15.6 days, respectively; P value not reported). Secondary: Not reported
Keratitis				

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Parks et al ⁶⁷ Ciprofloxacin 3 mg/mL vs cefazolin 50 mg/mL fortified with gentamicin sulfate 9.1 mg/mL	RETRO Patients with infectious keratitis	N=44 Duration not specified	Primary: Average time to healing, and duration of antibiotic therapy Secondary: Not reported	Primary: Average time to healing in the ciprofloxacin group was less than that seen in the cefazolin fortified with gentamicin sulfate group, however this was not found to be statistically significant (34±33 vs 45±71 days; <i>P</i> value not reported). The duration of antibiotic therapy in the ciprofloxacin group was also less than that seen in the cefazolin fortified with gentamicin sulfate group (27±15 vs 33±50 days; <i>P</i> value not reported). Secondary: Not reported
Multiple/Unspecified External Ocular Infection				
Bloom et al ⁶⁸ Ciprofloxacin treatment to affected eye(s) for 7 days vs tobramycin treatment to affected eye(s) for 7 days	DB, MC, RCT Patients with blepharitis and blepharoconjunctivitis	N=464 7 days	Primary: Eradication or reduction of potentially pathogenic bacteria, improvement or cure rate after 7 days, and adverse events Secondary: Not reported	Primary: Eradication or reduction of potentially pathogenic bacteria after seven days of treatment was reported in more patients in the ciprofloxacin group than in the tobramycin group (93.7 vs 88.9% respectively; <i>P</i> value not reported). More than 80% of patients in both groups were cured or improved after seven days. However, no statistically significant differences were seen between the two groups (<i>P</i> value not reported). No serious adverse events were reported in either group. Secondary: Not reported
Adenis et al ⁶⁹ Ciprofloxacin 0.3% vs fusidic acid 1%*	OL, PG, RCT Patients with bacterial conjunctivitis and blepharitis	N=39 7 days	Primary: Eradication of infecting organism, clinical cure rate, and adverse events Secondary:	Primary: The infecting organism was documented to be eradicated in more patients in the ciprofloxacin group than those in the fusidic acid group (81 vs 72%, respectively; <i>P</i> value not reported). Clinical cure rates were also found to be higher in the ciprofloxacin group when compared to the fusidic acid group (95 vs 89%,

