AN ONGOING CE PROGRAM of the University of Connecticut School of Pharmacy

EDUCATIONAL OBJECTIVES

After participating in this activity pharmacists will be able to:
- DISCUSS common ocular condition’s pathophysiology and causes
- IDENTIFY recent changes in available medications to treat ocular conditions
- DISTINGUISH each FDA-approved product by the condition that it treats
- DISCUSS barriers to care, adherence, and administration of eye drop waste
- MAXIMIZE the pharmacist’s role in identifying OTC products, referring patients for prescription strength medication, and counseling patients about both

After participating in this activity, pharmacy technicians will be able to:
- LIST basic facts about ocular conditions
- IDENTIFY reputable sources for patients who have ocular conditions to find information
- DIFFERENTIATE between over-the-counter and prescription drugs for ocular conditions
- IDENTIFY patients who need referral to the pharmacist for recommendations or referral

ABSTRACT: Ocular problems—many of which cause severe vision loss or blindness—are on the rise in the US. Common eye diseases include glaucoma, age-related macular degeneration, dry eye, conjunctivitis and blepharitis. Pharmacy staff may be the first providers a patient approaches to consult about an eye condition since many treatment options are available over-the-counter. Armed with knowledge of ophthalmic conditions and treatments, pharmacists can determine if patients are candidates for self-treatment, evaluate the appropriateness of pharmacotherapy, screen for medication-induced eye disorders, and promote proper medication adherence. Patients often use ophthalmic products; patient education should be a top priority for pharmacy staff.

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FACULTY DISCLOSURE: Drs. Nigro and Haftel have no actual or potential conflicts of interest associated with this article.

DISCLOSURE OF DISCUSSIONS of OFF-LABEL and INVESTIGATIONAL DRUG USE: This activity may contain discussion of off-label/unapproved use of drugs. The content and views presented in this educational program are those of the faculty and do not necessarily represent those of the University of Connecticut School of Pharmacy. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

INTRODUCTION

Ocular problems—many of which may cause severe vision loss or blindness—are on the rise in the US. A change in vision is common. Sensitivity to light and the need to wear glasses to see near or far are expected parts of aging. However, the development of certain age-related eye diseases including cataracts, diabetic retinopathy, glaucoma, and macular degeneration can significantly impair vision, further reducing quality of life and independence. Currently, 1.3 million people in the US are blind and more than $139 billion in healthcare costs are related to ocular problems. As the population continues to age, these numbers are expected to worsen.

Pharmacy staff may be the first providers a patient approaches to consult about his or her eye condition. Yet, many pharmacists and other healthcare providers express lack of confidence caring for patients with ocular conditions. With improved ophthalmic knowledge, pharmacists can help patients navigate overcrowded over-the-counter (OTC) aisles, understand proper use of eye care products, and improve overall satisfaction with their care.
EYE ANATOMY

The eye is the organ of sight. Although it is small, measuring one inch in diameter, the eye is composed of various muscles, nerves and structures. (See Figure 1) Normal vision relies on the coordinated interplay between the eye and brain to transform light into visual images.² The eye is often compared to a digital camera, since both transmit and focus light to create a picture. Here is a brief overview of the most common structural components and their functions:

- **Conjunctiva** - A thin layer of tissue and blood vessels located in the front of the eye to keep bacteria and foreign particles out of the eye.
- **Cornea** – A clear layer located in front of the iris to help transmit and focus light as it enters the eye.
- **Eyelid** – A thin fold of skin responsible for protecting the eye and keeping the cornea moist.
- **Eye lashes** – Fine hairs that grow at the base of the eyelid to protect the eye from foreign objects and particles.
- **Iris** – A ring shaped tissue with a central opening (pupil) that helps control the amount of light that enters the eye. It is the colored part of the eye.
- **Lens** – A crystalline, bendable structure located behind the iris and pupil that works with the cornea to automatically focus light onto the retina.
- **Macula** – A small, central area of the retina that contains specialized cells to see sharp, fine details through central vision.
- **Retina** – A light-sensing layer of nerves that line the back of the eye to convert optical images into electrical signals.
- **Optic disc** – A round area in the back of the eye where the optic nerve leaves the retina.
- **Optic nerve** – A grouping of fibers that carry electrical signals from the retina to the brain to create visual images.
- **Trabecular meshwork** – An area of tissue located around the base of the cornea responsible for draining the aqueous humor from the eye.
- **Vitreous humor** – A jelly-like fluid located behind the lens that helps protect the eye and keep the retina in place, maintaining the eye’s round shape.

