Therapeutic Class Overview
Ophthalmics, Antibiotics, and Combinations

INTRODUCTION

- Blepharitis is a chronic inflammatory condition of the eyelids, often presenting with 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 being *Staphylococcus* species. The mainstay of the treatment of blepharitis is patient education regarding eyelid hygiene as well as the use of ophthalmic antibiotics. Of note, blepharitis is a chronic condition without definitive cure; therefore, satisfactory results require a long-term commitment to treatment and appropriate expectations. Ophthalmic corticosteroids may also be used acutely to treat exacerbations (*American Academy of Ophthalmology [AAO] 2018b*).
- Bacterial conjunctivitis rarely causes permanent visual loss or structural damage, as mild cases may be self-limited, and will resolve without treatment in immunocompetent individuals. The most common causative pathogens seen with bacterial conjunctivitis include *Staphylococcus (S.) aureus, Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*. 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 (*AAO 2018c; American Optometric Association [AOA] 2007*).
- 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 *S. 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 (N.) gonorrhoeae* and *Chlamydia (C.) trachomatis*, systemic antibiotic therapy is necessary, and while not necessary, ophthalmic antibiotics are also typically used (*AAO 2018c; AOA 2007*).
- 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. Due to corneal scarring or topographic irregularity, many forms of this infection result 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 severe cases, patients should be followed daily until stabilization or clinical improvement is documented (*AAO 2018a*).
- Though not Food and Drug Administration (FDA)-approved for this indication, 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 (*AAO 2016; AAO 2017; AOA 2004*).
- Ophthalmic antibiotic and steroid combinations are included in this review.
- Medispan class: Ophthalmic Antibiotics, Ophthalmic Anti-infective Combinations, Ophthalmic Sulfonamides, and Ophthalmic Steroid Combinations.

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Aminoglycosides	
Gentak (gentamicin)* ointment & solution	✔
Tobrex (tobramycin) ointment & solution	✔ †
Macrolides	
Azasite (azithromycin) solution	-
erythromycin ointment	✔
Other	
Bacitracin ointment	✔
Bleph-10 (sulfacetamide sodium)§ ointment & solution	✔
Quinolones	
Besivance (besifloxacin) suspension	-
Ciloxan (ciprofloxacin) ointment & solution	✔ †
levofloxacin solution	✔
Moxeza, Vigamox (moxifloxacin) solution	✔ ‖
Ocuflox (ofloxacin) solution	✔
Zymaxid (gatifloxacin) solution	✔
Combinations	
Neo-Polycin (bacitracin/neomycin/polymyxin) ointment	✔
Neo-Polycin HC (bacitracin/neomycin/polymyxin/hydrocortisone) ointment	✔
AK-Poly-Bac, Polycin (bacitracin/polymyxin) ointment	✔
Blephamide (sulfacetamide/prednisolone 10-0.2%) ointment & suspension	-
sulfacetamide/prednisolone 10-0.23% (0.25%) solution	✔
Maxitrol (neomycin/polymyxin/dexamethasone) ointment & suspension	✔
neomycin/polymyxin/hydrocortisone suspension	✔
gramicidin/neomycin/polymyxin solution	✔
Pred-G (gentamicin/prednisolone) ointment & suspension	-
Polytrim (polymyxin/trimethoprim) solution	✔
Tobradex (tobramycin/dexamethasone 0.3-0.1%) ointment & suspension	✔ **
Tobradex ST (tobramycin/dexamethasone 0.3-0.05%) suspension	-
Zylet (tobramycin/loteprednol) suspension	-

*Gentak is a branded generic of gentamicin ophthalmic ointment.
†Solution only
§Brand name Bleph-10 is available in solution only; generics are available for solution and ointment.
‖Multiple generic versions of Vigamox are available; a single generic version of Moxeza is available.
**Suspension only

(*Drugs@FDA, 2020; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2020; Drug Facts and Comparisons, 2020; Clinical Pharmacology, 2020*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Agents within this review that contain ocular corticosteroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of corticosteroid use in certain infective conjunctivitis is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns; or penetration of foreign bodies.