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			Not reported	<p>respectively; <i>P</i> value not reported).</p> <p>Two patients in the ciprofloxacin group reported adverse events, mild discomfort and stinging on instillation, while one patient in the fusidic acid group reported moderate edema and discomfort (<i>P</i> value not reported).</p> <p>Secondary: Not reported</p>
<p>Adenis et al⁷⁰</p> <p>Ciprofloxacin 0.3% vs rifamycin 1%*</p>	<p>DB, PG, RCT</p> <p>Patients with bacterial conjunctivitis and blepharitis</p>	<p>N=41</p> <p>7 days</p>	<p>Primary: Clinical cure rate on day 7, bacteriological eradication rate, and adverse events</p> <p>Secondary: Not reported</p>	<p>Primary: Clinical cure rates on day seven were shown to be higher in the ciprofloxacin group than the rifamycin group, however this difference was not found to be statistically significant (53 vs 23%, respectively; <i>P</i>=0.061).</p> <p>Bacteriological eradication rates were similar in both groups (68 vs 77%, respectively; <i>P</i> value not reported).</p> <p>No serious adverse events were reported in either treatment group.</p> <p>Secondary: Not reported</p>
<p>Shulman et al⁷¹</p> <p>Neomycin/polymyxin B/ dexamethasone 3500 units/mL/6000 units/mL/0.1% vs dexamethasone 0.1%</p>	<p>DB</p> <p>Patients with bacterial blepharitis or conjunctivitis</p>	<p>N=111</p> <p>Duration not specified</p>	<p>Primary: Bacterial count, bacterial eradication, and reduction in symptoms</p> <p>Secondary: Not reported</p>	<p>Primary: The neomycin/polymyxin B/dexamethasone group showed a significantly greater decrease in bacterial counts and bacterial eradication when compared to dexamethasone (90 vs 50% and 34 vs 17% respectively; <i>P</i> values not reported).</p> <p>Neomycin/polymyxin B/dexamethasone was shown to significantly reduce conjunctival discharge when compared to dexamethasone 0.1% (<i>P</i> value not reported).</p> <p>Both groups were equally efficacious in alleviating other ocular signs and symptoms (<i>P</i> value not reported).</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
<p>Bron et al⁷²</p> <p>Ofloxacin 0.3% 1 drop into the affected eye(s) every 2 to 4 hours on days 1 and 2 and QID on days 3 through 7</p> <p>vs</p> <p>chloramphenicol 0.5%* 1 drop into the affected eye(s) every 2 to 4 hours on days 1 and 2 and QID on days 3 through 7</p>	<p>DB, MC, PG, RCT</p> <p>Patients with suspected bacterial ocular infection</p>	<p>N=167</p> <p>8 days</p>	<p>Primary: Clinical improvement as defined as a decline in symptoms of external ocular infection , microbiological improvement rate, and clinical improvement rate</p> <p>Secondary: Safety</p>	<p>Secondary: Not reported</p> <p>Primary: High rates of improvement were seen in both groups with no statistically or clinically significant differences seen with regard to microbiological, clinical or overall improvement rates of the initial culture-positive group (<i>P</i> value not reported).</p> <p>Microbiological improvement rates were similar between the ofloxacin group and the chloramphenicol group (85 vs 88%, respectively; <i>P</i> value not reported).</p> <p>Clinical improvement rates were also high for both the ofloxacin group and the chloramphenicol group (100 vs 95%, respectively; <i>P</i> value not reported).</p> <p>Secondary: No significant differences were seen between the two groups for any symptom present at visit three or with regard to adverse events (<i>P</i> value not reported).</p>
<p>Gwon et al⁷³</p> <p>Ofloxacin 0.3% 1 drop into the affected eye(s) every 2 to 4 hours on days 1 and 2 and QID on days 3 through 7</p> <p>vs</p> <p>gentamicin 0.3% 1 drop into the affected eye(s) every 2 to 4 hours on days 1 and 2 and QID on days 3 through 7</p>	<p>DB, RCT</p> <p>Patients with suspected external ocular bacterial infection including conjunctivitis, blepharitis, and blepharoconjunctivitis</p>	<p>N=194</p> <p>11 days</p>	<p>Primary: Clinical, microbiological, and overall improvement rates</p> <p>Secondary: Safety</p>	<p>Primary: Ofloxacin was found to have higher rates of clinical (98 vs 92%), microbiological (78 vs 67%), and overall (78 vs 63%) improvement rates when compared to gentamicin however none of these differences were statistically significant (<i>P</i>=0.089 for all outcomes).</p> <p>Secondary: Adverse events were reported in 3.2% of the ofloxacin group and in 7.1% of the gentamicin group with the most common reactions including burning, stinging, and photophobia (<i>P</i> value not reported).</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
<p>Gwon et al⁷⁴</p> <p>Ofloxacin 0.3% 1 drop into the affected eye(s) every 2 to 4 hours on days 1 and 2 and QID on days 3 through 10</p> <p>vs</p> <p>tobramycin 0.3% 1 drop into the affected eye(s) every 2 to 4 hours on days 1 and 2 and QID on days 3 through 10</p>	<p>DB, MC, RCT</p> <p>Patients with the presence of conjunctival hyperemia, either eyelid crusting or discharge, and positive bacterial culture</p>	<p>N=345</p> <p>11 days</p>	<p>Primary: Clinical, microbiological, and overall improvement rates</p> <p>Secondary: Change in cumulative summary score of 10 key biomicroscopic and symptomatologic variables, and safety</p>	<p>Primary: Ofloxacin was found to have higher rates of microbiological (85.2 vs 77.6%), and overall (84.0 vs 77.6%) improvement rates when compared to tobramycin at day 11, while tobramycin was shown to have a higher clinical improvement rate (98.9 vs 100%), however none of these differences were found to be statistically significant ($P=0.089$ for all outcomes).</p> <p>Secondary: The decrease in cumulative summary score was found to be significantly greater in the ofloxacin group when compared to the tobramycin group at visits on days three to five ($P<0.050$)</p> <p>Adverse reactions occurred more frequently in the tobramycin group, however this was not found to be significant (0.6 vs 2.9%, respectively; P value not reported).</p>
<p>Laibson et al⁷⁵</p> <p>Tobramycin ointment</p> <p>vs</p> <p>gentamicin sulfate ointment</p>	<p>DB, MC</p> <p>Patients with bacterial infections of the external eye</p>	<p>N=511</p> <p>Duration not specified</p>	<p>Primary: Efficacy evaluated by resolution of signs and symptoms and follow-up impression made by a physician, and adverse events</p> <p>Secondary: Not reported</p>	<p>Primary: Tobramycin ointment was found to be significantly more effective than gentamicin ointment when compared for resolution of signs and symptoms and follow-up impression made by a physician (P value not reported).</p> <p>Tobramycin ointment was associated with significantly less adverse events than gentamicin ointment (P value not reported).</p> <p>Secondary: Not reported</p>
<p>Leibowitz et al⁷⁶</p> <p>Tobramycin</p> <p>vs</p> <p>gentamicin</p>	<p>DB, MC, RCT</p> <p>Patients with superficial external eye disease</p>	<p>N=77</p> <p>10 days</p>	<p>Primary: Clinical cure or improvement, antibacterial effectiveness, and adverse events</p>	<p>Primary: A trend favoring the tobramycin group was seen with regard to clinical cure or improvement when compared to the gentamicin group, however this difference was not significant (97 vs 91.3%, respectively; $P>0.05$).</p> <p>Antibacterial effectiveness also favored tobramycin but was not found</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			Secondary: Not reported	to be statistically significant (87.8 vs 77.4%, respectively; $P>0.05$). Adverse events in the tobramycin and gentamicin groups were also not found to be significantly different (9.3 vs 17.6%; $P>0.05$). Secondary: Not reported
<p>Jacobson et al⁷⁷</p> <p>Tobramycin 0.3% 1 drop into the affected eye(s) every 2 hours while awake on day 1 and then QID on days 2 through 7</p> <p>vs</p> <p>norfloxacin 0.3%* 1 drop into the affected eye(s) every 2 hours while awake on day 1 and then QID on days 2 through 7</p>	<p>DB, MC, RCT</p> <p>Male and female patients, with a clinical diagnosis of acute bacterial conjunctivitis, keratoconjunctivitis, blepharitis, or blepharoconjunctivitis</p>	<p>N=120</p> <p>8 days</p>	<p>Primary: Pathogens eliminated after therapy</p> <p>Secondary: Safety</p>	<p>Primary: Almost all patients in both groups were evaluated as cured or improved after treatment (no values reported). Both groups had approximately 80% of all pathogens eliminated after therapy (P value not reported).</p> <p>Secondary: None of the side effects reported in either group were regarded as serious. Three patients in the tobramycin group reported having corneal stippling (P value not reported).</p>
<p>Foulks et al⁸</p> <p>Trimethoprim/polymyxin B 1 mg/mL/10,000 units/g applied to the affected eye(s) every three hours while awake for 10 days</p> <p>vs</p> <p>trimethoprim/sulfacetamide/polymyxin B 1 mg/g/5 mg/mL/</p>	<p>DB, RCT</p> <p>Patients with clinical signs and symptoms of surface ocular bacterial infections, ages two months and older</p>	<p>N=57</p> <p>10 days</p>	<p>Primary: Clinical improvement, and microbiologic improvement</p> <p>Secondary: Safety</p>	<p>Primary: Clinical improvements and cure rates at the final follow up visit were similar in the trimethoprim/polymyxin B and trimethoprim/sulfacetamide/polymyxin B groups with no statistically significant differences between the two with regard to either outcome (20 vs 29% and 80 vs 71% respectively; P value not reported).</p> <p>Differences in microbiologic responses were also not found to be statistically significant between the two groups (87 vs 93%, respectively; P value not reported).</p> <p>Secondary:</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
10,000 units/g* applied to affected eye(s) every three hours while awake for 10 days				Patients evaluated for safety showed an identical incidence of adverse events (<i>P</i> value not reported).
Prophylaxis of Ophthalmia Neonatorum				
Bell et al ⁷⁹ Erythromycin 0.5% ointment applied to eyes of child at birth vs silver nitration applied to eyes of child at birth vs no prophylaxis	DB, RCT Women from the University of Washington Medical Center-associated obstetric clinics	N=669 60 days	Primary: Frequency of conjunctivitis, and duration of prophylaxis Secondary: Not reported	Primary: After 2 months of observation it was found that infants who received prophylaxis had lower rates of conjunctivitis with only silver nitrate showing a statistically significant decrease, rates of conjunctivitis were 22% in the no prophylaxis group, 16% in the erythromycin group, and 14% in the silver nitrated group (<i>P</i> value not reported). Patients who received silver nitrate at birth had a 39% lower rate of conjunctivitis (HR, 0.61; 95% CI, 0.39 to 0.97), while those who received erythromycin had a 31% lower rate of conjunctivitis (HR, 0.69; 95% CI, 0.44 to 1.07). When cases of conjunctivitis were compared before and after two weeks of age, the protective effect of prophylaxis was found to be most effective prior to two weeks of age. The efficacy of erythromycin from day zero to day 14 was 9.0% as compared to 15.0% with no prophylaxis (<i>P</i> =0.050). This was not found to be statistically significant from days 15 to 60 (7.0 vs 8.0% respectively; <i>P</i> =0.920). Secondary: Not reported
Ali et al ⁸⁰ Erythromycin 0.5% ointment applied to eyes during the first few hours of birth vs betadine 2.5% applied to eyes	RCT Healthy newborns, without congenital eye abnormalities, from mother who had not used any form of antibiotics within the last 48 hours prior to	N=330 14 days	Primary: Rate of conjunctival symptoms Secondary: Not reported	Primary: The betadine group and erythromycin group had significantly less reports of conjunctival redness and tearing or serious or purulent discharge during the first 24 hours through two weeks of birth when compared to the group that did not receive prophylaxis (9.0% vs 18.4% vs 22.4%, respectively; <i>P</i> =0.030). Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
during the first few hours of birth vs no prophylaxis	delivery, without rupture of membranes for more than 18 hours, and absence of meconium aspiration			
Miscellaneous				
Stewart et al ⁸⁴ Dexamethasone/ neomycin/polymyxin B instilled 3 days prior to surgery and three weeks following surgery vs placebo instilled 3 days prior to surgery and three weeks following surgery	DB, PRO, RCT Patients undergoing planned extracapsular cataract extraction with intraocular lens implantation	N=23 Duration not known (>3 weeks)	Primary: Postoperative development of iritis/ excessive inflammation Secondary: Not reported	Primary: Five out of 13 patients in the placebo group developed significant iritis compared to none out of 10 patients in the dexamethasone/neomycin/polymyxin B group postoperatively (38 vs 0%; $P=0.027$). Two patients in the dexamethasone/neomycin/polymyxin B group compared to none in the placebo group experienced broken suture followed by iris prolapse postoperatively ($P>0.10$). Secondary: Not reported
Van Endt et al ⁸¹ Dexamethasone/ neomycin/polymyxin B vs gentamicin	PG, PRO, RCT Male and female patients undergoing cataract and posterior chamber lens implant surgery	N=112 34 days	Primary: Bacterial colony count, intra-ocular inflammation, and global assessment of success of therapy and local tolerance Secondary: Not reported	Primary: At day six to eight the bacterial colony count was significantly less in the gentamicin group when compared to the dexamethasone/neomycin/ polymyxin B group ($P=0.033$). No statistically significant difference was found between the two groups with regard to the degree of intra-ocular inflammation or the global assessment of the success of therapy and local tolerance by the study patients and doctors (P value not reported). Secondary: Not reported
Rhee et al ⁸³ Dexamethasone/tobramycin	DB, PG, RCT Patients with	N=40 5 days	Primary: Reduction in ocular symptom scores	Primary: All scores for ocular symptoms showed greater reductions in symptom scores in the dexamethasone/tobramycin group when

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
<p>0.1%/0.3% 1 drop into the affected eye(s) BID for 3 to 5 days</p> <p>vs</p> <p>loteprednol/tobramycin 0.5%/0.3% 1 drop into the affected eye(s) BID for 3 to 5 days</p>	<p>moderate blepharokeratoconjunctivitis in at least one eye defined as a total sum of scores >6 derived from grading of blepharitis, conjunctivitis, ocular discharge, and punctate epithelial keratitis</p>		<p>Secondary: Safety</p>	<p>compared to the loteprednol/tobramycin group. Scores for signs of blepharitis, conjunctivitis, and ocular discharge were significantly reduced ($P=0.017$, $P=0.013$ and $P=0.025$, respectively), while the reduction in the keratitis score was not found to be statistically significant ($P=0.065$).</p> <p>Secondary: No adverse events were reported in any patient in either treatment group.</p>
<p>White et al⁸⁵</p> <p>Loteprednol/tobramycin 0.5%/0.3% 1 drop in the affected eye(s) QID</p> <p>vs</p> <p>dexamethasone/ tobramycin 0.1%/0.3% 1 drop in the affected eye(s) QID</p>	<p>MC, PG, RCT, SB</p> <p>Patients with ocular inflammation associated with blepharokeratoconjunctivitis in at least one eye</p>	<p>N=276</p> <p>14 days</p>	<p>Primary: Change from baseline in the signs of symptoms composite score of ocular inflammation associated with blepharokeratoconjunctivitis</p> <p>Secondary: Visual acuity, biomicroscopy, intraocular pressure assessments and adverse events</p>	<p>Primary: The mean±SD change from baseline in the signs and symptoms composite score at day 15 was -15.2±7.3 for loteprednol/tobramycin and -15.6±7.7 for dexamethasone/tobramycin (P value not reported).</p> <p>Secondary: Patients in the dexamethasone/tobramycin group experienced a significant increase in intraocular pressure compared to patients in the loteprednol/tobramycin group at day seven, day 15, and overall (0.6±2.3 vs -0.1±2.2; $P=0.03$, 1.0±3.0 vs -0.1±2.4; $P=0.01$, and 2.3±2.3 vs 1.6±1.7; $P=0.02$, respectively).</p>
<p>Notivol et al⁸²</p> <p>Dexamethasone/ tobramycin 1 mg/mL/3 mg/mL 1 drop into the operated eye(s) QID for 21 days</p>	<p>DB, MC, PG, PRO</p> <p>Male and female patients of any race, ages 18 years and older, undergoing cataract extraction by</p>	<p>N=271</p> <p>21 days</p>	<p>Primary: Intraocular inflammation assessed at days 3, 8, 14 and 21</p> <p>Secondary: Evaluation of adverse</p>	<p>Primary: Inflammation scores between dexamethasone/tobramycin and dexamethasone/neomycin/polymyxin B were 0.08, 0.13 and 0.09 at days three, eight, 14, and 21 respectively ($P<0.70$ for all) and met the upper 95% CI to show noninferiority of dexamethasone/tobramycin.</p> <p>Inflammation scores were significantly lower in the dexamethasone/</p>