Pause and Ponder:
What concerns do you have about recommending and counseling patients on eye care products?
AN OCULAR OCTET
It is important for pharmacists to have a basic understanding of common ocular disorders and their associated treatments. Armed with knowledge, pharmacists can determine if a patient is a candidate for self-treatment (See Table 1),2 evaluate the appropriateness of pharmacotherapy selection, screen for actual and/or potential drug interactions and side effects, and counsel patients on the proper use of ocular medications. This section will highlight eight common eye diseases and outline available OTC and prescription remedies.

Acute Eye Injury
Healthcare providers treat more than 3 million eye injuries each year in the US.4 This may be an underestimation of the true prevalence since only emergency room (ER), urgent care centers, or medical offices report ocular injuries. Many patients presenting to the ER with acute eye injury require hospitalization.4

Superficial injury of the eye—such as corneal abrasion—is the most common injury and accounts for 42% of cases.4 Superficial injury can occur from a simple finger scratch or poke, a misplaced makeup brush, or even exposure to sand, dirt, and dust. Patients who experience corneal abrasions complain of pain, photophobia, a gritty feeling, and/or feeling like there is something in the eye. Most corneal abrasions will heal with 48 to 72 hours without any intervention. Historically, patients were instructed to wear an eye patch to cover the injured eye for protection from light and environmental factors. Current guidelines suggest that this action is unnecessary and offers no added benefit.5 In cases where an object penetrates the cornea, patients may require short courses of topical antibiotics for infection prevention or antiinflammatories for symptom relief.5

Other common injuries include foreign body on the external eye, contusion, and open wounds of the eye and adnexa (the supporting structures around the eye). Foreign objects, trauma or physical contact cause most eye injuries.6 Many injuries to the eye are minor, but if not cared for appropriately, sight threatening complications can develop.

It is important for patients to understand that they should receive prompt medical attention for almost all eye injuries; severe eye injuries are not suitable for self-care. Patients should be discouraged from removing large objects that are lodged in the eye or tending to major lacerations as this can potentially worsen vision if done incorrectly. Although it may be difficult, patients should not touch or rub the eye and surrounding area.7

Management of acute eye injuries will depend on the actual injury. Most treatments involve supporting the injury, including compression, ice, and rest. Wearing protective eyewear such as eye glasses can keep the eye area protected from infection or other foreign objects. In the case of a scratched eye, rinsing the eye with sterile saline solution will help keep it clean and reduce risk of infection. Lubricating eye drops can help minimize irritation. In some cases, topical antibiotics and pain relievers may be needed.

Table 1. Exclusions for Self-treatment of Ocular Conditions3

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt trauma to the eye</td>
</tr>
<tr>
<td>Exposure of eye to chemicals</td>
</tr>
<tr>
<td>Head lice</td>
</tr>
<tr>
<td>Hordeolum, chalazion, blepharitis</td>
</tr>
<tr>
<td>Macular degeneration</td>
</tr>
<tr>
<td>Signs and symptoms of infection of eyelids (i.e. red, thickened eyelids, scaling)</td>
</tr>
</tbody>
</table>

Ocular Vocabulary 101

Chalazion
- A noninfectious bump or nodule inside the upper or lower eyelid

Hordeolum
- An acute, infectious bump or nodule inside the upper or lower eyelid (stye)

Hypotrichosis
- Abnormal hair loss or reduction

Metamorphosis
- Distortion of straight lines to wavy or curvy

Ophthalmologist
- A medical doctor who specializes in eye and vision care. Ophthalmologists can diagnose and treat all eye diseases, perform surgery, and prescribe and fit glasses and contact lenses

Optometrist
- A healthcare professional who primarily conducts eye exams and vision tests. Optometrists can prescribe and dispense corrective lenses, identify eye abnormalities, and prescribe treatment for select eye disorders

Photophobia
- Sensitivity to light

Photopsia
- Presence of perceived flashes of light

Scotoma
- A partial loss of vision; a blind spot

Visual acuity
- Sharp, precise vision

Xanthopsia
- Yellow vision
Age-related Macular Degeneration

Age-related macular degeneration (AMD) is a chronic, progressive, degenerative disease of the macula that results in irreversible loss of central vision (See Figure 2). It is the leading cause of blindness worldwide and responsible for 46% of cases involving severe vision loss in Americans older than 40. Causes of AMD include a combination of heredity and environmental factors including aging, smoking, cardiovascular disease, Caucasian race, lifetime oxidative stress, and expression of vascular endothelial growth factors (VEGF).

Experts widely recognize two clinical forms of AMD; “dry” (non-exudative or atrophic) and “wet” (exudative or neovascular).

