Therapeutic Class Overview
Ophthalmic Antibiotics

Therapeutic Class

- **Overview/Summary:** Ophthalmic antibiotics are used to treat ocular infections including blepharitis, conjunctivitis, keratitis and several others. There are ophthalmic antibiotics available from a variety of 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. 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. The mainstay of blepharitis treatment is patient education regarding eye lid hygiene as well as the use of ophthalmic antibiotics.[2,3] Conjunctivitis occurs worldwide and affects all ages, social strata, and both genders.[4] Mild cases may be self limited as many cases will resolve without treatment in immunocompetent individuals although ophthalmic antibiotics are associated with earlier clinical and microbiological remission compared to placebo. All ophthalmic antibiotics, with the exception of ophthalmic levofloxacin 1.5%, are approved by the Food and Drug Administration to treat bacterial conjunctivitis.[5-25] 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.[26] 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. Untreated or severe bacterial keratitis can result in corneal perforation and may develop into endophthalmitis and result in the loss of the eye. 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 severe cases, patients should be followed daily until stabilization or clinical improvement is documented.[27]

Table 1. Current Medications Available in Therapeutic Class[5-25]

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
Single-Entity Agents			
Azithromycin ophthalmic (Azasite®)	Treatment of bacterial conjunctivitis	Ophthalmic solution: 1%	-
Bacitracin ophthalmic (Bacticin®*)	Treatment of superficial ocular infections involving the conjunctiva and/or cornea	Ophthalmic ointment: 500 units/g	✔
Besifloxacin ophthalmic (Besivance®)	Treatment of bacterial conjunctivitis	Ophthalmic suspension: 0.6%	-
Ciprofloxacin ophthalmic (Ciloxan®*)	Treatment of bacterial conjunctivitis, treatment of corneal ulcers (ointment)	Ophthalmic ointment: 0.3% Ophthalmic solution: 0.3%	✔ (solution)
Erythromycin ophthalmic (Ilotycin®*, Romycin®*)	Prophylaxis of ophthalmia neonatorum due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis,* treatment of superficial ocular infections involving the conjunctiva and/or cornea	Ophthalmic ointment: 0.5%	✔
Gatifloxacin ophthalmic (Zymaxid®)	Treatment of bacterial conjunctivitis	Ophthalmic solution: 0.5%	-
Gentamicin sulfate	Treatment of acute meibomianitis,	Ophthalmic ointment:	✔

Generic (Trade Name)	Food and Drug Administration-Approved Indications	Dosage Form/Strength	Generic Availability
ophthalmic (Garamycin®*, Genoptic®*, Gentak®*, Gentasol®*)	treatment of bacterial conjunctivitis, treatment of blepharitis, treatment of blepharoconjunctivitis, treatment of corneal ulcers, treatment of dacryocystitis, treatment of keratitis, treatment of keratoconjunctivitis	0.3% Ophthalmic solution: 0.3%	
Levofloxacin ophthalmic (Iquix®, Quixin®*)	Treatment of bacterial conjunctivitis, treatment of corneal ulcers	Ophthalmic solution: 0.5% 1.5%	✔ (0.5% solution)
Moxifloxacin hydrochloride ophthalmic (Moxeza®, Vigamox®)	Treatment of bacterial conjunctivitis	Ophthalmic solution: 0.5%	-
Ofloxacin ophthalmic (Ocuflox®*)	Treatment of bacterial conjunctivitis, treatment of corneal ulcers	Ophthalmic solution: 0.3%	✔
Sulfacetamide sodium ophthalmic (AKSulf®*, Bleph-10®*, Ocusulf®*, Sturzsulf®*, Sulster®*)	Adjunctive treatment in systemic sulfonamide therapy of trachoma (solution), treatment of bacterial conjunctivitis, treatment of superficial ocular infections	Ophthalmic ointment: 10% Ophthalmic solution: 10%	✔
Tobramycin ophthalmic (AKTob®*, Tobrasol®*, Tobrex®*)	Treatment of external infections of the eye and its adnexa	Ophthalmic ointment: 0.3% Ophthalmic solution: 0.3%	✔ (solution)
Combination Products			
Bacitracin zinc/polymyxin B sulfate ophthalmic (AK-Poly-Bac®*, Polysporin®*)	Treatment of superficial ocular infections involving the conjunctiva and/or cornea	Ophthalmic ointment: 500 units/g/10,000 units/g	✔
Polymyxin B sulfate/trimethoprim ophthalmic (Polytrim®*)	Treatment of bacterial conjunctivitis, Treatment of blepharoconjunctivitis, Treatment of superficial ocular infections	Ophthalmic solution: 10,000 units/mL/0.1%	✔
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc ophthalmic (Neosporin®*)	Treatment of bacterial conjunctivitis, treatment of blepharitis, treatment of blepharoconjunctivitis, treatment of keratitis, treatment of keratoconjunctivitis	Ophthalmic ointment: 0.35%/10,000 units/g/ 400 units/g	✔
Neomycin sulfate/polymyxin B sulfate/gramicidin ophthalmic (Neosporin®*)	Treatment of bacterial conjunctivitis, treatment of blepharitis, treatment of blepharoconjunctivitis, treatment of keratitis, treatment of keratoconjunctivitis	Ophthalmic solution: 1.75 mg/mL/10,000 units/mL/0.025 mg/mL	✔

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

Evidence-based Medicine

- Results from clinical trials have demonstrated that ophthalmic antibiotics are effective in treating and providing relief of conjunctivitis in pediatric and adult patients.[28-48] Several studies comparing ophthalmic 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.

- 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 treated with ophthalmic moxifloxacin had complete resolution of ocular signs and symptoms at 48 hours compared to treatment with ophthalmic polymyxin B sulfate/trimethoprim.[36] In a small meta-analysis, moxifloxacin was found to be associated with fewer drop-outs for treatment failure compared to ofloxacin (*P*=0.002).[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 treatments (*P* value not reported).[50]
- In patients with a corneal ulcer, ophthalmic ciprofloxacin was shown to be an efficacious treatment option.[51-53] Specifically, in one trial of patients with a diagnosis of infectious keratitis ophthalmic ciprofloxacin had a shorter average time to healing compared to ophthalmic cefazolin sodium fortified with gentamicin sulfate, although this was not found to be significant *(P* value not reported).[52]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
    - There is insufficient evidence to recommend treatment for blepharitis, and due to the self-limiting nature of the condition, a cure is not possible in most cases. An ophthalmic antibiotic ointment may be prescribed and applied on the eyelid margins one or more times daily or at bedtime for one or more weeks. The combination of tobramycin/dexamethasone ophthalmic suspension and azithromycin in a sustained-release system appear to reduce some of the symptoms of blepharitis, but are not approved for this indication.[3]
    - Bacterial conjunctivitis may be self-limiting and resolve spontaneously without treatment in immunocompetent adults. Ophthalmic antibacterial therapy is associated with earlier clinical and microbiological remission compared to placebo at days two to five of treatment. The choice of ophthalmic antibiotic is usually empirical and a five to seven day course of ophthalmic broad-spectrum antibiotic is usually effective. The most convenient or least expensive option can be selected. For severe bacterial conjunctivitis, the choice of ophthalmic antibiotic is guided by the results of laboratory tests.[26]
    - Ophthalmic broad-spectrum antibiotics are used initially for empiric treatment of bacterial keratitis. Therapy with an ophthalmic fluoroquinolones has been shown to be as effective as combination therapy with fortified ophthalmic antibiotics. Ciprofloxacin 0.3%, ofloxacin 0.3% and levofloxacin 1.5% are Food and Drug Administration-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 and potentially better than ciprofloxacin.[27]
    - Some pathogens (e.g., *Streptococci*, anaerobes) reportedly have variable susceptibility to ophthalmic fluoroquinolones and the prevalence of resistance to fluoroquinolones appears to be increasing. 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.[27]
- Other Key Facts:
    - There is at least one generic product available for treating each of the conditions outlined in outlined in Table 1.[1]
    - Both ophthalmic moxifloxacin formulations (Moxeza® and Vigamox®) are 0.5% solutions. Moxeza® may be administered twice daily while Vigamox® is to be administered three times daily for seven days.[15,16]
    - Ciprofloxacin and ofloxacin are considered second-generation fluoroquinolones, with levofloxacin being a third-generation fluoroquinolone. The fourth-generation fluoroquinolones include gatifloxacin, moxifloxacin and the newest fluoroquinolone, besifloxacin.[54,55]

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Therapeutic Class Review
Ophthalmic Antibiotics

Overview/Summary

Ophthalmic antibiotics are used to treat several ocular infections including blepharitis, conjunctivitis, keratitis and others. Ophthalmic antibiotics are available from several drug classes including aminoglycosides, macrolides, polypeptides, quinolones and sulfonamides.[1-22] In addition, many are available as combination products with other antibiotics or corticosteroids. This class review focuses on single-agent and combination ophthalmic antibiotic products. A list of available ophthalmic antibiotics is included in Table 1. Moreover, there is at least one generic product available for treating each of the conditions outlined in Table 2.[1-22]

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*, *Corynebacterium* and *Propionibacterium acnes* species. The mainstay of the treatment of blepharitis is patient education regarding eyelid hygiene as well as the use of ophthalmic antibiotics. 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.[23,24]

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 pneumonia*e, *Haemophilus influenza*e and *Moraxella catarrhalis*.[25] 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.[26] 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* 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 gonorrheae* and *Chlamydia trachomatis,* systemic antibiotic therapy is necessary, and while not necessary, ophthalmic antibiotics are also typically used.[26]

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.[27]

Thought not Food and Drug Administration approved, ophthalmic antibiotics are routinely used to prevent postoperative infections after eye surgeries such as refractive surgeries and cataract removal, while ophthalmic corticosteroids may also be used to reduce inflammation associated with surgeries.[28-30]

Medications

Table 1. Medications Included Within Class Review[1-22]

Generic Name (Trade name)	Medication Class	Generic Availability
Single-Entity Agents		
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 (Garamycin®*, Genoptic®*, Gentak®*, Gentasol®*)	Aminoglycoside antibiotic	✔
Levofloxacin ophthalmic (Iquix®†, Quixin®*†)	Quinolone antibiotic	✔ (0.5% solution)
Moxifloxacin hydrochloride ophthalmic (Moxeza®, Vigamox®)	Quinolone antibiotic	-
Ofloxacin ophthalmic (Ocuflox®*)	Quinolone antibiotic	✔
Sulfacetamide sodium ophthalmic (AKSulf®*, Bleph-10®*, Ocusulf®*, Sturzsulf®*, Sulster®*)	Miscellaneous anti-infective	✔
Tobramycin ophthalmic (AKTob®*, Tobrasol®*, Tobrex®*)	Aminoglycoside antibiotic	✔ (solution)
Combination Products		
Bacitracin zinc/polymyxin B sulfate ophthalmic (AK-Poly-Bac®*, Polysporin®*)	Polypeptide antibiotic	✔
Polymyxin B sulfate/trimethoprim ophthalmic (Polytrim®*)	Polypeptide antibiotic	✔
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc ophthalmic (Neosporin®*)	Polypeptide antibiotic	✔
Neomycin sulfate/polymyxin B sulfate/gramicidin ophthalmic (Neosporin®*)	Polypeptide antibiotic	✔

*Generic available in at least one dosage form or strength.
†Iquix® and Quixin® were discontinued by the manufacturer in November 2011.