Indication	Aminoglycosides		Macrolides		Other		Quinolones							Combinations										
	gentamicin	tobramycin	Azasite	erythromycin	bacitracin	sulfacetamide	ciprofloxacin	levofloxacin	ofloxacin	Besivance	Moxeza	Vigamox	Zymaxid	bacitracin/neomycin/polymyxin	bacitratin/neomycin/polymyxin/hydrocortisone	bacitracin/polymyxin	Blephamide	Maxitrol	neomycin/polymyxin/hydrocortisone	gramicidin/neomycin/polymyxin	Pred-G	polymyxin/trimethoprim	Tobradex; Tobradex ST	Zylet
Treatment of bacterial conjunctivitis			✔				✔	✔	✔	✔	✔	✔	✔											
Treatment of corneal ulcers							✔ †		✔															
Treatment of external infections of the eye and its adnexa caused by susceptible bacteria		✔												✔		✔ *				✔				
Treatment of superficial ocular infections involving the conjunctiva and/or cornea				✔	✔											✔ ‖								
Prophylaxis of ophthalmia neonatorum due to *N. gonorrhoeae* or *C. trachomatis*				✔ §																				
Treatment of ocular bacterial infections including conjunctivitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharitis, blepharoconjunctivitis, acute meibomianitis, and dacryocystitis	✔																							

Indication	Aminoglycosides		Macrolides		Other		Quinolones							Combinations										
	gentamicin	tobramycin	Azasite	erythromycin	bacitracin	sulfacetamide	ciprofloxacin	levofloxacin	ofloxacin	Besivance	Moxeza	Vigamox	Zymaxid	bacitracin/neomycin/polymyxin	bacitratin/neomycin/polymyxin/hydrocortisone	bacitracin/polymyxin	Blephamide	Maxitrol	neomycin/polymyxin/hydrocortisone	gramicidin/neomycin/polymyxin	Pred-G	polymyxin/trimethoprim	Tobradex; Tobradex ST	Zylet
Treatment of surface ocular infections, including acute bacterial conjunctivitis and blepharoconjunctivitis																						✔		
Treatment of conjunctivitis and other superficial ocular infections						✔																		
Adjunctive treatment with systemic treatment for trachoma						✔ †																		
Steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial ocular infection or a risk of bacterial ocular infection exists															✔		✔	✔	✔		✔		✔	✔

†solution only

§ The effectiveness of erythromycin in the prevention of ophthalmia caused by penicillinase-producing *N. gonorrhoeae* is not established.

*Polycin brand only

‖generic and AK-Poly-Bac brand only

(*Prescribing information: AK-Poly-Bac 2018; Azasite, 2017; bacitracin, 2019; bacitracin/neomycin/polymyxin, 2016; bacitracin/neomycin/polymyxin/hydrocortisone, 2016; bacitracin/polymyxin, 2020; Besivance, 2020; Bleph-10, 2017; Blephamide ointment, 2018; Blephamide suspension, 2017; Ciloxan ointment, 2019; Ciloxan solution, 2019; erythromycin, 2018; Gentak, 2017; gentamicin, 2017; levofloxacin, 2017; Maxitrol suspension, 2019; Maxitrol ointment, 2019; Moxeza, 2019; Neo-Polycin 2018; Neo-Polycin HC 2018; neomycin/polymyxin/gramicidin 2016; neomycin/polymyxin/hydrocortisone, 2019; Ocuflox, 2017; Polycin 2018; polymyxin/trimethoprim, 2020; Polytrim, 2019; Pred-G ointment, 2018; Pred-G suspension, 2018; sulfacetamide ointment, 2018; sulfacetamide solution, 2016; sulfacetamide/prednisolone solution, 2016; Tobradex ointment, 2020; Tobradex suspension, 2020; Tobradex ST, 2019; tobramycin 2020; Tobrex ointment, 2020; Tobrex solution, 2020; Vigamox, 2019; Zylet, 2019; Zymaxid, 2016*)