Dry AMD accounts for approximately 85% of cases and causes gradual, painless changes in the retinal pigment epithelium (RPE). Early in the disease, waste products accumulate within the macula resulting in local deposition of round, yellow, fat-like substances known as drusen. Upon exam, the macula shows pigmentation changes. In later stages, a process called geographic atrophy damages the retina. Symptoms include blurred central vision. Over time, fine details such as reading a book, driving at night, and recognizing faces becomes less clear. If not properly treated, dry AMD can progress to wet AMD.

Wet AMD accounts for only 15% of cases, but its presence indicates disease that is more advanced. Abnormal blood vessels grow under the retina and macula in a process called choroidal neovascularization. This occurs when VEGF binds to VEGF receptors on endothelial cells. These blood vessels can hemorrhage and leak fluid, causing the macula to elevate or detach, altering central vision. Symptoms include metamorphopsia and scotoma. Peripheral vision is often preserved. Patients may lose vision rapidly, sometimes over several weeks or months.

The American Academy of Ophthalmology endorses the classification of AMD based on the Age-Related Eye Disease Study (AREDS). The clinical features of dry AMD are most consistent with early disease and wet AMD corresponds well with advanced disease.

- **Category 1**: No AMD – No or few drusen (< 63 µm in diameter)
- **Category 2**: Early AMD – Multiple small drusen, few intermediate drusen (63 -124 µm in diameter), or mild RPE abnormalities
- **Category 3**: Intermediate AMD – Multiple intermediate drusen, at least one large drusen (125 µm or larger in diameter), or geographic atrophy not involving the center of the fovea
- **Category 4**: Advanced AMD - Geographic atrophy of the RPE or neovascular maculopathy

Goals of treatment are to minimize or reverse visual loss and functional impairment. In addition to lifestyle changes (i.e. smoking cessation, antioxidant-rich diet) and surgical procedures, several medication-based treatments exist. OTC antioxidant vitamins and minerals are recommended for those with intermediate or advanced AMD in at least one eye. Findings from the AREDS study show that high doses of vitamins C, E, and beta-carotene coupled with zinc and copper slow disease progression. Individuals at high risk of developing advanced AMD; taking supplements lowers risk by about 25%. Those with early AMD did not appear to benefit significantly from supplementation.

In 2013, researchers published the findings from the follow-up AREDS 2 study. Investigators sought to determine if adding omega-3 fatty acids and the antioxidants lutein and zeaxanthin to the original AREDS formulation would further reduce disease progression. Due to the growing safety concern that beta-carotene increases the risk of lung cancer in smokers, the researchers substituted lutein and zeaxanthin for beta-carotene in some formulations. The study found that adding omega-3 fatty acids had no effect on disease progression. The combination of lutein and zeaxanthin had no overall effect on AMD when added to the original AREDS formulation. They appear a safe alternative to beta-carotene.
### Table 2. Medications for the Treatment of Age-Related Macular Degeneration