Indications

Table 2. Food and Drug Administration-Approved Indications[1-22]

Indication	Single-Entity Agents														Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Adjunctive treatment in systemic sulfonamide therapy of trachoma													✔ *					
Prophylaxis of ophthalmia neonatorum due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*						✔												
Treatment of acute meibomianitis								✔										
Treatment of bacterial conjunctivitis	✔		✔	✔	✔		✔	✔	✔		✔	✔	✔			✔	✔	✔
Treatment of blepharitis								✔									✔	✔
Treatment of blepharoconjunctivitis								✔								✔	✔	✔
Treatment of corneal ulcers				✔				✔		✔		✔						
Treatment of dacryocystitis								✔										
Treatment of external infections of the eye and its adnexa														✔				
Treatment of keratitis								✔									✔	✔
Treatment of keratoconjunctivitis								✔									✔	✔
Treatment of superficial ocular infections													✔			✔		
Treatment of superficial ocular infections involving the conjunctiva and/or cornea		✔				✔									✔			

*Solution only.

Pharmacokinetics

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, maximum mean concentrations post-administration were reported to be more than 1,000 times lower than those reported after standard oral doses of the respective oral medications.[1-22]

Clinical Trials

Clinical trials have demonstrated that ophthalmic antibiotics are effective in treating and providing relief of bacterial conjunctivitis in pediatric and adult patients.[31-57] Several studies comparing ophthalmic antibiotics such as azithromycin, besifloxacin, ciprofloxacin, levofloxacin, moxifloxacin and bacitracin/ polymyxin B to either placebo or vehicle, have concluded that these medications resulted in significantly higher clinical resolution rates at days one through five.[31-42] However, one trial with ophthalmic bacitracin/ polymyxin B showed no significant difference in clinical resolution rate on days eight through 10 when compared to placebo.[41]

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/trimethoprim (*P*=0.001).[42] In another trial, there was no difference in clinical cure rate between treatment with ophthalmic polymyxin B/trimethoprim and ophthalmic moxifloxacin (P=0.59).[43] In a small meta-analysis, moxifloxacin was found to be associated with fewer drop-outs for treatment failure compared to ofloxacin (*P*=0.002).[44] 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).[46]

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.[36,39,46-52] While no difference was found between ophthalmic formulations of azithromycin and tobramycin with regard to clinical resolution and bacterial eradication, ophthalmic azithromycin produced the same clinical outcome with 65% fewer drops.[47] 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.[36,39,41-52]

In patients with a diagnosis of corneal ulcer or bacterial keratitis, ophthalmic ciprofloxacin was shown to be an efficacious treatment option.[68-60] 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, although this difference was not found to be significant (*P* value not reported).[60]

A number of studies consisted of patients with multiple diagnoses such as blepharitis, blepharoconjunctivitis, bacterial conjunctivitis, keratoconjunctivitis or symptoms of surface ocular infections. These studies found that the ophthalmic formulations of ciprofloxacin, gentamicin, ofloxacin, tobramycin solution and polymyxin B/trimethoprim were efficacious in resolving or curing multiple ocular infections.[60-71] 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 (*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).[65] In studies of patients with multiple diagnoses, the most commonly reported adverse events were similar 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 days zero to 14 was statistically significant when compared to no prophylaxis; however, the efficacy was not significant from days 15 to 60 (14 vs 9%; *P*=0.05 and 7 vs 8%; *P*=0.92 respectively).[72] In another study, ophthalmic erythromycin prophylaxis resulted in significantly fewer 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).[73]

In patients undergoing cataract and posterior chamber lens implant surgery, treatment with ophthalmic gentamicin resulted in lower bacterial colony count compared to ophthalmic neomycin/polymyxin B/dexamethasone at days six and eight (*P*=0.033); however, 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 (*P* value not reported).[74] In a separate study involving patients undergoing cataract extraction by either manual extraction or phacoemulsification with intraocular lens implantation, ophthalmic tobramycin/dexamethasone was non-inferior to ophthalmic neomycin/polymyxin B/dexamethasone concerning inflammation scores at days three, eight, 14 and 21. Inflammation scores in the ophthalmic tobramycin/dexamethasone group were significantly lower than scores seen in the ophthalmic neomycin/polymyxin B/gramicidin group at days eight, 14 and 21 (*P*<0.05 for all), and scores in the ophthalmic neomycin/polymyxin B/dexamethasone group were significantly lower than those seen in the ophthalmic neomycin/polymyxin B/gramicidin group at day eight (*P*<0.05).[75]

Table 3. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Conjunctivitis				
Abelson et al[31] Azithromycin 1% one drop into the affected eye(s) BID on days one and two and QD on days three through five vs vehicle one drop into the affected eye(s) BID on days one and two and QD on days three through five	Phase 3 DB, MC, PC, PG, RCT Patients ≥1 year of age with a positive clinical diagnosis of bacterial conjunctivitis with signs and symptoms present for less than three days and a best-corrected visual acuity score of ≥20/100 in each eye	N=685 5 days	Primary: Clinical resolution at the test-of-cure visit (visit three on day six or seven) Secondary: Bacterial eradication at visit three, as indicated by the absence of bacterial growth and incidence of adverse events	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). 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). 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).
Cochereau et al[46] Azithromycin 1.5% one drop into the affected eye(s) BID for three days vs tobramycin 0.3% one drop into the affected eye(s) every two hours up to eight times a day for two days, then QID for five days	IB, MC, NI, PG, RCT Patients ≥1 day old with a diagnosis of purulent bacterial conjunctivitis defined as bulbar injection and purulent discharge	N=1,043 9 days	Primary: Clinical efficacy, microbiological assessment and safety Secondary: Not reported	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). NI 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). 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). Adverse events reported were mile 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. Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Not reported
Abelson et al[47] Azithromycin 1% one drop into the affected eye(s) BID on days one and two and QD on days three through five vs tobramycin 0.3% one drop into the affected eye(s) QID for five days	Phase 3, AC, DB, MC, PRO, RCT Patients ≥1 year of age with purulent conjunctival discharge and conjunctival or palpebral injection of three days or less in duration, with a best corrected visual acuity of ≥20/100	N=743 5 days	Primary: Clinical resolution of signs and symptoms of infective bacterial conjunctivitis Secondary: Bacterial eradication and investigator ratings of clinical outcomes	Primary: Differences in clinical resolution between azithromycin and tobramycin were not statistically significant (79.9 vs 78.3%, respectively; *P*=0.783). Secondary: Bacterial eradication was not statistically significant between the azithromycin and tobramycin groups (88.1 vs 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.
Karpecki et al[32] Besifloxacin 0.6% one drop into the affected eye(s) TID for five days vs vehicle one drop into the affected eye(s) TID for five days	DB, MC, PC, PG, PRO, RCT Patients ≥1 year of age in good health, with a clinical diagnosis of acute bacterial conjunctivitis as evidenced by a minimum of grade one for purulent conjunctival discharge and a minimum of grade one for either bulbar or palpebral conjunctival injection in at least one eye on ocular examination, with pinhole visual acuity of ≥20/200 in	N=269 5 days	Primary: Clinical resolution defined as the absence of conjunctival discharge and bulbar conjunctival injection at visit three Secondary: Eradication of baseline bacterial infection, defined as the absence at visit three of bacterial species that were present at or above the threshold on day one, clinical resolution of baseline conjunctivitis at visit two, eradication of the	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). 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*=0.003, *P*=0.013 and *P*<0.001, respectively). 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, respectively).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	each eye and females of childbearing potential using a reliable method of contraception		baseline bacterial infection at visit two and improvements in investigators' ratings of global change in clinical signs and symptoms	
Tepedino et al[33] Besifloxacin 0.6% one drop into the affected eye(s) TID for five days vs vehicle one drop into the affected eye(s) TID for five days	DB, MC, VC Patients ≥1 year of age with clinical manifestations of acute bacterial conjunctivitis in at least one eye	N=957 9 days	Primary: Clinical resolution and microbial eradication of baseline bacterial infection at visit two (day five) Secondary: Clinical resolution and microbial eradication at visit three (day eight or nine), individual clinical outcomes at follow-up visits and safety	Primary: Clinical resolution rates were significantly higher in the besifloxacin 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. 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 compared to vehicle alone (88.4 vs 71.7%; *P*<0.0001). 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 to those treated with vehicle. 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). The investigators assessment of cure increased in both the 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),