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

Antibiotics

- Clinical trials have demonstrated that ophthalmic antibiotics are effective in treating and providing relief of bacterial conjunctivitis in pediatric and adult patients (*Abelson et al 2007; Abelson et al 2008; Bremond-Gignac et al 2014; Cochereau et al 2007; DeLeon et al 2012; Gross et al 1997; Hwang et al 2003; Karpecki et al 2009; Kernt et al 2005; McDonald et al, 2009; Schwab et al 2003; Sheikh et al 2012; Silver et al 2005; Silverstein et al 2011; Silverstein et al, 2012; Tauber et al 2011; Tepedino et al 2009; Williams et al 2013*). Several studies comparing ophthalmic antibiotics such as azithromycin, besifloxacin, levofloxacin, and moxifloxacin to placebo have concluded that these medications resulted in significantly higher clinical resolution rates at days 1 through 5 (*Abelson et al 2008; DeLeon et al 2012; Hwang et al 2003; Karpecki et al 2009; Silverstein et al 2011; Tauber et al 2011; Tepedino et al 2009*).
  - One clinical trial demonstrated that there was no difference in clinical cure rate between treatment with ophthalmic polymyxin B/trimethoprim and ophthalmic moxifloxacin in treating conjunctivitis in children (p = 0.59) (*Williams et al 2013*). In a 5-day trial, a higher percentage of patients receiving levofloxacin had microbial eradication at the final visit compared to patients receiving ofloxacin for the treatment of bacterial conjunctivitis (p = 0.034); however, clinical cure rates were similar between the 2 treatments (p value not reported) (*Schwab 2003*).
  - 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 (*Ableson et al 2007; Cochereau et al 2007, Gross et al 1997; McDonald et al 2009; Sanfilippo et al 2017; Silver et al 2005*). 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 (*Abelson et al 2007*). 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 (*Abelson et al 2007; Cochereau et al 2007; Gross et al 1997; McDonald et al 2009; Schwab et al 2003; Silver et al 2005; Williams et al 2013*).
  - 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 gentamicin, levofloxacin, ofloxacin, and tobramycin solution were efficacious in resolving or curing multiple ocular infections (*Gwon 1992 Sep; Gwon 1992 Dec; Kanda et al 2012*). 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 3 through 5 in patients with conjunctival hyperemia, eyelid crusting or discharge, and positive bacterial culture when compared to ophthalmic tobramycin ($p < 0.05$); however, by day 11, there were no significant differences between the 2 treatments with regard to clinical, microbial, and overall improvement rates (*Gwon 1992 Sep*). 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 *N. 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 0 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) (*Bell et al 1993*). 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 2 weeks of life when compared to no prophylaxis (18.4 vs 22.4%; p = 0.03) (*Ali et al 2007*).

Antibiotic-steroid combinations

- Clinical trials have demonstrated that ophthalmic antibiotic-steroid combination products are effective in treating patients with external ocular infections, including bacterial blepharitis, conjunctivitis, and blepharokeratoconjunctivitis (*Rhee et al 2007; Shulman et al 1996; White et al 2008*).
  - In one study involving patients with moderate blepharokeratoconjunctivitis, reductions in blepharitis and conjunctivitis symptom scores were greater with ophthalmic tobramycin/dexamethasone therapy compared to ophthalmic tobramycin/loteprednol therapy, while the reductions in keratitis symptom scores were similar between the 2 treatment groups (*Rhee et al 2007*).

- In another study, the reduction in composite symptom scores in patients with blepharokeratoconjunctivitis was similar between the tobramycin/dexamethasone and tobramycin/loteprednol groups; however, the increase in intraocular pressure was significantly greater with tobramycin/dexamethasone than tobramycin/loteprednol (White et al 2008). Another pooled analysis of data from 2 trials in patients with blepharokeratoconjunctivitis who were randomized to either tobramycin/dexamethasone or tobramycin/loteprednol found similar effects on blepharitis severity; however, tobramycin/loteprednol demonstrated a better safety profile with respect to intraocular pressure (Comstock 2017).
- Another study involving patients with moderate to severe acute blepharitis/blepharoconjunctivitis showed initial therapy with the combination of tobramycin/dexamethasone ST provides faster inflammation relief than ophthalmic azithromycin based on a statistically significant lower mean global score ($p = 0.0002$) (Torkildsen et al 2011).
- One study showed that when compared to dexamethasone alone, neomycin/polymyxin B/dexamethasone resulted in significantly greater bacterial eradication and decrease in bacterial count in patients with bacterial blepharitis or conjunctivitis; however, the reduction in signs and symptoms of ocular infection was similar between the 2 treatment groups (Shulman et al 1996).
- In a 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 3, 8, 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 8, 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 8 ($p < 0.05$) (Notivol et al 2004).
- 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 6 and 8 ($p = 0.033$); however, there was no significant difference between the 2 groups with regard to the degree of intraocular inflammation or the global assessment of the success of therapy and local tolerance (p value not reported) (Van Endt et al 1997). 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 3, 8, 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 8, 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 8 ($p < 0.05$) (Notivol et al 2004).