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
<p>vs</p> <p>dexamethasone/neomycin/polymyxin B 1 mg/mL/ 3500 units/mL/6000 units/mL 1 drop into the operated eye(s) QID for 21 days</p> <p>vs</p> <p>neomycin/polymyxin B/gramicidin 3500 units/mL/7500 units/mL/20 µg/mL 1 drop into the operated eye(s) QID for 21 days</p>	<p>either manual extraction or phacoemulsification with intraocular lens implantation</p>		<p>events including flare, conjunctival hyperemia, corneal edema, anterior vitreous reaction, ocular pain, physician's impression of inflammation, and presence of ciliary flush</p>	<p>tobramycin group when compared to the dexamethasone/neomycin/polymyxin B group at days eight, 14, and 21 (0.77, 0.54, 0.39 respectively; $P<0.050$ for all), and scores in the dexamethasone/neomycin/polymyxin B group were significantly lower than those seen in the neomycin/polymyxin B/gramicidin group at day eight (mean score difference, 0.51; $P<0.050$).</p> <p>Secondary: No statistically significant differences were seen in the mean scores of any variable between the dexamethasone/ tobramycin group and the dexamethasone/neomycin/ polymyxin B groups.</p> <p>The neomycin/polymyxin B/gramicidin group reported significantly lower events with regard to flare at day eight, conjunctival hyperemia at days three, eight, 14, and 21, corneal edema at days three, 14, and 21, ocular pain at days eight, 14, and 21, and physician's clinical impression of inflammation at days three, eight, 14, and 21 when compared to the dexamethasone/tobramycin group ($P<0.05$ for all).</p> <p>The percentage of patients with ciliary flush as days eight, 14, and 21 were significantly lower in the dexamethasone/tobramycin group than in the neomycin/polymyxin B/gramicidin group ($P<0.05$ for all).</p> <p>Scores in the dexamethasone/neomycin/polymyxin B group in relation to conjunctival hyperemia at days three, eight, 14, and 21, corneal edema at day 14, ocular pain at days eight, 14, and 21, and physician's impression at days eight, 14, and 21 were significantly lower than those reported in the neomycin/polymyxin B/gramicidin group ($P<0.05$ for all).</p>

*Agent not available in the United States.

Drug regimen abbreviations: BID=twice daily, QID=four times daily, TID=three times daily,

Study abbreviations: AC=active-controlled, CI=confidence interval, DB=double-blind, HR=hazard ratio, IB=investigator blind, HS=at bedtime, MA=meta-analysis, MC=multicenter, NI=non-inferiority, OL=open-label, PC=placebo-controlled, PG=parallel-group, PRO=prospective, R=randomized, RCT=randomized controlled trial, RETRO=retrospective, RR=risk ratio, SB=single blind, VC=vehicle control

Special Populations

While the ophthalmic agents included in this review are classified as pregnancy category B or C, it is unknown if they are excreted in human breast milk. No overall differences in safety or efficacy were observed in the elderly and no dose adjustments are required in renal or hepatic impairment.

Table 4. Special Populations^{1,4-37}

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Single Entity Products					
Azithromycin	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <1 year of age have not been established.	Not reported	Not reported	B	Not reported
Bacitracin	No overall differences in safety or efficacy observed in the elderly.	Not reported	Not reported	C	Not reported
Besifloxacin	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <1 year of age have not been established.	Not reported	Not reported	C	Not reported
Ciprofloxacin	No overall differences in safety or efficacy observed in the elderly. Ophthalmic ointment: Safety and efficacy in pediatric patients <2 years of age have not been established. Ophthalmic suspension: Safety and efficacy in pediatric patients <1 year of age have not been established.	Not reported	Not reported	C	Not reported
Erythromycin	Safety and efficacy has been established in newborn infants.	Not reported	Not reported	B	Not reported
Gatifloxacin	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <1 year of age have not been	Not reported	Not reported	C	Not reported

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
	established.				
Gentamicin sulfate	Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported
Levofloxacin	No overall differences in safety or efficacy observed in the elderly. Iquix®: Safety and efficacy in pediatric patients <6 years of age have not been established. Quixin®: Safety and efficacy in pediatric patients <1 year of age have not been established.	Not reported	Not reported	C	Not reported
Moxifloxacin hydrochloride	No overall differences in safety or efficacy observed in the elderly. Moxeza®: Safety and efficacy in pediatric patients <3 months of age have not been established. Vigamox®: Safety and efficacy in pediatric patients <1 year of age have not been established.	Not reported	Not reported	C	Not reported
Ofloxacin	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <1 year of age have not been established.	Not reported	Not reported	C	Not reported
Sulfacetamide sodium	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <2 months of age have not been established.	Not reported	Not reported	C	Not reported

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Tobramycin	Not reported.	Not reported	Not reported	B	Not reported
Combination Products					
Bacitracin zinc/ polymyxin B sulfate	Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported
Gentamicin sulfate/ prednisolone acetate	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported
Polymyxin B sulfate/ trimethoprim	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <2 months of age have not been established.	Not reported	Not reported	C	Not reported
Sulfacetamide sodium/ prednisolone acetate	Safety and efficacy in pediatric patients <6 years of age have not been established.	Not reported	Not reported	C	Not reported
Sulfacetamide sodium/ prednisolone sodium phosphate	Safety and efficacy in pediatric patients <6 years of age have not been established.	Not reported	Not reported	C	Not reported
Tobramycin/ dexamethasone	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients <2 years of age have not been established.	Not reported	Not reported	C	Not reported
Tobramycin/ loteprednol etabonate	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Unknown
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc	Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported
Neomycin	No overall differences in	Not reported	Not reported	C	Not

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
sulfate/ polymyxin B sulfate/ dexamethasone	safety or efficacy observed in the elderly. Ophthalmic ointment: Safety and efficacy in pediatric patients have not been established. Ophthalmic suspension: Safety and efficacy in pediatric patients <2 years of age have not been established.				reported
Neomycin sulfate/ polymyxin B sulfate/ gramicidin	Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported
Neomycin sulfate/ polymyxin B sulfate/ hydrocortisone	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported
Neomycin sulfate/ polymyxin B sulfate/ prednisolone acetate sulfate	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Excreted in human milk; use caution.
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc/ hydrocortisone	No overall differences in safety or efficacy observed in the elderly. Safety and efficacy in pediatric patients have not been established.	Not reported	Not reported	C	Not reported

Adverse Drug Events

In rare instances sulfonamides have caused fatalities due to adverse reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias.¹⁸

Table 5. Adverse Drug Events (%)^{1,4-37}

Adverse Event(s)	Single Entity Products													
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Suspension	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin
Cardiovascular														
Hyperemia	-	-	-	-	<1	-	-	-	-	<1	-	-	-	-
Central Nervous System														
Dizziness	-	-	-	-	-	-	-	-	-	-	-	✓	-	-
Hallucinations	-	-	-	-	-	-	-	✓	-	-	-	-	-	-
Headache	-	-	1 to 2	-	-	-	1 to 4	-	1 to 3	8 to 10	-	-	-	-
Itching	-	-	-	<10	-	-	-	-	-	-	-	✓	-	-
Itching pain	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Pruritus	-	-	-	-	<1	-	-	-	-	-	-	-	-	-
Dermatologic														
Contact dermatitis	<1	-	-	-	-	-	-	-	-	-	-	-	-	-
Dermatitis	-	-	-	-	<1	-	-	-	-	-	-	-	-	-
Hives	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Rash	✓	-	-	-	-	-	-	-	-	-	1 to 4	-	-	-
Endocrine and Metabolic														
Edema	-	-	-	-	<1	-	-	-	-	-	-	✓	-	-
Gastrointestinal														
Diarrhea	-	-	-	-	-	-	-	-	-	1 to 2	-	-	-	-
Dyspepsia	-	-	-	-	-	-	-	-	-	1 to 2	-	-	-	-
Nausea	-	-	-	<1	<1	-	-	-	-	1 to 2	-	✓	-	-
Ocular														
Blurred vision	✓	-	1 to 2	-	<1	-	-	-	-	1 to 2	-	✓	-	-
Burning	<1	-	-	✓	-	-	-	✓	-	-	-	-	✓	-