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				while at visit three, the rates were 83.9 and 66.0% (*P*=0.0002). A significantly greater percentage of eyes treated with vehicle experienced at least one ocular adverse event compared to those treated with besifloxacin (13.9 vs 9.2%; *P*=0.0047).
DeLeon et al[34] Besifloxacin 0.6% one drop into the affected eye(s) BID for three days vs vehicle one drop into the affected eye(s) BID for three days	DB, MC, PG, RCT, VC Patients ≥1 year of age with acute bacterial conjunctivitis in at least one eye based on the presence of grade one or greater purulent conjunctival discharge and bulbar conjunctival injection, pinhole visual acuity of ≥20/200 in both eyes in age-appropriate individuals and acceptable visual acuity by the investigator's judgment in children too young to provide reliable acuity measurements	N=474 7 days	Primary: Clinical resolution of conjunctivitis and eradication rates at day four or five in patients with bacterial conjunctivitis Secondary: Bacterial eradication and clinical resolution at day seven, individual clinical outcomes (ocular conjunctival discharge and bulbar conjunctival injection) at each follow-up visit, microbial and clinical outcomes for overall bacterial species and safety	Primary: By day four or five of treatment, bacterial eradication was significantly higher with besifloxacin compared to the vehicle (85.2 vs 54.6%; *P*<0.001). Similarly, a clinical resolution by days four or five was also significantly greater in the besifloxacin group compared to the vehicle group (65.9 vs 44.0%, respectively; *P*<0.001). Secondary: The rates of bacterial eradication at day seven continued to be significantly greater in the besifloxacin group compared to the vehicle group (85.2 vs 64.5%, respectively; *P*<0.001); however, rates of clinical resolution did not differ significantly between the treatment groups (76.3 and 66.7%; *P*=0.209). Significantly more patients treated with besifloxacin experienced a resolution of ocular discharge compared to patients who received vehicle at day four or five (77.8 vs 64.5%, respectively; *P*=0.012) and day seven (87.4 vs 77.3%; *P*=0.046). At day four or five, the proportion of patients treated with besifloxacin who experienced a resolution of bulbar conjunctival injection was significantly greater compared to those treated with vehicle (77.0 vs 51.8%; *P*<0.001), but not at day seven (84.4 vs 76.6%; *P*=0.259). Bacterial eradication and clinical resolution were significantly better with besifloxacin compared to vehicle for infections caused by either gram-positive or gram-negative organisms at day four or five of treatment.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				At day seven, only bacterial eradication was significantly better in besifloxacin-treated patients compared to those receiving vehicle and only for infections caused by gram-positive organisms. There were no significant differences between the besifloxacin and vehicle groups in the number of eyes with at least one ocular adverse event in either study eye. All ocular adverse events in the besifloxacin ophthalmic suspension and vehicle groups were of mild or moderate severity. The most frequently reported adverse event in the besifloxacin and vehicle groups was bacterial conjunctivitis (2.4% for both). Chalazion occurred in 0.8% of patients treated with besifloxacin compared to vehicle.
Silverstein et al[35] Besifloxacin 0.6% one drop into the affected eye(s) BID for three days vs vehicle one drop into the affected eye(s) BID for three days	DB, MC, PG, PRO, RCT, VC Patients ≥1 year of age with a clinical diagnosis of acute bacterial conjunctivitis with purulent discharge, crusty or sticky eyelids ocular surface redness and a minimum of grade one severity for both discharge and bulbar conjunctival injection in at least one eye	N=202 7 days	Primary: Clinical resolution and bacterial eradication of the baseline bacterial infection at visit two Secondary: Clinical resolution and bacterial eradication of the baseline bacterial infection at visit three and individual clinical outcomes at the follow-up visits	Primary: At visit two, clinical resolution of conjunctivitis in the study eye was significantly higher in the besifloxacin group compared to the vehicle group (69.8 vs 37.5%, respectively; *P*<0.001). The eradication of bacterial infection at visit two occurred in significantly more patients in the besifloxacin group compared to the vehicle group (86.8 vs 57.1%; *P*<0.001). 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). 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). 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).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				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*<0.001), but not at visit three (83.0 vs 73.2%; *P* value not reported).
Silverstein et al[53] Besifloxacin 0.6% one drop into the affected eye(s) BID or TID vs vehicle one drop into the affected eye(s) BID or TID or moxifloxacin 0.5% one drop into the affected eye(s) TID	PS on Karpecki et al, Tepedino et al, DeLeon et al and McDonald et al Patients ≥1 year of age with a clinical diagnosis of bacterial conjunctivitis as evidenced by a grade one or greater severity of both purulent ocular discharge and bulbar conjunctival injection in at least one eye, had culture-confirmed *Pseudomonas aeruginosa* infections and had pinhole visual acuity of ≥20/200	N=9 3 to 5 days	Primary: Clinical resolution and bacterial eradication of the baseline bacterial infection at visit two or three Secondary: Ocular and non-ocular adverse events, changes in visual acuity and biomicroscopy and ophthalmoscopy findings at follow-up visits	Primary: Of a total of 2,859 patients across of the four studies, nine patients had culture-confirmed *Pseudomonas aeruginosa* infections. Five of these patients received besifloxacin, all of whom had bacterial eradication of the baseline infections at visits two and three. Clinical resolution was reported in two of these patients by visit two and in four of these patients by visit three. Data on patients who received vehicle or moxifloxacin was not reported. Secondary: No adverse events were reported in the five patients who received besifloxacin. There were no clinically meaningful changes in visual acuity or any biomicroscopy or ophthalmoscopy findings.
McDonald et al[48] Besifloxacin 0.6% one drop into the affected eye(s) TID for five days vs moxifloxacin 0.5% one drop into the affected eye(s) TID for	DB, MC, NI, PG, RCT Patients ≥1 year of age in good health, with a clinical diagnosis of bacterial conjunctivitis as evidenced a grade of one or greater purulent conjunctival	N=1,161 8 days	Primary: Clinical resolution on day five and microbial eradication on day five of all accepted ocular bacterial species that were present at or above threshold at baseline	Primary: Findings on day five showed that there was no statistically significant difference in clinical resolution between the besifloxacin and moxifloxacin groups (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 five (93.3 vs 91.1%, respectively; *P*=0.124).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
five days	discharge and bulbar conjunctival injection in at least one eye, pinhole visual acuity of ≥20/200 in both eyes, willing to discontinue contact lens use during the study and females of childbearing potential using a reliable method of contraception		Secondary: Clinical resolution on day eight, microbial eradication on day eight of all accepted ocular bacterial species that were present at or above threshold at baseline and safety	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[49] Ciprofloxacin 3 mg/mL one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through seven vs tobramycin solution one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through seven	DB, MC, RCT Patients ≤12 years of age with bacterial conjunctivitis	N=257 7 days	Primary: Treatment efficacy assessed by microbiological culture and physicians' judgment of overall resolution Secondary: Safety	Primary: Microbiological eradication was shown to be higher in the ciprofloxacin group when compared to the tobramycin group; however, this difference was not significant (*P*=0.29). 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). Secondary: No serious adverse events were attributed to either treatment.
Leibowitz et al[36] (abstract) Ciprofloxacin 0.3%	Two MC, PRO, RCT Patients with bacterial conjunctivitis	N=288 Duration not specified	Primary: Antibacterial efficacy and eradication of bacterial pathogens	Primary: In one study, ciprofloxacin was shown to be significantly more effective than placebo (*P*<0.001) and eradicated or reduced the various bacterial pathogens in more patients when compared to

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs tobramycin 0.3% vs placebo			Secondary: Not reported	placebo (93.6 vs 59.5%; *P* value not reported). In a second study ciprofloxacin and tobramycin were found to be equally effective in antibacterial efficacy (94.5 vs 91.9%; *P* value not reported). Secondary: Not reported
Jauch et al[54] Gentamicin 0.3% vs tobramycin 0.3% vs chloramphenicol 0.5%* vs fusidic acid 1%* vs lomefloxacin 0.3%* vs norfloxacin 0.3%*	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 (*P* 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 (*P*=0.026 and *P*=0.016, respectively). Secondary: When lomefloxacin was compared to all other medications, poor tolerance for the medication was reported less often with lomefloxacin than with the other medications (1.5 vs 3.9%; *P* value not reported). Duration of any burning sensation was also significantly less with lomefloxacin when compared to all other medications (*P*=0.04).
Papa et al[55] Gentamicin 0.3% one to two drops into the affected eye(s)	AC, DB, PG, PRO, RCT Patients ≥3 years of	N=209 10 days	Primary: Clinical resolution of ocular infection as assessed by either	Primary: Netilmicin was shown to be significantly more effective than gentamicin in increasing the percentage of infections eradication over time (*P*=0.001).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
QID until resolution and up to 10 days with gentamicin ointment applied to affected eye(s) at bedtime vs netilmicin 0.3%* one to two drops into the affected eye(s) QID until resolution and up to 10 days with netilmicin ointment* applied to affected eye(s) at bedtime	age with suspected acute bacterial conjunctivitis		clinical or microbiologic parameters Secondary: Safety	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 (*P*=0.001 for both five and 10 days). Secondary: Adverse events were reported in four (3.9%) patients in the gentamicin group and two (1.9%) patients in the netilmicin group (*P* value not reported).Treatment tolerance was rated slightly higher in the netilmicin group as compared to the gentamicin group; however, this difference was not statistically significant (96.9 vs 70.9%; *P* value not reported).
Hwang et al[38] Levofloxacin 0.5% one to two drops into the affected eye(s) while awake on days one and two then every four hours while awake on days three through five vs placebo one to two drops into the affected eye(s) while awake on days one and two then every four hours while awake on days three through five	Phase 3, DB, MC, PC, RCT Patients ≥2 years of age with a clinical diagnosis of bacterial conjunctivitis characterized by purulent ocular discharge and redness in at least one eye	N=249 5 days	Primary: Antimicrobial efficacy, clinical efficacy, resolution of ocular signs and symptoms and safety Secondary: Not reported	Primary: Microbial eradication rates were significantly higher with levofloxacin at study visits one, two and three when compared to placebo (95 vs 49%; *P*<0.001, 92 vs 53%; *P*<0.001 and 90 vs 53%; *P*<0.001, respectively). Approximately twice as many patients in the treatment group achieved microbial eradication as those in the placebo group (*P*<0.001). Clinical cure rates were significantly greater in the levofloxacin group when compared to the placebo group both the final visit and the last observation made for patients who did not attend all visits (*P*=0.020 and *P*=0.026, respectively). Resolution of ocular signs and symptoms were consistently higher in the treatment group than with the placebo group at all study visits (*P* value not reported). Statistically significant differences were seen favoring the levofloxacin group with regard to resolution of the ocular signs of conjunctival discharge (*P*=0.027), bulbar conjunctival injection (*P*=0.018) and for the ocular symptoms of burning and stinging (*P*=0.008), itching (*P*=0.037) and photophobia (*P*=0.023).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				With regard to safety, 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 (*P* value not reported). Of the most common adverse events, only erythema and swelling was reported in significantly more patients in the levofloxacin group (*P*=0.672), while there was no statistically significant difference in the rate of conjunctival discharge, photophobia and burning or stinging (*P*=0.027, *P*=0.023 and *P*=0.008, respectively). Secondary: Not reported
Schwab et al[45] Levofloxacin 0.5% one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through five vs ofloxacin 0.3% one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through five	AC, DB, MC, RCT Patients ≥1 year of age with a diagnosis of bacterial conjunctivitis, characteristic purulent conjunctival discharge (≥1 on a four-point scale) and redness (≥1 on a four-point scale for bulbar and/or palpebral injection) in at least one eye	N=423 7 days	Primary: Microbial eradication and clinical cures Secondary: Evaluations of ocular signs and symptoms and safety	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). 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). Secondary: No significant differences were noted between the two treatment groups in resolution of baseline ocular signs at either the final visit or endpoint. 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). There were no significant differences between treatment groups in