CLINICAL GUIDELINES

- The AAO preferred practice pattern (PPP) states that bacterial keratitis should be treated with an ophthalmic antibiotic that may be selected based on the isolated organism; if no organism is identified, treatment with cefazolin or vancomycin plus either gentamicin or tobramycin or an ophthalmic fluoroquinolone alone is recommended. The AAO guideline also notes that fewer gram-positive cocci are resistant to ophthalmic gatifloxacin, moxifloxacin, and besifloxacin than other fluoroquinolones. Topical antibiotic eye drops are capable of achieving high tissue levels and are the preferred method of treatment in most cases. Ocular ointments may be useful at bedtime in less severe cases and may be useful for adjunctive therapy. Ointments lack solubility and are not able to penetrate into the cornea significantly for optimum therapeutic benefit (*AAO 2018a*).
- The AAO PPP recommends that initial treatment of blepharitis is to use warm compresses on the eyelids and incorporate eyelid cleansing, with or without hypochlorous acid based cleansers, and eyelid massage. The AAO PPP also states that topical ophthalmic antibiotics such as bacitracin or erythromycin ointments may reduce symptoms of blepharitis; the guideline also notes that tobramycin/dexamethasone ophthalmic suspension and ophthalmic azithromycin have been shown to reduce some signs and symptoms of blepharitis. To prevent resistance, topical antibiotics with different mechanisms of action can be used intermittently if needed (*AAO 2018b*).
- For the treatment of bacterial conjunctivitis, the AAO PPP states that indiscriminate use of topical antibiotics or corticosteroids should be avoided, because antibiotics can induce toxicity and corticosteroids can potentially prolong or worsen some infections. If treatment is warranted, it is recommended that the least expensive or most convenient broad-spectrum topical antibiotic be selected for a 5- to 7-day course of treatment. Systemic antibiotic therapy is necessary to treat conjunctivitis due to *N. gonorrhoeae* and *C. trachomatis*, and topical therapy may be used concomitantly (*AAO 2018c; AOA 2007*).

- Short-term use of ophthalmic corticosteroids is recommended to reduce inflammation in the treatment of blepharitis, conjunctivitis, and keratitis, and can be considered in postoperative prophylaxis (*AAO 2016; AAO 2018a; AAO 2018b; AAO 2018c*).
- The AAO cataract in the adult eye PPP states that postoperative regimens of topically applied antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), and oral analgesic agents vary among practitioners. There are no controlled investigations that establish optimal regimens for the use of topical agents. Therefore, it is the decision of the operating surgeon to use any or all of these products singly or in combination (*AAO 2016*).
- The United States Preventative Services Task Force (USPSTF) recommends ophthalmia neonatorum prophylaxis with erythromycin ophthalmic ointment for all newborns (*USPSTF 2019*).