#### OTC Antioxidants and Minerals

<table>
<thead>
<tr>
<th>Name</th>
<th>Strength</th>
<th>Dosage form</th>
<th>Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PreserVision AREDS 2 formula</td>
<td></td>
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<tr>
<td>PreserVision AREDS 2 chewables</td>
<td></td>
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<tr>
<td></td>
<td>Vitamin C 250 mg</td>
<td>Softgels</td>
<td>Take 1 softgel twice a day</td>
<td>Beta-carotene free and suitable for smokers</td>
</tr>
<tr>
<td></td>
<td>Vitamin E 200 IU</td>
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<tr>
<td></td>
<td>Zinc 40 mg</td>
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<tr>
<td></td>
<td>Copper 1 mg</td>
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<tr>
<td></td>
<td>Lutein 5 mg</td>
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<tr>
<td></td>
<td>Zeaxanthin 1 mg</td>
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<tr>
<td></td>
<td>(per 1 softgel or 1 chewable tablet)</td>
<td>Chewable tablets</td>
<td>Chew 1 tablet twice a day</td>
<td>Take with a full glass of water</td>
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<tr>
<td>PreserVision AREDS</td>
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<tr>
<td>Ocuvite Adult 50+</td>
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</tr>
<tr>
<td></td>
<td>Vitamin C 150 mg</td>
<td>Softgels</td>
<td>Take 1 softgel twice a day</td>
<td>Not recommended for smokers</td>
</tr>
<tr>
<td></td>
<td>Vitamin E 20 mg</td>
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<td></td>
<td>Zinc 9 mg</td>
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<td></td>
<td>Copper 1 mg</td>
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<tr>
<td></td>
<td>Omega-3 fatty acids 250 mg</td>
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<tr>
<td></td>
<td>Lutein 5 mg</td>
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<tr>
<td></td>
<td>Zeaxanthin 1 mg</td>
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<tr>
<td></td>
<td>(per softgel)</td>
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<td></td>
<td></td>
<td>Tablets</td>
<td>Take 2 tablets twice a day</td>
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<tr>
<td>I caps Eye vitamin and mineral supplement</td>
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<tr>
<td></td>
<td>Vitamin C 256 mg</td>
<td>Tablets</td>
<td>Take 2 tablets twice a day</td>
<td>Beta-carotene free and suitable for smokers</td>
</tr>
<tr>
<td></td>
<td>Vitamin E 215 IU</td>
<td></td>
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<tr>
<td></td>
<td>Zinc 42.3 mg</td>
<td></td>
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<tr>
<td></td>
<td>Copper 1.8 mg</td>
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<tr>
<td></td>
<td>Lutein 3.33 mg</td>
<td></td>
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<td></td>
<td>Zeaxanthin 1.67 mg</td>
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<td></td>
<td>(per 2 tablets)</td>
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<tr>
<td>VEGF Inhibitors</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Generic (Brand name)</th>
<th>Mechanism of action</th>
<th>Type</th>
<th>Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegaptanib</td>
<td>Binds to VEGF receptors on endothelial cells to inhibit neovascularization</td>
<td>Pegylated modified oligonucleotide</td>
<td>0.3 mg intravitreally every 6 weeks</td>
<td>Monitor for increases in IOP 2-7 days post injection</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Recombinant humanized monoclonal IgG1 antibody</td>
<td>Recombinant humanized monoclonal IgG1 antibody</td>
<td>1.25 mg intravitreally every 4 to 6 weeks</td>
<td>Off-label use; not FDA approved for macular degeneration</td>
</tr>
<tr>
<td>Ranibizumab</td>
<td>Fab fragment of bevacizumab</td>
<td>Fab fragment of bevacizumab</td>
<td>0.5 mg intravitreally every 4 weeks</td>
<td>One-third the size of bevacizumab; shorter t½ and higher VEGF binding affinity vs. bevacizumab</td>
</tr>
<tr>
<td>Afiblercept</td>
<td>N/A</td>
<td>N/A</td>
<td>2 mg intravitreally every 4 to 8 weeks</td>
<td>Higher potency, binding affinity and duration of action vs. other VEGF inhibitors</td>
</tr>
</tbody>
</table>

OTC = over the counter; VEGF = Vascular endothelial growth factor; t½ = half-life; IOP = intraocular pressure
In neovascular AMD, intravitreal injection therapy with VEGF inhibitors is the preferred first-line therapy. Historically, the treatment armamentarium for AMD was limited to photodynamic therapy (PDT). PDT combines a photo sensing dye and laser therapy to destroy abnormal blood vessel growth. Although PDT slows disease progression, it does not improve visual acuity. Four VEGF inhibitors have been studied in the treatment of neovascular AMD; pegaptanib, bevacizumab, ranibizumab, and afilbercept. (See Table 2) These agents offer the benefit of slowing vision loss, and in some cases improve visual acuity. Despite improvements in vision, VEGF inhibitors raise several safety concerns. Repeated intravitreal injections can cause increased intraocular pressure (IOP), eye pain, ocular hemorrhage, retinal detachment, sensitivity to light, and endophthalmitis.

Blepharitis and Uveitis

Blepharitis is a common ocular disorder that affects 37% to 47% of patients seen in ophthalmologist and optometrist settings. When the eyelid’s sebaceous glands become clogged, inflammation ensues resulting in red, irritated, and itchy eyes. Two types of blepharitis exist. Anterior blepharitis describes inflammation of the outside of the eyelid, near the base of the lashes. Seborrheic dermatitis and staphylococcus bacteria are the two most common causes. Inflammation of the meibomian glands in the inner eyelid causes posterior blepharitis. Seborrhic dermatitis and acne/roacea increase risk of developing posterior blepharitis. Blepharitis is not contagious and rarely causes vision loss.

Practicing good eyelid hygiene helps reduce the risk of both types of blepharitis. Keeping the eyelids clean can help minimize infection. Applying warm eyelid compresses several times daily will loosen any crusts. Patients can also be instructed to clean their eyelids by gently rubbing a 1:10 solution of baby shampoo: warm water along the base of the lid, rinsing, and repeating as necessary.

For bacterial, severe, or refractory cases, patients can apply topical bacitracin or erythromycin to the eyelid one or more times daily for a several weeks. A short course of topical corticosteroids can also be used to help reduce ocular inflammation. If topical treatments fail to improve symptoms, oral tetracyclines (doxycycline, minocycline) can be tried until symptoms resolve, usually within two to six weeks. Despite adequate eyelid hygiene and treatment, most cases of blepharitis will recur.