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				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%).
Lichtenstein et al[39] (abstract) Levofloxacin 0.5% one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through five vs ofloxacin 0.3% one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through five vs placebo one drop into the affected eye(s) every two hours on days one and two and every four hours on days three through five	DB, MC, PG, RCT Patients 1 to 16 years of age with a diagnosis of bacterial conjunctivitis	N=167 10 days	Primary: Rate of microbial eradication Secondary: Not reported	Primary: At the last observation, the levofloxacin 0.5% group showed higher rates of microbial eradication when compared to the ofloxacin 0.3% group (*P* value not reported). In children two to 11 years of age, this finding was statistically significant in favor of levofloxacin 0.5% when compared to both ofloxacin 0.3% and placebo (87 vs 62%; *P*<0.032 and 88 vs 24%; *P*<0.001). No statistically significant differences were observed between the three groups in the other age subgroups. Secondary: Not reported
Tauber et al[40] Moxifloxacin 0.5% one drop into the affected eye(s) BID for three days	DB, MC, PG, RCT, VC Patients ≥28 days of age with a diagnosis of bacterial conjunctivitis in one or	N=1,180 6 days	Primary: Clinical cure rate and eradication rates by species Secondary:	Primary: Patients treated with moxifloxacin BID 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 BID was significantly more effective than

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs placebo one drop into the affected eye(s) BID for three days	both eyes based on bulbar conjunctival injection and discharge (score ≥1 on a four-point scale for each sign) and matting		Not reported	vehicle in eradicating the three principle conjunctivitis pathogens, *H influenzae* (98.5 vs 59.6%; *P*<0.001), *S pneumoniae* (86.4 vs 50.0%; *P*<0.001) and *S aureus* (94.1 vs 80.0%; *P*<0.001). Secondary: Not reported
Silver et al[50] Moxifloxacin 0.5% one drop into the affected eye(s) TID for four days vs ofloxacin 0.3% one drop into the affected eye(s) QID for four days vs ciprofloxacin 0.3% one drop into the affected eye(s) TID for four days vs vehicle	MA Patients of any race with a diagnosis of bacterial conjunctivitis	N=1,978 7 to 9 days	Primary: Safety Secondary: Not reported	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 group (2.8 vs 2.1%; *P* value not reported). 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 fewer patients in the moxifloxacin group when compared to the vehicle group (1.9 vs 2.2%; *P* value not reported). The most common systemic adverse event reported in pediatric patients was increased cough that occurred in more patients in the moxifloxacin group than the vehicle group (3.2 vs 2.8%; *P* value not reported). Similar rates of adverse events were reported in a study comparing moxifloxacin to ofloxacin with regard to keratitis, corneal infiltrate and ocular hyperemia (*P* value not reported). 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 (*P* value not reported). Secondary: Not reported
Kodjikian et al[44] (abstract)	MA (five RCT) Patients with a clinical	N=not reported	Primary: Clinical efficacy and drop-out rates for all	Primary: Treatment with moxifloxacin was 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

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Moxifloxacin vs ofloxacin vs levofloxacin	diagnosis of acute bacterial conjunctivitis in one or more eyes	Duration not reported	reasons including lack of efficacy Secondary: Not reported	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 a lower risk of therapy discontinuation compared to treatment with placebo (OR, 2.22; 95% CI, 1.62 to 3.03; *P*<0.001). In comparison to ofloxacin, patients treated with moxifloxacin had fewer dropouts for reasons other than treatment failure (OR, 1.92; 95% CI, 1.28 to 2.89; *P*=0.02) and fewer dropouts for treatment failure (OR, 2.53; 95% CI, 1.41 to 4.56; *P*=0.002). Secondary: Not reported
Kernt et al[56] Enhanced viscosity tobramycin 0.3% one drop into the affected eye(s) BID for seven days vs tobramycin 0.3% one drop into the affected eye(s) QID for seven days	IB, MC, PG, RCT Male and female patients with a negative pregnancy test prior to study entry who agreed to use birth control throughout the study, ≥1 year of age with bacterial conjunctivitis based on clinical observation	N=276 12 days	Primary: Percentage of patients with sustained cure/ presumed bacterial eradication based on final clinical judgment at test-of-cure visit Secondary: Lid erythema/swelling, palpebral conjunctiva, bulbar conjunctiva, conjunctival discharge/exudates, tearing and epithelial disease; microbiology and safety	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 vs 99%, respectively; *P*=0.604). 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). 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). Adverse events reported were mild to moderate in severity and were 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 (*P* value not reported).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Gigliotti et al[41] (abstract) Bacitracin/polymyxin applied to affected eye(s) QID for seven days vs placebo applied to affected eye(s) QID for seven days	DB, RCT Patients 1 month to 18 years of age with acute conjunctivitis	N=102 10 days	Primary: Clinical cure rate and bacterial pathogen eradication Secondary: Not reported	Primary: During days three through five, significantly more patients in the bacitracin/polymyxin 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 and placebo groups was not significant (91 vs 72%; *P* value not reported). It was found that the bacterial pathogen was eradicated in significantly more patients in the treatment group than the placebo group on days three to five, as well as on days eight to 10 (72 vs 19% and 79 vs 31%, respectively; *P*<0.001 for both). Secondary: Not reported
Sheikh et al[37] 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%*	MA Patients ≥1 month of age 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 at days three through five, bacitracin/ polymyxin was favored (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, 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

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs vehicle				
Lohr et al[51] (abstract) Polymyxin B/trimethoprim vs gentamicin vs sulfacetamide sodium	R Patients with culture-positive conjunctivitis	N=158 17 days	Primary: Patients cured and symptom improvement at days three to six after the start of treatment, patients cured and symptom improvement at days two to seven after completion of therapy and bacteriologic response at days two to seven after completion of therapy Secondary: Not reported	Primary: Clinical response at days three to six after the start of treatment was similar among the polymyxin B/trimethoprim, gentamicin and sulfacetamide sodium groups with regard to patients cured (47, 49 and 41%, respectively; *P* value not reported) as well as symptom improvement (45, 46 and 48%, respectively; *P* value not reported). At days two to seven after completion of therapy, clinical response (84, 88 and 89%, respectively; *P* value not reported) and symptom improvement (9, 9 and 4%; *P* value not reported) were also similar among all groups. Bacteriologic response at days two to seven after completion of therapy was similar as well for all groups (83, 68 and 72%; *P* value not reported). Secondary: Not reported
Granet et al[42] (abstract) Polymyxin B/trimethoprim one drop into the affected eye(s) QID for seven days vs moxifloxacin 0.5% one drop into the affected eye(s) TID for seven days	MC, RCT Patients ≤18 years of age with a clinical diagnosis of bacterial conjunctivitis	N=56 7 days	Primary: Relief of all signs and symptoms of bacterial conjunctivitis Secondary: Safety	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/trimethoprim group (81 vs 44%; *P*=0.001). Secondary: No adverse events were reported in either group.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Williams et al[43] Polymyxin B/trimethoprim one drop into the affected eye(s) QID for seven days vs moxifloxacin 0.5% one drop into the affected eye(s) TID for seven days	SB, RCT Patients 1 to 18 years of age with acute conjunctivitis	N=114 7 days	Primary: Clinical cure rate Secondary: Not reported	Primary: At the four-to-six day follow-up visit, 72 and 77% of patients in the polymyxin B/trimethoprim and moxifloxacin groups were considered clinically cured, defined as a complete resolution of all signs and symptoms of conjunctivitis (*P*=0.59). Treatment with polymyxin B/trimethoprim was shown to be NI to moxifloxacin with a NI margin of 20% (difference, -0.05; 90% CI, -0.20 to 0.11). At the seven-to-ten day follow-up visit, 96 and 95% of patients in the polymyxin B/trimethoprim and moxifloxacin groups were considered clinically cured (*P* value not reported). Bacteriologist cure rate was 61% in the polymyxin B/trimethoprim group and 79% in the moxifloxacin group (*P*=0.52). Secondary: Not reported
Gibson[52] (abstract) Polymyxin B/trimethoprim 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 polymyxin B/trimethoprim group and the neomycin/polymyxin B/gramicidin group (*P* value not reported). However, neomycin/polymyxin B/gramicidin was found to be significantly more efficacious than chloramphenicol in reducing signs and symptoms (*P*=0.03). Secondary: Not reported
Behrens-Baumann et al[57] Polymyxin B sulfate/ trimethoprim 10,000 units/g/5 mg/g applied QID to the lower conjunctival sac(s) for seven days	DB, PG, RCT Patients with a clinical diagnosis of bacterial conjunctivitis	N=42 10 days	Primary: Reduction in severity rating score Secondary: Safety	Primary: No significant difference was seen between the two groups with regard to reduction in severity rating score (*P*>0.1). Secondary: Three (7%) patients from the polymyxin B sulfate/trimethoprim group experienced adverse events: one patient reported stinging/burning,