Adverse Event(s)	Single Entity Products													
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Suspension	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin
Chemical conjunctivitis	◀	.	.
Chemical keratitis	◀	.	.
Chemosis	1 to 4	.	.	<1
Conjunctival epithelial defects	◀
Conjunctival erythema	△3
Conjunctival hemorrhage	1 to 4
Conjunctival hyperemia	.	.	.	<10	.	.	.	◀	◀	.
Conjunctival irritation	5 to 10
Conjunctival redness	.	.	2
Conjunctivitis	1 to 6	.	.	.
Corneal erosion	<1	<1
Corneal infiltrates	.	.	.	<1
Corneal staining	.	.	.	<1	<1
Corneal ulcer	◀	.	<1	.	.	◀	.
Crystals/scales	.	.	.	<10
Decreased vision	.	.	.	<1	1 to 3	1 to 2
Decreased visual acuity	<1	.	1 to 4	.	.	.	1 to 6	.	.	.
Diplopia	<1
Dry eye	<1	.	.	.	<1	.	1 to 4	.	.	.	1 to 6	.	.	.
Dryness	◀	.	.
Epitheliopathy	<1
Eye discharge	1 to 4
Eye discomfort	.	.	.	✓	2	1 to 2
Eye irritation	1 to 2	.	1 to 2	.	<1	✓	1 to 4	.	.	1 to 2	1 to 2	.	✓	.
Eye pain	.	.	1 to 2	.	<1	.	1 to 4	✓	.	.
Eye pruritus	.	.	1 to 2
Eyelid edema	1 to 4
Eyelid swelling	◀

Adverse Event(s)	Single Entity Products													
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Suspension	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin
Floaters	<1
Foreign body sensation	.	.	.	<10	<1	.	.	.	1 to 3	.	.	<	.	.
Irritation upon instillation	<1	<
Keratoconjunctivitis	<1
Keratopathy	.	.	.	<1	2
Keratitis	.	.	.	<1	.	.	5 to 10	.	.	.	1 to 6	.	.	.
Lid edema	.	.	.	<1	<1	<1
Lid erythema	<1	<1
Lid itching	<3
Lid margin crusting	.	.	.	<10
Lid margin hyperemia	<1
Lid swelling	<3
Non-specific conjunctivitis	<	<	.
Ocular discharge	<1
Ocular discomfort	1 to 3	1 to 2	1 to 6	.	.	.
Ocular dryness	<1
Ocular hyperemia	1 to 6	.	.	.
Ocular infection	1 to 2
Ocular itching	<1
Ocular pain	1 to 3	1 to 2	1 to 6	.	.	.
Ocular pruritus	1 to 6	.	.	.
Papillary conjunctivitis	5 to 10
Periocular swelling	<
Punctate keratitis	<1
Redness	<	1 to 4	<	<	.
Stinging	<	<	.
Stinging upon instillation	<1
Subconjunctival hemorrhage	1 to 6	.	.	.

Adverse Event(s)	Single Entity Products													
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Suspension	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin
Tearing	-	-	-	<1	<1	-	5 to 10	-	-	-	1 to 6	✓	-	-
Transient ocular burning	-	-	-	-	-	-	-	-	1 to 3	-	-	✓	-	-
Transient ocular discomfort	-	-	-	-	-	-	-	-	-	-	-	✓	-	-
Visual activity reduction	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
White crystalline precipitates	-	-	-	17	-	-	-	-	-	-	-	-	-	-
Respiratory														
Increased cough	-	-	-	-	-	-	-	-	-	-	1 to 4	-	-	-
Nasal congestion	<1	-	-	-	-	-	-	-	-	-	-	-	-	-
Pharyngitis	-	-	-	-	-	-	-	-	1 to 3	-	1 to 4	-	-	-
Rhinitis	-	-	-	-	-	-	-	-	-	-	1 to 4	-	-	-
Other														
Allergic reactions	✓	-	-	<1	<1	-	-	✓	<1	-	-	-	✓	-
Bad taste following instillation	-	-	-	<10	-	-	-	-	-	-	-	-	-	-
Dysgeusia	<1	-	-	-	-	-	-	-	-	-	-	-	-	-
Fever	-	-	-	-	-	-	-	-	1 to 3	1 to 2	1 to 4	-	-	-
Hypersensitivity reactions	-	-	-	-	-	✓	-	-	-	-	-	-	-	-
Infection	-	-	-	-	-	-	-	-	-	1 to 2	1 to 4	-	-	-
Otitis media	-	-	-	-	-	-	-	-	-	-	1 to 4	-	-	-
Photophobia	-	-	-	<1	<1	-	-	-	1 to 3	-	-	✓	-	-
Pyrexia	-	-	-	-	-	-	-	-	-	-	1 to 2	-	-	-
Secondary infections	-	-	-	-	-	-	-	-	-	-	-	-	✓	-
Taste perversion	-	-	-	-	<1	-	1 to 4	-	-	8 to 10	-	-	-	-
Thrombocytopenic purpura	-	-	-	-	-	-	-	✓	-	-	-	-	-	-
Throat irritation	-	-	-	-	-	-	-	-	-	1 to 2	-	-	-	-

✓ Percent not specified.

- Event not reported or incidence <1%.

Table 6. Adverse Drug Events (%)^{1,4-37}

Adverse Event(s)	Combination Products														
	Bacitracin Zinc/Polymyxin B Sulfate	Gentamicin Sulfate/Prednisolone Acetate	Polymyxin B Sulfate/Trimethoprim	Sulfacetamide Sodium/Prednisolone Acetate	Sulfacetamide Sodium/Prednisolone Sodium Phosphate	Tobramycin/Dexamethasone 0.3%/0.1%	Tobramycin/Dexamethasone 0.3%/0.05%	Tobramycin/Loteprednol Etabonate	Neomycin Sulfate/Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/Polymyxin B Sulfate/Dexamethasone Ointment	Neomycin Sulfate/Polymyxin B Sulfate/Dexamethasone Solution	Neomycin Sulfate/Polymyxin B Sulfate/Gramicidin	Neomycin Sulfate/Polymyxin B Sulfate/Hydrocortisone	Neomycin Sulfate/Polymyxin B Sulfate/Prednisolone Acetate Sulfate	Neomycin Sulfate/Polymyxin B Sulfate/Bacitracin Zinc/Hydrocortisone
Cardiovascular															
Increase in blood pressure	-	-	-	-	-	-	0.5 to 1.0	-	-	-	-	-	-	-	-
Central Nervous System															
Headache	-	-	-	-	-	-	0.5 to 1.0	14	-	-	-	-	-	-	-
Itching	<	-	<	-	-	<4	-	<4	<	-	-	<	<	-	<
Dermatologic															
Circumocular rash	-	-	<	-	-	-	-	-	-	-	-	-	-	-	-
Ocular															
Burning	-	<	<	-	-	-	-	9	-	-	-	-	-	-	-
Conjunctival erythema	<	-	-	-	-	<4	-	-	<	-	-	<	<	<	<
Conjunctival hyperemia	-	-	-	-	-	-	<4	-	-	-	<	-	-	<	-
Conjunctivitis	-	-	-	-	-	-	-	-	-	-	<	-	-	<	-
Corneal deposits	-	-	-	-	-	-	-	<4	-	-	-	-	-	-	-
Corneal ulcer	-	-	-	-	-	-	-	-	-	-	<	-	-	<	-
Discharge	-	-	-	-	-	-	-	<4	-	-	-	-	-	-	-
Discomfort	-	-	-	-	-	-	-	<4	-	-	-	-	-	-	-
Elevation in intraocular pressure	-	<	-	<	<	<	<	10	-	<	<	-	-	<	-
Eye irritation	-	<	-	-	<	-	<4	-	-	-	-	-	-	-	-
Eye pruritus	-	-	-	-	-	-	<4	-	-	-	-	-	-	-	-
Eyelid disorder	-	-	-	-	-	-	-	<4	-	-	-	-	-	-	-
Eyelid edema	-	-	-	-	-	-	<4	-	-	-	-	-	-	-	-
Irritation upon instillation	<	-	-	-	-	-	-	-	<	-	-	<	-	-	-