SAFETY SUMMARY

- Products are contraindicated if there is a hypersensitivity to any component.
- Warnings/precautions of anti-infective agents include the following: 1) do not wear contact lenses while infected; 2) prolonged use may result in overgrowth of non-susceptible organisms, including fungi; and 3) cutaneous sensitization may occur with products containing neomycin.
  - The most frequent adverse effects were burning, stinging, and irritation upon instillation, redness, blurred vision, itching, swelling, tearing, eye pain, and photophobia. Non-ocular reactions can occur and include headache, pharyngitis, dizziness, and allergic reactions.
- Prolonged use of corticosteroids may result in the following: development of glaucoma, corneal or scleral thinning which can lead to perforation, suppression of host response causing secondary infection, and/or purulent infections of the eye may be masked or activity enhanced.
  - If using these products for longer than 10 days, IOP should be monitored. Use after cataract surgery may delay healing.
  - Blephamide (sulfacetamide/prednisolone) may cause acute anterior uveitis in susceptible individuals. The p-aminobenzoic acid present in purulent exudates competes with sulfonamides and can reduce their effectiveness.
- Reactions occurring most often from the presence of the anti-infective ingredient are allergic sensitization reactions including itching, swelling, and conjunctival erythema. The reactions due to the corticosteroid component are elevation of IOP with possible development of glaucoma, and infrequent optic nerve damage; posterior subcapsular cataract formation; and delayed wound healing.
- These agents are minimally absorbed; therefore, drug interactions are not likely to occur.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Usual Recommended Frequency	Comments
Azasite (azithromycin)	Ophthalmic solution: 1%	Twice daily, 8 to 12 hours apart for the first 2 days, then once daily for the next 5 days	Safety and efficacy have not been established in children < 1 year of age.
Bacitracin	Ophthalmic ointment: 500 units/gram	Apply directly into the conjunctival sac 1 to 3 times daily	No data in pediatric patients.
Besivance (besifloxacin)	Ophthalmic suspension: 0.6%	Three times daily, 4 to 12 hours apart for 7 days	Safety and efficacy have not been established in children < 1 year.
Bleph-10 (sulfacetamide sodium)	Ophthalmic ointment: 10% Ophthalmic solution: 10%	**Ointment**: every 3 to 4 hours and at bedtime for 7 to 10 days **Solution**: every 2 to 3 hours for 7 to 10 days *Trachoma*: every 2 hours; must also use systemic administration	Safety and efficacy have not been established in infants < 2 months of age.
Ciloxan (ciprofloxacin)	Ophthalmic ointment: 0.3% Ophthalmic solution: 0.3%	**Corneal ulcers**: *Solution*: every 15 minutes for the first 6 hours, every 30 minutes for the remainder of the first day. Second day: every hour	**Ointment**: Safety and efficacy have not been established in children < 2 years of age. **Solution**: Safety and efficacy have been established in all

Drug	Available Formulations	Usual Recommended Frequency	Comments
		Third through 14th day: every 4 hours **Conjunctivitis**: *Ointment*: 3 times daily for first 2 days, then twice daily for the next 5 days *Solution*: every 2 hours while awake for 2 days, then every 4 hours while awake for next 5 days	ages.
Erythromycin	Ophthalmic ointment: 0.5%	**Superficial infections**: Apply directly to the infected structure up to 6 times daily, depending on the severity of the infection. **Prophylaxis of neonatal gonococcal or chlamydial conjunctivitis:** apply into each lower conjunctival sac.	For neonates: The ointment should not be flushed from the eye following instillation.
Gentak (gentamicin)	Ophthalmic ointment: 0.3% Ophthalmic solution: 0.3%	**Ointment**: 2 or 3 times a day **Solution**: every 4 hours *Severe infections:* dosage may be increased to as much as every hour.	Safety and efficacy in neonates have not been established.
Levofloxacin	Ophthalmic solution: 0.5%*	Every 2 hours while awake, up to 8 times per day on days 1 and 2, then every 4 hours while awake, up to 4 times per day for days 3 to 7	Safety and efficacy have not been established in children < 6 year of age.
Moxeza, Vigamox (moxifloxacin)	Ophthalmic solution: 0.5% (Moxeza - twice daily formulation), 0.5% (Vigamox - 3 times daily formulation)	**Moxeza**: twice daily for 7 days **Vigamox**: 3 times daily for 7 days	**Moxeza**: Safety and efficacy have not been established in infants < 4 months of age. **Vigamox**: Safety and efficacy have been established in all ages.
Ocuflox (ofloxacin)	Ophthalmic solution: 0.3%	**Conjunctivitis**: every 2 to 4 hours days 1 and 2, then 4 times daily for days 3 through 7 **Corneal ulcers:** *Days 1 and 2*: every 30 minutes, while awake *Days 3 through 7 to 9*: hourly, while awake *Days 7 to 9 through treatment completion*: 4 times daily	Safety and efficacy have not been established in children < 1 year of age.
Tobrex (tobramycin)	Ophthalmic ointment: 0.3% Ophthalmic solution: 0.3%	**Ointment**: *Mild to moderate disease*: 2 or 3 times a day *Severe infections*: every 3 to 4 hours until improvement, following which treatment should be reduced prior to discontinuation. **Solution**: *Mild to moderate disease*: every 4 hours *Severe infections*: hourly until improvement, following which	Safety and efficacy have not been established in infants < 2 months of age.