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs chloramphenicol 10 mg/g* applied QID to the lower conjunctival sac(s) for seven days				one reported increases in transient grittiness and conjunctival hyperemia, and one reported periorbital edema (*P* value not reported).
Corneal Ulcer				
Kosrirukvongs et al[68] (abstract) Ciprofloxacin 0.3% applied into the affected eye(s) every 15 minutes for the first six 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 six 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 statistically significant (70.6 vs 62.5%, respectively; *P* value not reported). The mean duration for healing after treatment was less in the ciprofloxacin group, but this difference was not statistically significant (14.6 vs 15.6 days, respectively; *P* value not reported). Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Booranapong et al[69] (abstract) 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).
Keratitis				
Parks et al[60] (abstract) Ciprofloxacin 3 mg/mL vs cefazolin 50 mg/mL fortified with gentamicin 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 in the cefazolin fortified with gentamicin group; however, this was not found to be statistically significant (34±33 vs 45±71 days; *P* value not reported). The duration of antibiotic therapy in the ciprofloxacin group was also less than that seen in the cefazolin fortified with gentamicin group (27±15 vs 33±50 days; *P* value not reported). Secondary: Not reported
Multiple/Unspecified External Ocular Infection				
Bloom et al[61] (abstract) Ciprofloxacin to affected eye(s) for seven days vs tobramycin to affected eye(s) for seven 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 seven 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; *P* 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 (*P* value not reported). No serious adverse events were reported in either group. Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				Not reported
Adenis et al[62] (abstract) 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: Not reported	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; *P* 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%, respectively; *P* value not reported). 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 (*P* value not reported). Secondary: Not reported
Adenis et al[63] (abstract) Ciprofloxacin 0.3% vs rifamycin 1%*	DB, PG, RCT Patients with bacterial conjunctivitis and blepharitis	N=41 7 days	Primary: Clinical cure rate on day seven, bacteriological eradication rate and adverse events Secondary: Not reported	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; *P*=0.061). Bacteriological eradication rates were similar in both groups (68 vs 77%, respectively; *P* value not reported). No serious adverse events were reported in either treatment group. Secondary: Not reported
Kanda et al[64] Levofloxacin 0.5%	MC, RETRO Patients who received ophthalmic levofloxacin for	N=6,686 (safety) N=5,929 (efficacy)	Primary: Adverse events and clinical response Secondary:	Primary: Forty-six adverse events were reported in 42 patients, with an overall incidence of 0.63%. The most commonly reported adverse events were ocular disorders such as blepharitis (0.1%), eye irritation (0.09%) and punctuate keratitis (0.07%). None of the reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
	blepharitis, dacryocystitis, hordeolum, conjunctivitis, tarsadenitis, keratitis and/or corneal ulcer	Median 29 days for dacryo-cystitis; 8 to 9 days for all other infections	Not reported	adverse events were considered serious. A clinical response was observed in 95.5% of the 5,929 patients. Patients who were treated for dacryocystitis had a significantly lower response rate (88.3%) compared to patients treated for other diagnoses (overall, 95.8%; *P*<0.001). Secondary: Not reported
Gwon[65] Ofloxacin 0.3% one drop into the affected eye(s) every two to four hours on days one and two and QID on days three through seven vs gentamicin 0.3% one drop into the affected eye(s) every two to four hours on days one and two and QID on days three through seven	DB, RCT Patients with suspected external ocular bacterial infection including conjunctivitis, blepharitis and blepharoconjunctivitis	N=194 11 days	Primary: Clinical, microbiological and overall improvement rates Secondary: Safety	Primary: Ofloxacin had 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 (*P*=0.089 for all outcomes). 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 (*P* value not reported).
Gwon[66] Ofloxacin 0.3% one drop into the affected eye(s) every two to four hours on days one and two and QID on days three through 10 vs tobramycin 0.3% one drop into	DB, MC, RCT Patients with the presence of conjunctival hyperemia, either eyelid crusting or discharge and positive bacterial culture	N=345 11 days	Primary: Clinical, microbiological and overall improvement rates Secondary: Change in cumulative summary score of 10 key biomicroscopic and symptomatologic variables and safety	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 statistically significant (*P*=0.089 for all outcomes). Secondary: The decrease in cumulative summary score was found to be significantly greater in the ofloxacin group when compared to the

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
the affected eye(s) every two to four hours on days one and two and QID on days three through 10				tobramycin group at visits on days three to five (*P*<0.050). Adverse reactions occurred more frequently in the tobramycin group; however, this difference was not significant (0.6 vs 2.9%, respectively; *P* value not reported).
Bron et al[67] Ofloxacin 0.3% one drop into the affected eye(s) every two to four hours on days one and two and QID on days three through seven vs chloramphenicol 0.5%* one drop into the affected eye(s) every two to four hours on days one and two and QID on days three through seven	DB, MC, PG, RCT Patients with suspected bacterial ocular infection	N=167 8 days	Primary: Clinical improvement as defined as a decline in symptoms of external ocular infection, microbiological improvement rate and clinical improvement rate Secondary: Safety	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 (*P* value not reported). Microbiological improvement rates were similar between the ofloxacin group and the chloramphenicol group (85 vs 88%, respectively; *P* value not reported). Clinical improvement rates were also high for both the ofloxacin group and the chloramphenicol group (100 vs 95%, respectively; *P* value not reported). Secondary: No significant differences were seen between the two groups for any symptom present at visit three or with regard to adverse events (*P* value not reported).
Laibson et al[68] (abstract) Tobramycin ointment vs gentamicin ointment	DB, MC Patients with bacterial infections of the external eye	N=511 Duration not specified	Primary: Efficacy evaluated by resolution of signs and symptoms and follow-up impression made by a physician and adverse events Secondary: Not reported	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). Tobramycin ointment was associated with significantly fewer adverse events than gentamicin ointment (*P* value not reported). Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Leibowitz et al[69] (abstract) Tobramycin vs gentamicin	DB, MC, RCT Patients with superficial external eye disease	N=77 10 days	Primary: Clinical cure or improvement, antibacterial effectiveness and adverse events Secondary: Not reported	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 statistically significant (97.0 vs 91.3%, respectively; *P*>0.05). Antibacterial effectiveness also favored tobramycin but was not statistically significant (87.8 vs 77.4%, respectively; *P*>0.05). Adverse events in the tobramycin and gentamicin groups were also not significantly different (9.3 vs 17.6%; *P*>0.05). Secondary: Not reported
Jacobson et al[70] Tobramycin 0.3% one drop into the affected eye(s) every two hours while awake on day one and then QID on days two through seven vs norfloxacin 0.3%* one drop into the affected eye(s) every two hours while awake on day one and then QID on days two through seven	DB, MC, RCT Patients with a clinical diagnosis of acute bacterial conjunctivitis, keratoconjunctivitis, blepharitis, or blepharoconjunctivitis	N=120 8 days	Primary: Pathogens eliminated after therapy Secondary: Safety	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). 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).
Foulks et al[71] Polymyxin B/trimethoprim 10,000 units/g/1 mg/mL applied to the affected eye(s) every three hours while awake	DB, RCT Patients ≥2 months of age with clinical signs and symptoms of surface ocular	N=57 10 days	Primary: Clinical improvement and microbiologic improvement Secondary:	Primary: Clinical improvements and cure rates at the final follow up visit were similar in the polymyxin B/trimethoprim and polymyxin B/ trimethoprim/sulfacetamide 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).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
for 10 days vs polymyxin B/trimethoprim/ sulfacetamide 10,000 units/g/1 mg/g/5 mg/mL* applied to affected eye(s) every three hours while awake for 10 days	bacterial infections		Safety	Differences in microbiologic responses were also not statistically significant between the two groups (87 vs 93%, respectively; *P* value not reported). Secondary: Patients evaluated for safety showed an identical incidence of adverse events (*P* value not reported).
Prophylaxis of Ophthalmia Neonatorum				
Ali et al[73] Erythromycin 0.5% ointment applied to eyes during the first few hours of birth vs betadine 2.5% applied to eyes during the first few hours of birth vs no prophylaxis	RCT Healthy newborns without congenital eye abnormalities from mothers who had not used any form of antibiotics within the last 48 hours prior to delivery, without rupture of membranes for more than 18 hours and absence of meconium aspiration	N=330 14 days	Primary: Rate of conjunctival symptoms Secondary: Not reported	Primary: The betadine group and erythromycin group had significantly fewer 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 and 18.4 vs 22.4%, respectively; *P*=0.030). Secondary: Not reported
Bell et al[72] Erythromycin 0.5% ointment applied to eyes of child at birth vs silver nitration applied to eyes of child at birth	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 two 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 nitrate group (*P* 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