Adverse Event(s)	Combination Products														
	Bacitracin Zinc/Polymyxin B Sulfate	Gentamicin Sulfate/Prednisolone Acetate	Polymyxin B Sulfate/Trimethoprim	Sulfacetamide Sodium/Prednisolone Acetate	Sulfacetamide Sodium/Prednisolone Sodium Phosphate	Tobramycin/Dexamethasone 0.3%/0.1%	Tobramycin/Dexamethasone 0.3%/0.05%	Tobramycin/Loteprednol Etabonate	Neomycin Sulfate/Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/Polymyxin B Sulfate/Dexamethasone Ointment	Neomycin Sulfate/Polymyxin B Sulfate/Dexamethasone Solution	Neomycin Sulfate/Polymyxin B Sulfate/Gramicidin	Neomycin Sulfate/Polymyxin B Sulfate/Hydrocortisone	Neomycin Sulfate/Polymyxin B Sulfate/Prednisolone Acetate Sulfate	Neomycin Sulfate/Polymyxin B Sulfate/Bacitracin Zinc/Hydrocortisone
Keratitis	∠
Photophobia	<4
Posterior subcapsular cataract formation	.	∠	.	.	∠	∠	.	∠	.	∠	∠
Stinging	.	∠	∠	9
Superficial punctuate keratitis	.	∠	∠	>10
Tearing	.	.	∠
Vision disorders	.	.	∠	<4	.	.	∠
Other															
Allergic reactions	∠	.	.	.
Allergic sensitizations	.	∠	.	∠	∠	.	.	.	∠	∠	∠	.	∠	∠	∠
Anaphylaxis	∠	∠	.	∠	∠	∠	∠	∠
Delayed wound healing	.	∠	.	.	∠	∠	∠	∠	∠	∠	∠
Hypersensitivity reactions	.	.	∠	.	.	<4	.	<4	∠	.	∠	∠	∠	∠	∠
Secondary infections	.	∠	.	∠	∠	.	∠	.	∠	.	∠	∠	∠	∠	∠
Swelling	∠	<4	.	.	∠	.	∠	∠	∠	∠	∠

∠ Percent not specified.
 - Event not reported or incidence <1%.

Contraindications/Precautions^{1,4-37}

Patients with known hypersensitivity to any component of an antibiotic medication should avoid use of the ophthalmic formulation of that medication and the agent should be discontinued at the first sign of skin rash or hypersensitivity. Prolonged use of ophthalmic antibiotics may result in overgrowth of non-susceptible organisms. If super-infection occurs, use of the ophthalmic antibiotic should be discontinued and an alternative therapy should be started. Patients with suspected or confirmed bacterial conjunctivitis should avoid the use of contact lenses.^{1,4-37}

Prolonged use of ophthalmic corticosteroids may result in ocular hypertension and/or glaucoma with damage to the optic nerve, defects in visual acuity and fields, and in posterior subcapsular cataract formation. Ophthalmic corticosteroids should be used with caution in patients with glaucoma and intraocular pressure should be monitored routinely when used for 10 or more days. The use of topical corticosteroids may delay healing and increase the incidence of bleb formation after cataract surgery. Ophthalmic corticosteroids may also suppress the host response and increase the hazard of secondary ocular infections when used for extended periods of time. Acute purulent eye infections may be masked or enhanced by the use of ophthalmic corticosteroid medications. The use of ophthalmic corticosteroids in the presence of thin corneal or sclera tissue may lead to perforations and perforations have been known to occur with these agents.^{20,21,23-29} Ophthalmic ointments may retard corneal healing.

Ophthalmic corticosteroids should be used with caution in the treatment of herpes simplex keratitis since they can exacerbate the severity of viral infections of the eye. They are not effective for the treatment of mustard gas keratitis or Sjogren's keratoconjunctivitis. Fungal infections of the cornea may develop with prolonged use of ophthalmic corticosteroids. If there is any persistent corneal ulceration with ophthalmic corticosteroid use, then fungal invasion should be considered. Concomitant use of ophthalmic corticosteroids and ophthalmic aminoglycosides may result in sensitivity to the topically applied aminoglycosides. If a sensitivity reaction does occur, the ophthalmic corticosteroid medication should be discontinued.^{20,21,23-29}

A significant percentage of staphylococcal isolates have been found to be completely resistant to sulfonamides.^{23,24}

Drug Interactions^{1,4-37}

Since ophthalmic medications have minimal systemic absorption, studies have not been conducted to assess drug interactions associated with these medications.

Dosage and Administration**Table 7. Dosing and Administration**⁴⁻³⁷

Generic Name	Adult Dose	Pediatric Dose	Availability
Single Entity Products			
Azithromycin	<u>Bacterial conjunctivitis:</u> Instill one drop twice-daily for two days then one drop daily for five days	Safety and efficacy in pediatric patients <1 year of age have not been established.	Ophthalmic solution: 1% (2.5 mL)
Bacitracin	<u>Acute infection:</u> Apply a ¼ in to ½ in ribbon every three to four hours into conjunctival sac(s) <u>Mild-to-moderate infection:</u> Apply a ¼ in to ½ in ribbon two to three times daily for seven to 10 days	No specific pediatric information available.	Ophthalmic ointment: 500 units/g (3.5, 3.75 g)

Generic Name	Adult Dose	Pediatric Dose	Availability
Besifloxacin	<u>Bacterial conjunctivitis:</u> Instill one drop three times daily four to 12 hours apart for seven days	Safety and efficacy in pediatric patients <1 year of age have not been established.	Ophthalmic suspension: 0.6% (5 mL)
Ciprofloxacin	<u>Bacterial conjunctivitis:</u> Ophthalmic ointment: apply ½ inch ribbon into conjunctival sac(s) three times daily for one day then a ½ inch ribbon two times daily for five days Ophthalmic solution: instill one to two drops into conjunctival sac(s) every two hours while awake for two days, then one drop every four hours for five days <u>Corneal ulcer:</u> Ophthalmic solution: on day one instill two drops every 15 minutes for the first six hours then two drops every 30 minutes for the remainder of the day, then on day two instill two drops every hour, and then two drops every four hours for days three through 12	Ophthalmic ointment: safety and efficacy in pediatric patients <2 years of age have not been established. Ophthalmic solution: safety and efficacy in pediatric patients <1 year of age have not been established.	Ophthalmic ointment: 0.3% (3.5 g) Ophthalmic solution: 0.3% (2.5, 5, 10 mL)
Erythromycin	<u>Bacterial conjunctivitis and corneal ulcer:</u> Apply 1 cm ribbon directly to eye(s) up to six times daily	<u>Prophylaxis of neonatal ophthalmia:</u> Apply 1 cm ribbon into lower conjunctival sac(s)	Ophthalmic ointment: 0.5% (3.5 g)
Gatifloxacin	<u>Bacterial conjunctivitis:</u> On day one instill one drop every two hours while awake up to eight times daily, then on days two through seven instill one drop up to four times daily while awake (Zymaxid®)	Safety and efficacy in pediatric patients <1 year of age have not been established.	Ophthalmic solution: 0.5% (2.5 mL)
Gentamicin sulfate	Ophthalmic ointment: apply ½ in ribbon to affected eye(s) two to three times daily Ophthalmic solution: Instill one to two drops every four hours, may be increased to two drops once every hour in severe infection	Safety and efficacy in pediatric patients have not been established.	Ophthalmic ointment: 0.3% (3.5 g) Solution: 0.3% (5, 15 mL)
Levofloxacin	<u>Bacterial conjunctivitis:</u> Quixin®: on days one and two instill one to two drops every two	Quixin®: safety and efficacy in pediatric patients <1 year of	Ophthalmic solution: 0.5% (5 mL) (Quixin®)

Generic Name	Adult Dose	Pediatric Dose	Availability
	<p>hours while awake up to eight times per day, then on days three through seven instill one to two drops every four hours while awake up to four times daily</p> <p><u>Corneal ulcer:</u> Iquix[®]: on days one through three instill one to two drops every 30 minutes to two hours while awake and approximately four to six hours after retiring, then on days four through completion instill one to two drops every one to four hours while awake</p>	<p>age have not been established.</p> <p>Iquix[®]: safety and efficacy in pediatric patients <6 years of age have not been established.</p>	<p>1.5% (5 mL) (Iquix[®])</p>
<p>Moxifloxacin hydrochloride</p>	<p><u>Bacterial conjunctivitis:</u> Moxeza: instill one drop three times daily for seven days</p> <p>Vigamox[®]: instill one drop three times daily for seven days</p>	<p>Moxeza[®]: Safety and efficacy in pediatric patients <3 months of age have not been established.</p> <p>Vigamox[®]: Safety and efficacy in pediatric patients <1 year of age have not been established.</p>	<p>Ophthalmic solution: 0.5% (3 mL)</p>
<p>Ofloxacin</p>	<p><u>Bacterial conjunctivitis:</u> On days one and two instill one to two drops every two to four hours and on days three through seven instill one to two drops four times daily</p> <p><u>Corneal ulcer:</u> On days one and two instill one to two drops every 30 minutes while awake and awaken four to six hours after retiring to instill one to two drops, then on days three through seven to nine instill one to two drops hourly while awake, then on days seven to nine through treatment completion instill one to two drops four times daily</p>	<p>Safety and efficacy in pediatric patients <1 year of age have not been established.</p>	<p>Ophthalmic solution: 0.3% (1, 5, 10 mL)</p>
<p>Sulfacetamide sodium</p>	<p>Ophthalmic ointment: apply ½ in ribbon into the conjunctival sac(s) every three to four hours and at bedtime</p>	<p>Safety and efficacy in pediatric patients <2 months of age have not been established.</p>	<p>Ophthalmic ointment: 10% (3.5 g)</p> <p>Ophthalmic solution: 1% (5, 10 mL)</p>