Drug	Available Formulations	Usual Recommended Frequency	Comments
		treatment should be reduced prior to discontinuation	
Zymaxid (gatifloxacin)	Ophthalmic solution: 0.5%	Every 2 hours while awake up to 8 times on day 1, then 2 to 4 times per day while awake on days 2 through 7	Safety and efficacy have not been established in children < 1 year of age.
Combinations			
bacitracin/ neomycin/ polymyxin	Ophthalmic ointment: bacitracin zinc 400 units, neomycin 3.5 mg, polymyxin B sulfate 10,000 units per gram	Every 3 or 4 hours for 7 to 10 days, depending on the severity of the infection	Safety and efficacy have not been established in pediatric patients.
bacitracin/ neomycin/ polymyxin/ hydrocortisone	Ophthalmic ointment: bacitracin zinc 400 units/neomycin sulfate 3.5 mg/polymyxin B sulfate 10,000 units/hydrocortisone 10 mg per gram	Every 3 or 4 hours depending on the severity of the condition	Not more than 8 grams should be prescribed initially.
Blephamide (sulfacetamide/ prednisolone)	Ophthalmic ointment: sulfacetamide 10%/ prednisolone 0.2% Ophthalmic suspension: sulfacetamide 10%/ prednisolone 0.2%	**Ointment** Apply 3 or 4 times daily and once or twice at night to the conjunctival sac(s) **Suspension** Every 4 hours during the day and at bedtime into the conjunctival sac(s)	Ointment: Not more than 8 grams should be prescribed initially. Suspension: Not more than 20 mL should be prescribed initially; shake well before using.
gramicidin/ neomycin/ polymyxin	Ophthalmic solution: neomycin sulfate 1.75 mg, polymyxin B sulfate 10,000 units, gramicidin 0.025 mg per mL	Every 4 hours for 7 to 10 days *Severe infections*: may increase to every hour	Safety and efficacy have not been established in pediatric patients.
Maxitrol (neomycin/ polymyxin/ dexamethasone)	Ophthalmic ointment: neomycin 3.5 mg/ polymyxin B sulfate 10,000 units/dexamethasone 0.1% per gram Ophthalmic suspension: neomycin 3.5 mg/polymyxin B sulfate 10,000 units/ dexamethasone 0.1% per mL	**Ointment** Up to 3 or 4 times daily into the conjunctival sac(s) **Suspension** *Mild disease:* Up to 4 to 6 times daily in the conjunctival sac(s) *Severe disease*: Drops may be used hourly, being tapered to discontinuation as the inflammation subsides.	Ointment: Not more than 8 grams should be prescribed initially. Suspension: Not more than 20 mL should be prescribed initially.
neomycin/ polymyxin/ hydrocortisone	Ophthalmic suspension: neomycin sulfate 3.5 mg/polymyxin B sulfate 10,000 units/hydrocortisone10 mg per mL	Every 3 to 4 hours into the affected eye(s) depending on the severity of the infection	Not more than 20 mL should be prescribed initially.
Polysporin (bacitracin/ polymyxin)	Ophthalmic ointment: bacitracin zinc 500 units, polymyxin B sulfate 10,000 units per gram	Every 3 or 4 hours for 7 to 10 days, depending on the severity of the infection	No data in pediatric patients.

Drug	Available Formulations	Usual Recommended Frequency	Comments
Polytrim (polymyxin/ trimethoprim)	Ophthalmic solution: polymyxin B sulfate 10,000 units, trimethoprim 1 mg per mL	*Mild to moderate infections*: Every 3 hours (maximum of 6 doses per day) for a period of 7 to 10 days	Safety and efficacy have not been established in infants < 2 months of age.
Pred-G (gentamicin/ prednisolone)	Ophthalmic ointment: gentamicin 0.3%/ prednisolone acetate 0.6% Ophthalmic suspension: gentamicin 0.3%/ prednisolone acetate 1%	**Ointment** Apply 1 to 3 times daily in the conjunctival sac(s) **Suspension** Instill 2 to 4 times daily into the conjunctival sac(s). During the initial 24 to 48 hours, the dosing may be increased up to every hour.	Ointment: Not more than 8 grams should be prescribed initially. Suspension: Not more than 20 mL should be prescribed initially.
Tobradex, Tobradex ST (tobramycin/ dexamethasone)	Ophthalmic ointment: tobramycin 0.3%/ dexamethasone 0.1% Ophthalmic suspension: tobramycin 0.3%/ dexamethasone 0.1% Ophthalmic ST suspension: tobramycin 0.3%/ dexamethasone 0.05%	**Ointment** Up to 3 or 4 times daily into the conjunctival sac(s) **Suspension** Every 4 to 6 hours into the conjunctival sac(s); during the initial 24 to 48 hours, the dosage may be increased to every 2 hours **ST Suspension** Every 4 to 6 hours into the conjunctival sac(s); during the initial 24 to 48 hours, the dosage may be increased to every 2 hours	Ointment: Not more than 8 grams should be prescribed initially. Suspension, ST Suspension: Not more than 20 mL should be prescribed initially. Shake well before using.
Zylet (tobramycin/ loteprednol)	Ophthalmic suspension: tobramycin 0.3%/ loteprednol etabonate 0.5%	Every 4 to 6 hours into the conjunctival sac(s); during the initial 24 to 48 hours, the dosing may be increased to every 1 to 2 hours	Not more than 20 mL should be prescribed initially. Shake vigorously before using.