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs no prophylaxis				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 birth, the protective effect of prophylaxis was found to be most effective prior to 2 weeks of birth. The efficacy of erythromycin from days zero to 14 was 9.0% as compared to 15.0% with no prophylaxis (*P*=0.050). This was not found to be statistically significant from days 15 to 60 (7.0 vs 8.0%, respectively; *P*=0.920). Secondary: Not reported
Miscellaneous				
Parekh et al[76] Besifloxacin 0.6% one drop into the operated eye(s) TID vs moxifloxacin 0.5% one drop into the operated eye(s) QID	MC, RETRO Patients undergoing cataract surgery and using besifloxacin or moxifloxacin as prophylaxis	N=746 Duration varied	Primary: Safety and surgical outcomes Secondary: Not reported	Primary: No adverse reactions were reported in either treatment group. Surgical outcomes were similar between the two treatment groups. The proportion of eyes with an unexpected elevation in intraocular pressure was similar between the besifloxacin and moxifloxacin groups (6.3 vs 9.9%; *P*=0.318). Unexpected anterior chamber reactions were reported in four patients in the besifloxacin group and none in the moxifloxacin group (*P*=0.062). Final visual acuity was similar between the two groups (*P*=0.299). Unexpected corneal findings, such as abnormal postoperative endothelial morphology, corneal edema and would healing, were reported in 3.0 and 0.8% of patients in the besifloxacin and moxifloxacin groups, respectively (*P*=0.937). Secondary: Not reported
Van Endt et al[74] (abstract) Gentamicin	PG, PRO, RCT Patients undergoing cataract and posterior chamber lens implant	N=112 34 days	Primary: Bacterial colony count, intraocular inflammation and global assessment of	Primary: At days six to eight, the bacterial colony count was significantly lower in the gentamicin group when compared to the neomycin/polymyxin B/dexamethasone group (*P*=0.033).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs neomycin/polymyxin B/ dexamethasone	surgery		success of therapy and local tolerance Secondary: Not reported	No statistically significant difference was found between the two groups with regard to the degree of intraocular inflammation or the global assessment of the success of therapy and local tolerance as rated by the patients and physicians (*P* value not reported). Secondary: Not reported
Notivol et al[75] Tobramycin/dexamethasone 3 mg/mL/1 mg/mL one drop into the operated eye(s) QID for 21 days vs neomycin/polymyxin B/ dexamethasone 3,500 units/mL/6,000 units/mL/1 mg/mL one drop into the operated eye(s) QID for 21 days vs neomycin/polymyxin B/ gramicidin 3,500 units/mL/7,500 units/mL/20 µg/mL one drop into the operated eye(s) QID for 21 days	DB, MC, PG, PRO Patients ≥18 years of age undergoing cataract extraction by either manual extraction or phacoemulsification with intraocular lens implantation	N=271 21 days	Primary: Intraocular inflammation assessed at days three, eight, 14 and 21 Secondary: Evaluation of adverse events including flare, conjunctival hyperemia, corneal edema, anterior vitreous reaction, ocular pain, physician's impression of inflammation and presence of ciliary flush	Primary: Inflammation scores between tobramycin/dexamethasone and neomycin/polymyxin B/dexamethasone 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% confidence interval to show noninferiority of tobramycin/ dexamethasone. Inflammation scores were significantly lower in the tobramycin/ dexamethasone group when compared to the neomycin/polymyxin B/ dexamethasone group at days eight, 14 and 21 (0.77, 0.54 and 0.39, respectively; *P*<0.050 for all), and scores in the neomycin/polymyxin B/dexamethasone 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). Secondary: No statistically significant differences were seen in the mean scores of any variable between the tobramycin/dexamethasone group and the neomycin/polymyxin B/dexamethasone groups. The neomycin/polymyxin B/gramicidin group reported significantly lower incidence of 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 tobramycin/dexamethasone group (*P*<0.05 for all). The percentage of patients with ciliary flush as days eight, 14 and 21

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				was significantly lower in the tobramycin/dexamethasone group than in the neomycin/polymyxin B/gramicidin group (P<0.05 for all). Scores in the neomycin/polymyxin B/dexamethasone 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).

*Agent not available in the United States.
Drug regimen abbreviations: BID=twice daily, QD=once 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, MA=meta-analysis, MC=multicenter, NI=non-inferiority, OL=open-label, OR=odds ratio, PC=placebo-controlled, PG=parallel-group, PRO=prospective, PS=post-hoc study, R=randomized, RCT=randomized controlled trial, RETRO=retrospective, RR=risk ratio, SB=single blind, VC=vehicle control

Special Populations

Table 4. Special Populations[1-22]

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Single-Entity Agents					
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. No specific pediatric information available.	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	No overall differences in safety or efficacy observed in the elderly. 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.	Not reported	Not reported	C	Not reported

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
	Safety and efficacy in pediatric patients<1 year of age have not been 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	Not reported	Not reported	C	Not reported

Generic Name	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
	pediatric patients <2 months of age have not been established.				
Tobramycin	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	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
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
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 sulfate/ polymyxin B sulfate/ gramicidin	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.[14,15]

Table 5. Adverse Drug Events[1-22]

Adverse Event(s)	Single-Entity Agents														Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Cardiovascular																		
Hyperemia	-	-	-	-	<1	-	-	-	-	<1	-	-	-	-	-	-	-	-
Central Nervous System																		
Dizziness	-	-	-	-	-	-	-	-	-	-	-	✔	-	-	-	-	-	-
Hallucinations	-	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-
Headache	-	-	1 to 2	-	-	-	✔	-	1 to 3	8 to 10	-	-	-	-	-	-	-	-
Itching	-	-	-	<10	-	-	-	-	-	-	-	✔	-	-	✔	✔	✔	✔
Itching pain	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pruritus	-	-	-	-	<1	-	-	-	-	-	-	-	-	-	-	-	-	-
Dermatologic																		
Circumocular rash	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	-
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	-	✔	-	-	-	-	-	-

Adverse Event(s)	Single-Entity Agents														Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Burning	<1	-	-	✔	-	-	-	✔	-	-	-	-	✔	-	-	✔	-	-
Chemical conjunctivitis	-	-	-	-	-	-	-	-	-	-	-	✔	-	-	-	-	-	-
Chemical keratitis	-	-	-	-	-	-	-	-	-	-	-	✔	-	-	-	-	-	-
Chemosis	-	-	-	-	-	-	✔	-	-	<1	-	-	-	-	-	-	-	-
Conjunctival epithelial defects	-	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-
Conjunctival erythema	-	-	-	-	-	-	-	-	-	-	-	-	-	<3	✔	-	✔	✔
Conjunctival hemorrhage	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-	-
Conjunctival hyperemia	-	-	-	<10	-	-	-	✔	-	-	-	-	✔	-	-	-	-	-
Conjunctival irritation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Conjunctival redness	-	-	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Conjunctivitis	-	-	-	-	-	-	≥1	-	-	-	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 6	-	-	-	-	-	-	-
Diplopia	-	-	-	-	-	-	-	-	-	<1	-	-	-	-	-	-	-	-
Dry eye	<1	-	-	-	<1	-	✔	-	<1	-	1 to 6	✔	-	-	-	-	-	-
Epitheliopathy	-	-	-	-	<1	-	-	-	-	-	-	-	-	-	-	-	-	-
Eye discharge	<1	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-	-
Eye discomfort	-	-	-	✔	2	-	-	-	1 to 3	1 to 2	1 to 6	-	-	-	-	-	-	-
Eye irritation	1 to 2	-	1 to 2	-	<1	✔	≥1	-	-	1 to 2	1 to 2	-	✔	-	-	-	-	-
Eye pain	-	-	1 to 2	-	<1	-	≥1	-	1 to 3	1 to 2	1 to 6	✔	-	-	-	-	-	-
Eye pruritus	-	-	1 to 2	-	-	-	-	-	-	-	1 to 6	-	-	-	-	-	-	-
Eyelid edema	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-	-
Eyelid swelling	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Adverse Event(s)	Single-Entity Agents														Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Floaters	-	-	-	-	-	-	-	-	-	<1	-	-	-	-	-	-	-	-
Foreign body sensation	-	-	-	<10	<1	-	-	-	1 to 3	-	-	✔	-	-	-	-	-	-
Increased lacrimation	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-	-
Irritation upon instillation	<1	-	-	-	-	-	-	✔	-	-	-	-	-	-	✔	-	✔	✔
Keratoconjunctivitis	-	-	-	-	<1	-	-	-	-	-	-	-	-	-	-	-	-	-
Keratopathy	-	-	-	<1	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Keratitis	-	-	-	<1	-	-	✔	-	-	-	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 hyperemia	-	-	-	-	-	-	-	-	-	-	1 to 6	-	-	-	-	-	-	-
Ocular infection	-	-	-	-	-	-	-	-	-	1 to 2	-	-	-	-	-	-	-	-
Ocular itching	-	-	-	-	-	-	-	-	<1	-	-	-	-	-	-	-	-	-
Papillary conjunctivitis	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-	-
Periocular swelling	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Punctate keratitis	<1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Redness	-	-	-	-	-	✔	-	-	-	-	-	✔	-	-	-	✔	-	-
Stinging	-	-	-	-	-	-	-	-	-	-	-	✔	✔	-	-	✔	-	-
Stinging upon instillation	<1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Subconjunctival hemorrhage	-	-	-	-	-	-	-	-	-	-	1 to 6	-	-	-	-	-	-	-
Tearing	-	-	-	<1	<1	-	-	-	-	-	1 to 6	✔	-	-	-	✔	-	-
Transient ocular burning	-	-	-	-	-	-	-	-	1 to 3	-	-	✔	-	-	-	-	-	-
Transient ocular discomfort	-	-	-	-	-	-	-	-	-	-	-	✔	-	-	-	-	-	-
Vision disorders	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	-

Adverse Event(s)	Single-Entity Agents														Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
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	-	-	-	✔	-	-	-	-	✔
Allergic sensitizations	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	-
Anaphylaxis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	✔	✔
Bad taste following instillation	-	-	-	<10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dysgeusia	<1	-	-	-	-	-	≥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	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	-	-	-	-
Swelling	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	✔	✔
Taste perversion	-	-	-	-	<1	-	-	-	-	8 to 10	-	-	-	-	-	-	-	-
Throat irritation	-	-	-	-	-	-	-	-	-	1 to 2	-	-	-	-	-	-	-	-
Thrombocytopenic purpura	-	-	-	-	-	-	-	✔	-	-	-	-	-	-	-	-	-	-

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

Contraindications

Table 6. Contraindications[1-22]

Contraindication	Single-Entity Agents													Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Hypersensitivity to any components of the product	✔	✔	-	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	-	✔	✔	✔

Warnings/Precautions

Table 7. Warnings and Precautions[1-22]

Warning/Precaution	Single-Entity Agents													Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Anaphylaxis and hypersensitivity with systemic use; consider risks when administered systemically and discontinue if allergic reactions occur	✔	-	-	✔	✔	-	✔	-	✔	✔	✔	✔	✔	-	-	-	-	-
Bacterial keratitis associated with use of topical ophthalmic products in multiple-dose containers; instruct patients to avoid product contamination	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✔
Cartilage lesions or erosions in weight-bearing joints; associated with systemic quinolone therapy	-	-	✔	-	-	-	-	-	-	-	-	✔	-	-	-	-	-	-
Contact lens use; avoided if there are signs and symptoms of bacterial conjunctivitis	✔	-	✔	✔	✔	-	✔	✔	✔	✔	✔	-	-	✔	-	✔	-	✔