Generic Name	Adult Dose	Pediatric Dose	Availability
	<p><u>Conjunctivitis and other superficial ocular infections:</u> Ophthalmic solution: instill one or two drops into conjunctival sac(s) every two to three hours initially for seven to 10 days</p> <p><u>Trachoma:</u> Ophthalmic solution: instill two drops into the conjunctival sac(s) every two hours, must be accompanied by systemic administration</p>		10% (2, 2.5, 5, 15 mL) 30% (15 mL)
Tobramycin	<p><u>Conjunctivitis and other superficial ocular infections:</u> Ophthalmic ointment: apply two to three times daily, for severe infections can apply every three to four hours</p> <p><u>Mild-to-moderate infections:</u> Ophthalmic solution: instill one or two drops every four hours</p> <p><u>Severe infections:</u> Ophthalmic solution: instill two drops hourly until improvement, following which treatment should be reduced prior to discontinuation</p>	No specific pediatric information available.	Ophthalmic ointment: 0.3% (3.5 g) Ophthalmic solution: 0.3% (5 mL)
Combination Products			
Bacitracin zinc/ polymyxin B sulfate	Apply every three to four hours for seven to 10 days	Safety and efficacy in pediatric patients have not been established.	Ophthalmic ointment: 500 units/g /10,000 units/g (3.5 g)
Gentamicin sulfate/ prednisolone acetate	<p>Ophthalmic ointment: apply a ½ in ribbon into the conjunctival sac(s) one to three times daily</p> <p>Ophthalmic suspension: instill one drop into the conjunctival sac(s) two to four times daily; during the initial 24 to 48 hours the dosing frequency may be increased up to one drop per hour</p>	Safety and efficacy in pediatric patients have not been established.	Ophthalmic ointment: 0.3%/0.6% (3.5 g) Ophthalmic suspension: 0.3%/1.0% (5, 10 mL)
Polymyxin B sulfate/ trimethoprim	<u>Bacterial conjunctivitis and bacterial blepharoconjunctivitis:</u> Instill one drop every three hours with a maximum of six doses per day, for seven to 10 days	Safety and efficacy in pediatric patients <2 months of age have not been established.	Ophthalmic solution: 10,000 units/mL/ 0.1% (10 mL)
Sulfacetamide sodium/ prednisolone	<u>Bacterial conjunctivitis and corneal ulcer:</u> Ophthalmic ointment: apply a ½ in	Safety and efficacy in pediatric patients <6 years of age	Ophthalmic ointment: 10%/0.2% (3.5 g)

Generic Name	Adult Dose	Pediatric Dose	Availability
acetate	<p>ribbon in the conjunctival sac(s) three to four times daily and one to two times at night</p> <p>Ophthalmic suspension: shake before using, instill 2 drops into the conjunctival sac(s) every 4 hours during the day and at bedtime</p>	have not been established.	Ophthalmic suspension: 10%/0.2% (5, 10 mL)
Sulfacetamide sodium/ prednisolone sodium phosphate	<p><u>Bacterial conjunctivitis and corneal ulcer:</u> Instill two drops in the eye(s) every four hours</p>	Safety and efficacy in pediatric patients <6 years of age have not been established.	Ophthalmic solution: 10%/0.23% (5, 10 mL)
Tobramycin/ dexamethasone	<p><u>Bacterial conjunctivitis and corneal ulcer:</u> Ophthalmic ointment: apply a small amount, approximately a ½ in ribbon, into the conjunctival sac(s) up to three or four times daily</p> <p>Ophthalmic suspension, 0.3%/0.1%: instill one to two drops into conjunctival sac(s) every four to six hours, dosage may be increased to one to two drops every two hours during the initial 24 to 28 hours</p> <p>Ophthalmic suspension, 0.3%/0.05%: instill one drop into conjunctival sac(s) every four to six hours, during the initial 24 to 48 hours the dosage may be increased to one drop every two hours</p>	Safety and efficacy in pediatric patients <2 years of age have not been established.	<p>Ophthalmic ointment: 0.3%/0.1% (3.5 g)</p> <p>Ophthalmic suspension: 0.3%/0.1% (2.5, 10 mL)</p> <p>0.3%/0.05% (2.5, 5, 10 mL)</p>
Tobramycin/ loteprednol etabonate	<p><u>Bacterial conjunctivitis and corneal ulcer:</u> Instill one to two drops into the conjunctival sac(s) every four to six hours, during the initial 24 to 48 hours the dosing may be increased to every one to two hours, frequency should be decreased gradually as warranted by improvement in clinical signs</p>	Safety and efficacy in pediatric patients have not been established.	Ophthalmic suspension: 0.3%/0.5% (2.5, 5, 10 mL)
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc	Apply every three to four hours for seven to 10 days	Safety and efficacy in pediatric patients have not been established.	Ophthalmic ointment: 0.35%/10,000 units/g /400 units/g (3.5 g)

Neomycin sulfate/ polymyxin B sulfate/ dexamethasone	<u>Bacterial conjunctivitis and corneal ulcer:</u> Ophthalmic ointment: apply a small amount, approximately a ½ in ribbon, into the conjunctival sac(s) up to three times daily Ophthalmic suspension: instill one to two drops in the conjunctival sac(s), may be used hourly in severe disease, and up to six times daily in mild disease	Ophthalmic ointment: safety and efficacy in pediatric patients have not been established. Ophthalmic suspension: safety and efficacy in pediatric patients <2 years of age have not been established.	Ophthalmic ointment: 0.35%/10,000 units/g /0.1% (3.5 g) Ophthalmic suspension: 3.5mg/mL/10,000 units/mL/0.1% (5 mL)
Neomycin sulfate/ polymyxin B sulfate/ gramicidin	Instill one to two drops every four hours for seven to 10 days, may be increased to as much as two drops ever hour in severe infections	Safety and efficacy in pediatric patients have not been established.	Ophthalmic solution: 1.75 mg/mL/10,000 units/mL/0.025 mg/mL (10 mL)
Neomycin sulfate/ polymyxin B sulfate/ hydrocortisone	<u>Bacterial conjunctivitis and corneal ulcer:</u> Instill one to two drops in affected eye(s) every three to four hours, depending on the severity of the condition	Safety and efficacy in pediatric patients have not been established.	Ophthalmic suspension: 0.35%/10,000 units/mL /1% (7.5 mL)
Neomycin sulfate/ polymyxin B sulfate/ prednisolone acetate sulfate	<u>Bacterial conjunctivitis and corneal ulcer (eye treatment):</u> Instill one to two drops every three to four hours or more frequently as required, may require administration every 30 minutes for acute infections <u>Bacterial conjunctivitis and corneal ulcer (eyelid treatment):</u> Instill one to two drops into the eye every three to four hours, close the eye and rub the excess on the lids and lid margins	Safety and efficacy in pediatric patients have not been established.	Ophthalmic suspension: 0.35%/10,000 units/mL/ 0.5% (5 mL)
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc/ hydrocortisone	<u>Bacterial conjunctivitis and corneal ulcer:</u> Apply ointment in affected eye(s) every three to four hours, depending on the severity of the condition	Safety and efficacy in pediatric patients have not been established.	Ophthalmic ointment: 0.35%/10,000 units/g/ 400 units/g/1% (3.5 g)

Clinical Guidelines

Table 8. Clinical Guidelines

Clinical Guideline	Recommendation(s)
American Academy of Ophthalmology: Preferred	<ul style="list-style-type: none"> There is insufficient evidence to make definitive recommendations for the treatment of blepharitis, and cure is not possible in most cases. Treatments that are helpful include the following:

Clinical Guideline	Recommendation(s)
<p>Practice Pattern: Blepharitis (2011)³</p>	<ul style="list-style-type: none"> ○ Warm compresses. ○ Eyelid hygiene. ○ Antibiotics (topical and/or systemic). ○ Ophthalmic anti-inflammatory agents (e.g., corticosteroids, cyclosporine). <ul style="list-style-type: none"> • These treatment options are often used in combination. • Eyelid hygiene is especially useful for anterior blepharitis, and warm compresses are especially helpful for posterior blepharitis. • Optimal treatment regimens often require a trial and error approach. • An ophthalmic antibiotic ointment such as ophthalmic bacitracin or ophthalmic erythromycin can be prescribed and applied on the eyelid margins one or more times daily or at bedtime for one or more weeks. The frequency and duration of treatment should be guided by the severity of the blepharitis and response to treatment. In severe cases or for patients who do not tolerate ointment, metronidazole gel applied to the eyelid skin is an alternative treatment, although it has not been approved by the Food and Drug Administration (FDA) for this indication. • The combination of tobramycin/dexamethasone ophthalmic suspension and azithromycin in a sustained-release system has been evaluated and appears to reduce some of the symptoms of blepharitis, but its use for this indication has not been approved by the FDA. • For patients with meibomian gland dysfunction, whose chronic signs and symptoms are not adequately controlled with eyelid hygiene, an oral tetracycline can be prescribed. Macrolide antibiotics also have anti-inflammatory activity. • Treatments can be intermittently discontinued and reinstated, based on the severity of the patient's blepharitis and tolerance for the medication, and to allow re-colonization of normal flora. • Ophthalmic corticosteroid eye drops or ointments are typically applied several times daily to the eyelids or ocular surface. • Once the inflammation is controlled, the ophthalmic corticosteroid can be tapered and discontinued and then used intermittently to maintain patient comfort. • The minimal effective dose of ophthalmic corticosteroid should be utilized, and long-term ophthalmic corticosteroid therapy should be avoided if possible. • Potential adverse effects of ophthalmic corticosteroid use, including the risk for developing increased intraocular pressure and cataracts may be minimized by using a site-specific ophthalmic corticosteroid such as ophthalmic loteprednol etabonate and ophthalmic corticosteroids with limited ocular penetration, such as ophthalmic fluorometholone. • Topical cyclosporine may be helpful in some patients with posterior blepharitis. • Artificial tears may improve symptoms when used as an adjunct to eyelid hygiene and medications. If used more than four times per day, non-preserved tears should be used to avoid preservative toxicity.
<p>American Academy of Ophthalmology: Preferred Practice Pattern: Conjunctivitis (2011)³⁹</p>	<p><u>Mild bacterial conjunctivitis</u></p> <ul style="list-style-type: none"> • May be self-limited and resolve spontaneously without treatment in immunocompetent adults. • Ophthalmic antibacterial therapy is associated with earlier clinical and microbiological remission compared with placebo at days two to five of treatment. The advantages persist over six to 10 days, but the benefit