*A generic levofloxacin 1.5% ophthalmic solution was approved in February 2019 by the FDA; however, it is not available at this time. The branded 1.5% solution has been discontinued, and no other generics of this strength are currently approved.

See the current prescribing information for full details

CONCLUSION

- Ophthalmic antibiotics are used to treat ophthalmic infections, including blepharitis, conjunctivitis, and keratitis as well as several others. Classes of ophthalmic antibiotics include aminoglycosides, macrolides, quinolones, and other miscellaneous and combination products. For all FDA-approved indications, but not all products, a generic ophthalmic antibiotic is available.
- Ophthalmic antibiotic-steroid combination products are indicated for the treatment of steroid-responsive ocular inflammatory conditions where the presence or risk of a superficial bacterial ocular infection exists. At least 1 generic is available in each formulation: ointment, solution, and suspension.
- In comparative clinical trials, no one ophthalmic antibiotic has been shown to be more effective than another in bacterial eradication, clinical resolution, clinical response, or symptom improvement and no one ophthalmic antibiotic-steroid combination product has been shown to be more effective than another with regard to symptom improvement or reduction of postoperative inflammation.
- In clinical 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.
- Ophthalmic antibiotics and combinations 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. Steroid-containing ophthalmic products

may also increase the risk of IOP elevation, cataract formation, and delayed healing after cataract surgeries, and should be used with caution.

- Guidelines published by the AAO recommend that topical ophthalmic antibiotics such as bacitracin or erythromycin ointments may be used to reduce symptoms of blepharitis; the guideline also notes that tobramycin/dexamethasone ophthalmic suspension and ophthalmic azithromycin have been shown to reduce some signs and symptoms of blepharitis. To prevent resistance, topical antibiotics with different mechanisms of action can be used intermittently if needed (*AAO 2018b*).
- Guidelines state that keratitis should be treated with an ophthalmic antibiotic that may be selected based on the isolated organism, and if no organism is identified, treatment with cefazolin or vancomycin plus either gentamicin or tobramycin or an ophthalmic fluoroquinolone alone is recommended. The AAO guideline also notes that fewer gram-positive cocci are resistant to ophthalmic gatifloxacin, moxifloxacin, and besifloxacin than other fluoroquinolones (*AAO 2018a*).
- For the treatment of bacterial conjunctivitis, indiscriminate use of topical antibiotics or corticosteroids should be avoided, because antibiotics can induce toxicity and corticosteroids can potentially prolong or worsen some infections. If treatment is warranted, it is recommended that the least expensive or most convenient broad-spectrum antibiotic be selected for a 5- to 7-day course of treatment, if needed. Systemic antibiotic therapy is necessary to treat conjunctivitis due to *N.gonorrhoeae* and *C. trachomatis*, and topical therapy may be used concomitantly (*AAO 2018c; AOA 2007*).
- Short-term use of ophthalmic corticosteroids is recommended by treatment guidelines to reduce inflammation in the treatment of blepharitis, conjunctivitis, and keratitis and can be considered in postoperative prophylaxis (*AAO 2016; AAO 2018a; AAO 2018b; AAO 2018c*).
- The AAO cataract practice pattern states that postoperative regimens of topically applied antibiotics, corticosteroids, NSAIDs, and oral analgesic agents vary among practitioners. There are no controlled investigations that establish optimal regimens for the use of topical agents (*AAO 2016*).

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