Warning/Precaution	Single-Entity Agents														Combination Products			
	Azithromycin	Bacitracin	Besifloxacin	Ciprofloxacin Solution	Ciprofloxacin Ointment	Erythromycin	Gatifloxacin	Gentamicin Sulfate	Levofloxacin 0.5%	Levofloxacin 1.5%	Moxifloxacin Hydrochloride	Ofloxacin	Sulfacetamide Sodium	Tobramycin	Bacitracin Zinc/ Polymyxin B Sulfate	Polymyxin B Sulfate/ Trimethoprim	Neomycin Sulfate/ Polymyxin B Sulfate/Bacitracin Zinc	Neomycin Sulfate/ Polymyxin B Sulfate/ Gramicidin
Cross-reactions to kanamycin, paramomycin, streptomycin and possibly gentamycin; avoid use	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✔
Deep-seated ocular infection; avoid use in patients with these conditions or if infections are likely to become systemic	-	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Growth of resistant organisms with prolonged use; discontinue use and institute alternative therapy if super-infection occurs	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Hypersensitivity or irritation; discontinue use and begin appropriate therapy	-	-	-	-	-	-	-	✔	-	-	-	-	✔	✔	-	✔	✔	✔
Ophthalmia neonatorum; not indicated for the prophylaxis or treatment of this condition	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	-
Ophthalmic ointments may slow corneal healing and cause blurred vision; use with caution	-	-	-	-	✔	-	-	✔	-	-	-	-	✔	✔	✔	-	✔	-
Precipitate formation; development does not preclude continued treatment with the agent	-	-	-	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Reduced effectiveness by para-aminobenzoic acid present in purulent exudates; monitor therapy	-	-	-	-	-	-	-	-	-	-	-	-	✔	-	-	-	-	-
Topical ophthalmic use only; do not administer systemically, inject subconjunctivally or introduce into the anterior chamber of the eye	✔	-	✔	✔	✔	-	✔	✔	✔	✔	✔	✔	✔	✔	-	✔	✔	✔

Drug Interactions

Since ophthalmic medications have minimal systemic absorption, studies have not been conducted to assess drug interactions associated with these medications. [1-22]

Dosage and Administration

Table 8. Dosing and Administration[1-22]

Generic Name	Adult Dose	Pediatric Dose	Availability
Single-Entity Agents			
Azithromycin	Treatment of bacterial conjunctivitis: Ophthalmic solution: 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%
Bacitracin	Treatment of superficial ocular infections involving the conjunctiva and/or cornea: Ophthalmic ointment: Apply a thin ribbon every three to four hours for seven to 10 days	No specific pediatric information available.	Ophthalmic ointment: 500 units/g
Besifloxacin	Treatment of bacterial conjunctivitis: Ophthalmic suspension: 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%
Ciprofloxacin	Treatment of bacterial conjunctivitis: 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 Treatment of corneal ulcer: 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% Ophthalmic solution: 0.3%
Erythromycin	Treatment of superficial ocular infections involving the conjunctiva and/or cornea: Ophthalmic ointment: Apply 1-cm ribbon directly to infected eye(s) up to six times daily	Prophylaxis of ophthalmia neonatorum due to *Neisseria gonorrhoeae* or *Chlamydia*	Ophthalmic ointment: 0.5%

Generic Name	Adult Dose	Pediatric Dose	Availability
		trachomatis: Apply a 1-cm ribbon into each lower conjunctival sac Safety and efficacy has been established in newborn infants.	
Gatifloxacin	Treatment of bacterial conjunctivitis: Ophthalmic solution: 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	Safety and efficacy in pediatric patients <1 year of age have not been established.	Ophthalmic solution: 0.5%
Gentamicin sulfate	Treatment of acute meibomianitis, bacterial conjunctivitis, blepharitis, blepharoconjunctivitis, corneal ulcers, keratitis, keratoconjunctivitis and dacryocystitis: Ophthalmic ointment: Apply ½ inch 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% Ophthalmic solution: 0.3%
Levofloxacin	Treatment of bacterial conjunctivitis: Ophthalmic solution: On days one and two, instill one to two drops every two 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	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.	Ophthalmic solution: 0.5% 1.5%
Moxifloxacin hydrochloride	Treatment of bacterial conjunctivitis: Moxeza®: instill one drop twice daily for seven days Vigamox®: instill one drop three times daily for seven days	Moxeza®: Safety and efficacy in pediatric patients <3 months of age have not been established. Vigamox®: Safety and efficacy in pediatric patients	Ophthalmic solution: 0.5%

Generic Name	Adult Dose	Pediatric Dose	Availability
		<1 year of age have not been established.	
Ofloxacin	Treatment of bacterial conjunctivitis: Ophthalmic solution: 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 Treatment of corneal ulcer: Ophthalmic solution: 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	Safety and efficacy in pediatric patients <1 year of age have not been established.	Ophthalmic solution: 0.3%
Sulfacetamide sodium	Treatment of bacterial conjunctivitis and other superficial ocular infections: Ophthalmic ointment: Apply ½ inch ribbon into the conjunctival sac(s) every three to four hours and at bedtime for seven to 10 days Ophthalmic solution: instill one or two drops into conjunctival sac(s) every two to three hours initially for seven to 10 days Adjunctive treatment in systemic sulfonamide therapy of trachoma: Ophthalmic solution: instill two drops into the conjunctival sac(s) every two hours, must be accompanied by systemic administration	Safety and efficacy in pediatric patients <2 months of age have not been established.	Ophthalmic ointment: 10% Ophthalmic solution: 10%
Tobramycin	Treatment of external infections of the eye and its adnexa: Ophthalmic ointment: Mild to moderate infections, apply ½ inch ribbon into the affected eye(s) two to three times daily; severe infections, apply ½ inch ribbon into the affected eye(s) every three to four hours until improvement, following which treatment should	Safety and efficacy in pediatric patients <2 months of age have not been established.	Ophthalmic ointment: 0.3% Ophthalmic solution: 0.3%

Generic Name	Adult Dose	Pediatric Dose	Availability
	be reduced prior to discontinuation Ophthalmic solution: Mild to moderate infections, instill one or two drops every four hours; severe infections, instill two drops every hour until improvement, following which treatment should be reduced prior to discontinuation		
Combination Products			
Bacitracin zinc/ polymyxin B sulfate	Treatment of superficial ocular infections involving the conjunctiva and/or cornea: Ophthalmic ointment: 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
Polymyxin B sulfate/ trimethoprim	Treatment of bacterial conjunctivitis, blepharoconjunctivitis and other superficial ocular infections: Ophthalmic solution: 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%
Neomycin sulfate/ polymyxin B sulfate/ bacitracin zinc	Treatment of bacterial conjunctivitis, blepharitis, blepharoconjunctivitis, keratitis and keratoconjunctivitis: Ophthalmic ointment: 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
Neomycin sulfate/ polymyxin B sulfate/ gramicidin	Treatment of bacterial conjunctivitis, blepharitis, blepharoconjunctivitis, keratitis and keratoconjunctivitis: Ophthalmic solution: 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

Clinical Guidelines

Table 9. Clinical Guidelines

Clinical Guideline	Recommendation(s)
American Academy of Ophthalmology: **Preferred Practice Pattern: Blepharitis (2011)**[24]	• 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: o Warm compresses. o Eyelid hygiene. o Antibiotics (topical and/or systemic). o Ophthalmic anti-inflammatory agents (e.g., corticosteroids, cyclosporine).

Clinical Guideline	Recommendation(s)
	• 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.
American Academy of Ophthalmology: **Preferred Practice Pattern: Conjunctivitis (2011)**[26]	Seasonal allergic conjunctivitis • Treatment of conjunctivitis is ideally directed at the root cause. Indiscriminate use of topical antibiotics or corticosteroids should be avoided because antibiotics can induce toxicity, and corticosteroids can potentially prolong adenoviral infections and worsen herpes simplex virus infections. • Treat mild allergic conjunctivitis with an over-the-counter (OTC) antihistamine/vasoconstrictor or second-generation topical histamine H_1-receptor antagonist. The guideline does not give preference to one OTC antihistamine/vasoconstrictor or antihistamine vs another. The guideline does not address the role of prescription vasoconstrictors in the management of allergic conjunctivitis.

Clinical Guideline	Recommendation(s)
	• If the condition is frequently recurrent or persistent, use mast-cell stabilizers. The guideline does not give preference to one mast-cell stabilizer vs another. • Medications with antihistamine and mast-cell stabilizing properties may be utilized for either acute or chronic disease. The guideline does not give preference to one antihistamine/mast-cell stabilizer vs another. • If the symptoms are not adequately controlled, a brief course (one to two weeks) of low-potency topical corticosteroid may be added to the regimen. The lowest potency and frequency of corticosteroid administration that relieves the patient's symptoms should be used. • Ketorolac, a nonsteroidal anti-inflammatory drug (NSAID), is also FDA approved for the treatment of allergic conjunctivitis. • Additional measures include allergen avoidance and using cool compresses, oral antihistamines and artificial tears, which dilute allergens and treat coexisting tear deficiency. Frequent clothes washing and bathing before bedtime may also be helpful. • Consultation with an allergist or dermatologist may be helpful for patients with disease that cannot be adequately controlled with topical medications and oral antihistamines. <u>Vernal/atopic conjunctivitis</u> • General treatment measures include modifying the environment to minimize exposure to allergens or irritants and using cool compresses and ocular lubricants. Topical and oral antihistamines and topical mast-cell stabilizers may be beneficial in maintaining comfort. • For acute exacerbations, topical corticosteroids are usually necessary to control severe symptoms. The minimal amount of corticosteroid should be used based on patient response and tolerance. Topical cyclosporine is effective as adjunctive therapy to reduce the amount of topical corticosteroid used to treat severe atopic keratoconjunctivitis. For entities such as vernal keratoconjunctivitis, which may require repeat short-term therapy with topical corticosteroid, patients should be informed about potential complications of corticosteroid therapy, and general strategies to minimize corticosteroid use should be discussed. • For severe sight-threatening atopic keratoconjunctivitis that is not responsive to topical therapy, systemic immunosuppression may be warranted. Eyelid involvement may be treated with pimecrolimus or tacrolimus. Patients should be told to keep these medications away from the conjunctival and corneal surface and from the tear film. Both agents are rarely associated with the development of skin cancer and lymphoma. • Frequency of follow-up visits is based on the severity of disease presentation, etiology and treatment. Consultation with a dermatologist is often helpful. If corticosteroids are prescribed, baseline and periodic measurement of intraocular pressure and papillary dilation should be performed to evaluate for glaucoma and cataract(s). <u>Mild bacterial conjunctivitis</u> • Mild bacterial conjunctivitis may be self-limited and resolve spontaneously without treatment in immunocompetent adults. • Ophthalmic antibacterial therapy is associated with earlier clinical and microbiological remission compared to placebo at days two to five of treatment. The advantages persist over six to 10 days, but the benefit