Clinical Guideline	Recommendation(s)
	<p>over placebo lessens over time.</p> <ul style="list-style-type: none"> • The choice of ophthalmic antibiotic is usually empirical. • A five to seven day course of ophthalmic broad-spectrum antibiotic is usually effective. • The most convenient or least expensive option can be selected. <p><u>Severe bacterial conjunctivitis</u></p> <ul style="list-style-type: none"> • Characterized by copious purulent discharge, pain, and marked inflammation of the eye. • The choice of ophthalmic antibiotic is guided by the results of laboratory tests. • MRSA has been isolated with increasing frequency from patients with bacterial conjunctivitis. Many MRSA organisms are resistant to commercially available ophthalmic antibiotics. • Systemic antibiotic therapy is necessary to treat conjunctivitis due to <i>Neisseria gonorrhoeae</i> and <i>Chlamydia trachomatis</i>. • If corneal involvement is present, the patient should also be treated topically for bacterial keratitis.
<p>American Academy of Ophthalmology: Preferred Practice Pattern: Bacterial Keratitis (2011)⁴⁰</p>	<p><u>Initial treatment</u></p> <ul style="list-style-type: none"> • Ophthalmic antibiotic eye drops are the preferred method of treatment in most cases of bacterial keratitis. • Ophthalmic ointments may be useful at bedtime in less severe cases and also may be useful for adjunctive therapy. • Ophthalmic broad-spectrum antibiotics are used initially in the empiric treatment of bacterial keratitis. • The recommended ophthalmic empiric treatments include: <ul style="list-style-type: none"> ○ No organism identified or multiple types of organisms: ophthalmic cefazolin sodium (with gentamicin sulfate or tobramycin) or ophthalmic fluoroquinolones (fewer gram-positive cocci are resistant to gatifloxacin and moxifloxacin hydrochloride than other fluoroquinolones). ○ Gram-positive cocci: ophthalmic cefazolin sodium, vancomycin (for resistant <i>Enterococcus</i> and <i>Staphylococcus</i> species and penicillin allergy), ophthalmic bacitracin (for resistant <i>Enterococcus</i> and <i>Staphylococcus</i> species and penicillin allergy), or ophthalmic fluoroquinolones (fewer gram-positive cocci are resistant to gatifloxacin and moxifloxacin hydrochloride than other fluoroquinolones). ○ Gram-negative rods: ophthalmic formulations of tobramycin or gentamicin sulfate, ceftazidime, or fluoroquinolones. ○ Gram-negative cocci: ophthalmic ceftazidime, ceftriaxone sodium, or fluoroquinolones (systemic therapy is necessary for suspected gonococcal infection). ○ Nontuberculous mycobacteria: ophthalmic amikacin sulfate, azithromycin, clarithromycin, or fluoroquinolones. ○ Nocardia: ophthalmic amikacin sulfate, sulfacetamide sodium, or trimethoprim/sulfamethoxazole. • Single-drug therapy using an ophthalmic fluoroquinolone has been shown to be as effective as combination therapy with ophthalmic antibiotics that are fortified by increasing their concentration over commercially available topical antibiotics. Ciprofloxacin 0.3%, ofloxacin 0.3% and levofloxacin 1.5% are Food and Drug Administration

Clinical Guideline	Recommendation(s)
	<p>approved for this indication. The fourth generation fluoroquinolones have not been approved for the treatment of bacteria keratitis, however, both agents have performed at least as well as standard therapy, fortified cefazolin/tobramycin combination therapy and potentially better than ciprofloxacin.</p> <ul style="list-style-type: none"> • Some pathogens (e.g., <i>Streptococci</i>, anaerobes) reportedly have variable susceptibility to ophthalmic fluoroquinolones and the prevalence of resistance to fluoroquinolones appears to be increasing. • Combination fortified-antibiotic therapy is an alternative to consider for severe infection and for eyes unresponsive to initial treatment. • Treatment with more than one agent may be necessary for nontuberculous mycobacteria; infection with this pathogen has been reported in association with Laser in Situ Keratomileusis (LASIK). • Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) has been isolated with increasing frequency from patients with bacterial keratitis and has been reported following kerato-refractive surgery. Ophthalmic fluoroquinolones are generally poorly effective against MRSA ocular isolates. MRSA isolates are generally sensitive to ophthalmic vancomycin. • Systemic antibiotics are rarely needed, but they may be considered in severe cases where the infectious process has extended to adjacent tissues (e.g., the sclera) or when there is impending or frank perforation of the cornea. • Systemic therapy is necessary in cases of gonococcal keratitis. <p><u>Modification of therapy</u></p> <ul style="list-style-type: none"> • Efficacy of the regimen is judged primarily by clinical response. The results of cultures and sensitivity testing may have an impact on therapeutic decision making, especially if the patient is not responding to initial therapy. • Dual antibiotic treatment designed to achieve broad-spectrum coverage may become unnecessary once the causative organism has been isolated. • The initial therapeutic regimen should be modified (change in type, concentration or frequency of antibiotic) when the eye shows a lack of improvement or stabilization within 48 hours. • Most antibiotic eye drops should not be tapered below three to four times a day, because low doses are sub-therapeutic and may increase the risk of developing antibiotic resistance. <p><u>Corticosteroid therapy</u></p> <ul style="list-style-type: none"> • Ophthalmic corticosteroid therapy may have a beneficial role in treating some cases of infectious keratitis due to the probable suppression of inflammation, which may reduce subsequent corneal scarring and associated visual loss. • Potential disadvantages of ophthalmic corticosteroid use include infection reoccurrence, local immunosuppression, inhibition of collagen synthesis predisposing to corneal melting, and increased intraocular pressure. • There is no conclusive evidence that ophthalmic corticosteroids alter clinical outcome. • Despite risks involved, it is believed that sensible use of ophthalmic

Clinical Guideline	Recommendation(s)
	<p>corticosteroids can reduce morbidity.</p> <ul style="list-style-type: none"> • Patients being treated with ophthalmic corticosteroids at the time of presentation of suspected bacterial keratitis should have their ophthalmic corticosteroid regimen reduced or eliminated until the infection has been controlled. • Inflammation may temporarily increase as ophthalmic corticosteroids are reduced. • The minimum amount of ophthalmic corticosteroid required should be used to achieve control of inflammation. • Ophthalmic corticosteroids should not be part of initial treatment of presumed bacterial ulcers, and ideally they should not be used until the organism has been determined by cultures. • The use of ophthalmic corticosteroids in the initial treatment of corneal ulcers has been determined to be a risk factor for requiring a penetrating keratoplasty. • Ophthalmic antibiotics, which are generally administered more frequently than ophthalmic corticosteroids during treatment of active infection, are continued at high levels and tapered gradually. • Patient compliance is essential, intraocular pressure must be monitored frequently, and the patient should be examined within one to two days after initiation of ophthalmic corticosteroid therapy.
<p>American Academy of Ophthalmology: Preferred Practice Pattern: Refractive Errors and Refractive Surgery (2011)⁸⁶</p>	<p><u>Photorefractive keratectomy</u></p> <ul style="list-style-type: none"> • Topical antibiotics are administered to minimize the risk of postoperative infection. • Topical corticosteroids are generally started immediately after surgery and tapered over a period of days to weeks, and sometimes months. If corticosteroid treatment is prolonged, the intraocular pressure should be monitored. • Although postoperative pain may be reduced by the use of a bandage, contact lens, and nonsteroidal anti-inflammatory drugs (NSAIDs) drops, patients may still require prescription oral analgesics. • Since NSAID drops may delay corneal epithelialization, they should be applied judiciously. • Sterile corneal infiltrates associated with the use of NSAID drops without the concomitant use of topical corticosteroids have been described. • Periodic examinations are necessary to monitor ocular status and to check for corticosteroid-related side effects such as elevated intraocular pressure. <p><u>LASIK</u></p> <ul style="list-style-type: none"> • Topical antibiotics are administered to minimize the risk of postoperative infection. • Corticosteroids are generally used for a short time postoperatively. • Frequent lubrication is recommended in the postoperative period. • Diffuse lamellar keratitis is a noninfectious aggregation of inflammatory cells and treatment is commonly guided by the severity of the inflammation. Increasing frequency of topical corticosteroid administration with a closer follow-up is practiced by most surgeons.
<p>American Academy of Ophthalmology: Preferred Practice</p>	<p><u>Infection prophylaxis</u></p> <ul style="list-style-type: none"> • Two emerging concerns are the increasing resistance of <i>Staphylococcus</i> species (the most common cause of endophthalmitis)

Clinical Guideline	Recommendation(s)
<p>Pattern: Cataract in the Adult Eye (2011)⁸⁷</p>	<p>to a broad spectrum of antibiotics, including the latest generation fluoroquinolones, and the increased occurrence of acute endophthalmitis more than a week after surgery.</p> <ul style="list-style-type: none"> • Prophylactic strategies that have been used include applying topical antibiotic eye drops before surgery, applying 5% povidone iodine to the conjunctival cul de sac, preparing the periocular skin with 10% povidone iodine, careful sterile draping of the eyelid margins and eyelashes, adding antibiotics to the irrigating solution, instilling intracameral antibiotics at the close of surgery, injecting subconjunctival antibiotics, and applying topical antibiotic eye drops after surgery. • Because of the lack of and impracticality of sufficiently large prospective clinical trials, there is insufficient evidence to recommend a specific antibiotic drug or method of delivery for endophthalmitis prophylaxis. • Systemic antibiotics are rarely used; however, it has been shown that certain oral fluoroquinolone antibiotics penetrate the blood/ocular barrier adequately to reach levels above the minimum inhibitory concentrations for many organisms inside the eye, and oral antibiotics that penetrate well into the eye may be beneficial. <p><u>Postoperative follow-up</u></p> <ul style="list-style-type: none"> • Postoperative regimens of topically applied antibiotics, corticosteroids and NSAIDs vary among practitioners. • No controlled investigations establish optimal regimens for the use of topical agents. • The operating surgeon is responsible for making the decision whether to use any or all of the topical products singly or in combination. • Complications of postoperative medications include elevated IOP with corticosteroids and allergic reactions to antibiotics. Significant corneal reactions, including epithelial defects and stromal ulceration and melting, have rarely been reported with topical ocular nonsteroidal anti-inflammatory drugs (NSAIDs). <p><u>Cystoid macular edema</u></p> <ul style="list-style-type: none"> • Topical anti-inflammatory agents are used in an attempt to reduce the inflammatory response to cataract surgery and to treat established cystoid macular edema. • There is evidence that topically applied NSAIDs alone or in combination with corticosteroids is more effective than topical corticosteroids alone in preventing and treating cystoid macular edema.
<p>American Optometric Association: Care of the Adult Patient with Cataract (2004)⁸⁸</p>	<ul style="list-style-type: none"> • A combination of topical and oral antiglaucoma, antibiotic and anti-inflammatory medications may be administered to the patient before, during and after an operation. • Topical corticosteroids may be used to suppress inflammation associated with cataract surgery. • To control inflammation associated with anterior uveitis, topical corticosteroids such as prednisolone acetate 1% may be used every 2-4 hours depending on the degree of inflammation.

Conclusions

Ophthalmic antibiotics are used to treat ophthalmic infections including blepharitis, conjunctivitis, keratitis as well as several others. There are ophthalmic antibiotics available from the aminoglycoside, macrolide, polypeptide, quinolone, sulfonamide and miscellaneous antibiotic drug classes. These agents are

available as single agents or in combination with other ophthalmic antibiotics or ophthalmic steroids. All ophthalmic antibiotics, with the exception of ophthalmic levofloxacin 1.5%, are approved for the treatment of bacterial conjunctivitis.⁴⁻³⁷ It should be noted that for all of the indications listed in Table 2, there is at least one generic option available for treatment.¹

Head-to-head studies have failed to consistently show that any one ophthalmic antibiotic is significantly more effective than another with regard to bacterial eradication, clinical resolution, clinical response, efficacy, microbial eradication, physician's judgment of resolution, severity rating, or symptom improvement for any indication.^{45-52,55,56,65-67,70,72,76,78} In all studies, adverse events were mild with no significant difference seen with regard to the rate of adverse events. Common adverse events reported include burning, ocular discomfort, stinging, and tearing.⁴¹⁻⁸⁵

The majority of ophthalmic antibiotic medications have been studied in pediatric populations greater than one year of age, with ophthalmic sulfacetamide sodium and ophthalmic polymyxin B sulfate/trimethoprim having safety and efficacy data in patients older than two months of age.^{1,22-24} Ophthalmic antibiotics are not intended to be used for prolonged periods of time in order to avoid overgrowth of non-susceptible organisms and reduce the risk of resistance. Should super-infection occur, the ophthalmic antibiotic should be discontinued and an alternative therapy should be initiated.^{1,4-37}

Guidelines published by the American Academy of Ophthalmology recommend that blepharitis be treated with ophthalmic bacitracin or ophthalmic erythromycin and note that macrolide antibiotics may have anti-inflammatory activity with regard to the treatment of blepharitis.³ In addition, the guidelines state that keratitis should be treated with a broad-spectrum ophthalmic antibiotic that may be selected based on the isolated organism and if no organism is identified, treatment with ophthalmic fluoroquinolones is recommended. The American Academy of Ophthalmology guideline also notes that fewer gram-positive cocci are resistant to ophthalmic gatifloxacin and moxifloxacin hydrochloride.⁴⁰ For the treatment of conjunctivitis, it is recommended that the least expensive or most convenient broad-spectrum antibiotic be selected for a five to seven day course of treatment.³⁹

Appendix I: Utilization Within This Drug Class for DVHA: April 1, 2011 to September 30, 2011

Medication	Unique utilizers	# of Rx's	Market Share (%)	Plan Cost \$	Avg \$/Rx
Polymyxin B/ Trimethoprim	1,189	1,213	35.13%	\$17,767.39	\$14.65
Erythromycin	803	857	24.82%	\$17,330.99	\$20.22
Gentamycin sulfate	343	373	10.80%	\$2,634.02	\$7.06
Sulfacetamide sodium	303	307	8.89%	\$2,034	\$6.63
Ofloxacin	205	245	7.10%	\$3,511.46	\$14.33
Ciprofloxacin	159	173	5.01%	\$3,383.44	\$19.56
Tobramycin sulfate	121	124	3.59%	\$945.23	\$7.62
Bacitracin/ Polymyxin	34	44	1.27%	\$1,269.36	\$28.85
Bacitracin	25	41	1.19%	\$2,922.06	\$71.27
Gentak	26	28	0.81%	\$568.73	\$20.31
AK-Tob	18	18	0.52%	\$138.73	\$7.71
Vigamox	7	8	0.23%	\$674.39	\$84.30
Al-Poly-Bac	6	8	0.23%	\$152.76	\$19.10
Neomycin/ Polymyxin/ Gramicidin	5	5	0.14%	\$120.75	\$24.15
Neomycin/Bacitracin/ Polymyxin	4	4	0.12%	\$164.79	\$41.20
Azsite	3	3	0.09%	\$249.70	\$83.23

Medication	Unique utilizers	# of Rx's	Market Share (%)	Plan Cost \$	Avg \$/Rx
Ciloxan	1	1	0.03%	\$88.34	\$88.34
Zirgan	1	1	0.03%	\$171.67	\$171.67
Class Total:	---	3,453	100%	\$54,127.77	\$15.68

Recommendations

No changes to the current Department of Vermont Health Access (DVHA) approval criteria for ophthalmic antibiotics (below) are proposed.

Aminoglycosides:

- Single Agent: The patient has had a documented side effect, allergy or treatment failure with at least ONE preferred ophthalmic aminoglycoside. (If a product has an AB rated generic, there must have also been a trial of the generic formulation)
- Combination Product: The patient has had a documented intolerance with generic tobramycin/dexamethasone ophthalmic.

Macrolides:

- The patient has had a documented side effect, allergy or treatment failure with generic erythromycin. (If a product has an AB rated generic, there must have also been a trial of the generic formulation)

Miscellaneous Antibiotics:

- The patient has had a documented side effect, allergy or treatment failure with at least TWO preferred ophthalmic miscellaneous antibiotics. (If a product has an AB rated generic, there must have also been a trial of the generic formulation)

Quinolones:

- The patient has had a documented side effect, allergy or treatment failure with ciprofloxacin or ofloxacin.
- AND
- If the request is for Quixin, the patient also has a documented intolerance to generic levofloxacin 0.5 %.
- OR
- The request is for Vigamox or Zymar as part of a regimen to prevent postoperative infection in patients receiving any ophthalmologic surgery.

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