Clinical Guideline	Recommendation(s)
	over placebo lessens over time. • 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. Severe bacterial conjunctivitis • Severe bacterial conjunctivitis is 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. • Methicillin-resistant *Staphylococcus aureus* (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 *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. • If corneal involvement is present, the patient should also be treated topically for bacterial keratitis. Herpes simplex virus conjunctivitis • Topical and/or oral antiviral treatment is recommended for herpes simplex virus conjunctivitis to prevent corneal infection. • Possible options include topical ganciclovir 0.15% gel applied three to five times per day, trifluridine 1% solution applied five to eight times per day, or oral acyclovir 200 to 400 mg administered five times per day. • Oral valacyclovir and famciclovir also can be used. • Topical antiviral agents may cause toxicity if used for more than two weeks • Topical corticosteroids potentiate herpes simplex virus infection and should be avoided. • Follow-up care management within one week of treatment is advised and should include an interval history, visual acuity measurement, and slit-lamp biomicroscopy. • Neonates require prompt consultation with the pediatrician or primary care physician, because systemic herpes simplex virus infection is a life-threatening condition.
American Optometric Association: **Optometric Clinical Practice Guideline: Care of the Patient With Conjunctivitis (2007)**[77]	Allergic conjunctivitis (includes atopic keratoconjunctivitis, simple allergic conjunctivitis, seasonal or perennial conjunctivitis and vernal conjunctivitis) • The treatment of allergic conjunctivitis is based upon identification of specific antigens and elimination of specific pathogens, when practical, and upon the use of medications that decrease or mediate the immune response. The use of supportive treatment, including unpreserved lubricants and cold compresses, may provide symptomatic relief. • The following agents are useful in treating allergic conjunctivitis: topical corticosteroids (numerous products listed), vasoconstrictors/antihistamines (specific products not listed), antihistamines (azelastine, emedastine and levocabastine*), NSAIDs (ketorolac), mast cell stabilizers (cromolyn, lodoxamide, nedocromil and pemirolast), antihistamines/mast cell stabilizers (ketotifen and olopatadine) and immunosuppressants; and systemic immunosuppressants and antihistamines. • Topical corticosteroids are effective in relieving the acute symptoms of allergy; however, their use should be limited to the acute suppression of

Clinical Guideline	Recommendation(s)
	symptoms because of the potential for adverse side effects with prolonged use (e.g., cataract formation and elevated intraocular pressure). • Topical vasoconstrictors/antihistamines cause vascular constriction, decrease vascular permeability and reduce ocular itching by blocking histamine H_1 receptors. The guideline does not address the role of prescription vasoconstrictors in the management of allergic conjunctivitis. • Topical antihistamines competitively bind with histamine receptor sites and reduce itching and vasodilation. Azelastine, emedastine and levocabastine* are effective in reducing the symptoms of allergic conjunctivitis, and emedastine may be more efficacious than levocabastine*. • Topical diclofenac and ketorolac, which are both NSAIDS, are effective in reducing the signs and symptoms associated with allergic conjunctivitis, although only ketorolac is FDA approved for this indication. • Nedocromil, an effective treatment for seasonal allergic conjunctivitis, is more effective than cromolyn (2%†) in treating vernal conjunctivitis. Nedocromil was less effective than fluorometholone in treating severe vernal keratoconjunctivitis but has fewer side effects. Lodoxamide has demonstrated a greater improvement in the signs and symptoms of allergic eye disease, including vernal keratoconjunctivitis, than cromolyn (2† or 4%). Pemirolast has FDA approval as a treatment to relieve (to prevent) itching associated with allergic conjunctivitis. • Ketotifen and olopatadine are selective histamine H_1-receptor antagonists that also have mast cell stabilizing properties. Olopatadine may be more effective than other mast cell stabilizing agents in targeting the subtype of mast cell found in the conjunctiva. Compared to ketorolac or ketotifen, olopatadine is more effective in relieving the itching and redness associated with acute allergic conjunctivitis. • Systemically administered cyclosporine may be an effective treatment for patients with severe atopic keratoconjunctivitis. Topical cyclosporine is an alternative to topical corticosteroids for treatment of patients with severe atopic keratoconjunctivitis. Topical cyclosporine may also be beneficial in patients with vernal keratoconjunctivitis who have failed conventional therapy. • Systemic antihistamines are useful when the allergic response is associated with lid edema, dermatitis, rhinitis or sinusitis. They should be used with caution because of the sedating and anticholinergic effects of some first-generation antihistamines. Newer antihistamines are much less likely to cause sedation, but their use may result in increased ocular surface dryness. <u>Viral conjunctivitis</u> • Most viral conjunctivitis is related to adenoviral infection; however, no antiviral agent has been demonstrated to be effective in treating these infections. • Topical NSAID therapies have shown no benefit in reducing viral replication, decreasing the incidence of sub-epithelial infiltrates, or alleviating symptoms. • Topical antibiotics are not routinely used to treat viral conjunctivitis, unless there is evidence of secondary bacterial infection.

Clinical Guideline	Recommendation(s)
	• The treatment of herpes simplex conjunctivitis may include the use of antiviral agents such as trifluridine, although there is no evidence that this therapy results in a lower incidence of recurrent disease or keratitis. • Supportive therapy, including lubricants and cold compresses, which may be as effective as antiviral drugs, eliminates the potential for toxic side effects. • Topical steroids are specifically contraindicated for treating herpes simplex conjunctivitis.
American Academy of Ophthalmology: **Preferred Practice Pattern: Bacterial Keratitis (2011)**[27]	Initial treatment • 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 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: o 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). o Gram-positive cocci: ophthalmic cefazolin sodium, vancomycin (for resistant *Enterococcus* and *Staphylococcus* species and penicillin allergy), ophthalmic bacitracin (for resistant *Enterococcus* and *Staphylococcus* species and penicillin allergy) or ophthalmic fluoroquinolones (fewer gram-positive cocci are resistant to gatifloxacin and moxifloxacin hydrochloride than other fluoroquinolones). o Gram-negative rods: ophthalmic formulations of tobramycin or gentamicin sulfate, ceftazidime or fluoroquinolones. o Gram-negative cocci: ophthalmic ceftazidime, ceftriaxone sodium or fluoroquinolones (systemic therapy is necessary for suspected gonococcal infection). o Nontuberculous mycobacteria: ophthalmic amikacin sulfate, azithromycin, clarithromycin or fluoroquinolones. o 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 FDA-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. • Some pathogens (e.g., *Streptococci*, 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

Clinical Guideline	Recommendation(s)
	reported in association with laser in situ keratomileusis. • 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. <u>Modification of therapy</u> • 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. <u>Corticosteroid therapy</u> • 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 corticosteroids can reduce morbidity. • 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

Clinical Guideline	Recommendation(s)
	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.
American Academy of Ophthalmology: **Preferred Practice Pattern: Refractive Errors and Refractive Surgery (2012)**[28]	Surface ablation techniques • 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 NSAID 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. Laser in situ keratomileusis • 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. • Symptoms of post-laser in situ keratomileusis epitheliopathy (reduced best corrected visual acuity, fluctuating vision, foreign-body sensation and discomfort) typically improve with time, but in certain cases they may persist for months or years. Supplemental lubrication, topical cyclosporine eye drops and punctal occlusion may be helpful in such cases. • Diffuse lamellar keratitis is a noninfectious aggregation of inflammatory cells, and treatment is commonly guided by the severity of the inflammation. Increasing the frequency of topical corticosteroid administration with a closer follow-up is practiced by most surgeons.
American Academy of Ophthalmology: **Preferred Practice Pattern: Cataract in the Adult Eye (2011)**[29]	Infection prophylaxis • Two emerging concerns are the increasing resistance of *Staphylococcus* species (the most common cause of endophthalmitis) to a broad spectrum of antibiotics, including the latest generation fluoroquinolones, and the increased occurrence of acute endophthalmitis more than a week after surgery. • 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.

Clinical Guideline	Recommendation(s)
	• 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. Postoperative follow-up • 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 intraocular pressure with corticosteroids and allergic reactions to antibiotics. Significant corneal reactions, including epithelial defects and stromal ulceration and melting, have rarely been reported with topical NSAIDs. Cystoid macular edema • 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.
American Optometric Association: **Care of the Adult Patient with Cataract (2004)**[30]	• A combination of topical and oral anti-glaucoma, 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 two to four hours depending on the degree of inflammation.

*Product is not available in the United States.
†Cromolyn 4% but not 2% is available in the United States. The concentrations of cromolyn that were used in the original clinical studies are noted in this table.

Conclusions

Ophthalmic antibiotics are used to treat ophthalmic infections, including blepharitis, conjunctivitis, keratitis as well as several others. Ophthalmic antibiotics are available from the aminoglycoside, macrolide, polypeptide, quinolone, sulfonamide and miscellaneous antibiotic drug classes. These agents are available as single-entity agents or in combination with ophthalmic antibiotics or ophthalmic steroids. All ophthalmic antibiotics that are currently available on the market are approved for the treatment of bacterial conjunctivitis.[1-22] For all of the all indications listed in Table 2, there is at least one generic option available for treatment.[22]

The results from head-to-head studies do not consistently show any one ophthalmic antibiotic as significantly more effective than another with regard to bacterial eradication, clinical resolution, clinical response, severity rating or symptom improvement for any indication.[36,39,42-52,65,66,68,74,75] 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.[31-76]

The majority of ophthalmic antibiotic medications have been studied in pediatric populations one year of age and older, 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] 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.[1-22]

Guidelines published by the American Academy of Ophthalmology recommends 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.[24] 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 an ophthalmic fluoroquinolone is recommended. The American Academy of Ophthalmology guideline also notes that fewer gram-positive cocci are resistant to ophthalmic gatifloxacin and moxifloxacin hydrochloride.[27] 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.[26] Short-term use of ophthalmic corticosteroids are recommended by treatment guidelines to reduce inflammation in the treatment of blepharitis, conjunctivitis, keratitis and in postoperative prophylaxis.[24,26-30]

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