Uveitis is defined as intraocular inflammation of the uvea. The uvea provides necessary nourishment and blood supply to the retina. It is located in the center of the eye and contains the iris, choroid, and ciliary body. Unlike blepharitis, uveitis can cause irreversible, sight-reducing tissue damage. It is estimated that 35% of patients with uveitis exhibit blindness or vision loss in at least one eye. Uveitis can occur at any age, although the average age of onset is 40 years. Several types of uveitis exist. The most common form, anterior uveitis, affects the iris and anterior vitreous. Many factors contribute to the development of uveitis: eye injury, viral or bacterial infection, and comorbid inflammatory disorders such as rheumatoid arthritis. Most causes are idiopathic. Eye complaints include redness, pain, blurred vision, photophobia, and presence of floaters. Such symptoms can present suddenly and can rapidly worsen.

Treatment of anterior uveitis depends on whether the cause is believed to be infectious or non-infectious. Infectious uveitis is treated with appropriate antibiotics or antivirals. Topical (or in some cases systemic) corticosteroids are the mainstay of treatment. (See Table 3) They are normally tapered over six to eight weeks to control local inflammation rapidly, since untreated inflammation can result in macular edema. If symptoms recur when steroids are tapered or discontinued, therapy should continue. Higher potency steroids like prednisolone acetate 1% may be needed to achieve adequate concentration in the aqueous humor. Patients are instructed to instill one drop into the affected eye(s) every one to two hours until inflammation resolves. Topical NSAIDs can be used if steroids are contraindicated, but are not preferred (See Table 3). Drugs known to dilate the eye and paralyze the ciliary muscle are used short term until inflammation has subsided; they help to control pain. (See Table 4) Any increases in IOP should be managed with appropriate eye drops. Beta-blockers are used most often. Prostaglandins should be reserved for last because of their association with inflammation.
### Pause and Ponder:
What ocular conditions do you counsel on the most?

#### Table 3. Anti-Inflammatory Topical drugs\(^{5,27,38}\)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drugs in Class Generic (Brand)</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
<th>Clinical Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical antihistamines</td>
<td>Azelastine 0.05% solution (Optivar)</td>
<td>Histamine receptor antagonist</td>
<td>Dry eyes, burning in the eye, blurred vision</td>
<td>Alaway and Zaditor are available over the counter</td>
</tr>
<tr>
<td></td>
<td>Olopatadine 0.1% solution (Patanol) or 0.2% solution (Pataday)</td>
<td>Mixed mast cell stabilizer and histamine receptor antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ketotifen 0.025% Solution (Zaditor and Alaway)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical mast cell stabilizers</td>
<td>Cromolyn 4% solution (Crolom)</td>
<td>Blocks release of histamine from sensitized mast cells</td>
<td>Burning in the eye</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lodoxamide 0.1% solution (Alomide)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical steroids</td>
<td>Prednisolone acetate 1% (Pred Forte)</td>
<td>Unknown mechanism of action, but similar to systemic corticosteroids. Involves decreasing inflammation</td>
<td>Raised intraocular pressure, blurred vision, increased tears, wound healing defect, secondary infection</td>
<td>Avoid overuse due to possible systemic steroid effects</td>
</tr>
<tr>
<td></td>
<td>Fluorometholone 0.1% solution, suspension and ointment (FML)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Loteprednol 0.5% gel, ointment or solution (Lotemax)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical NSAIDs</td>
<td>Ketorolac 0.4% and 0.5% solution (Acular and Acular LS)</td>
<td>Blocks prostaglandin complex formation and production, resulting in potent analgesia</td>
<td>Burning in the eye, corneal edema, infection, irri-</td>
<td>Only use for a maximum of 5 days at a time</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 0.1% solution (Voltaren)</td>
<td></td>
<td>tation, iritis</td>
<td>Cannot be used while patient is wearing contact lenses</td>
</tr>
</tbody>
</table>

#### Table 4. Medications Used for Dilation\(^{38}\)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drugs in Class Generic (Brand)</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
<th>Clinical Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycloplegics</td>
<td>Cyclopentolate 0.5%-2% Atropine 1% (Isopto Atropine)</td>
<td>Blocks action of the sphincter muscle, leading to pupil dilation and paralysis of the ciliary muscle</td>
<td>Blurred vision, burning sensation of the eye, photophobia</td>
<td>Press down on nasolacrimal duct after instillation to avoid systemic effects</td>
</tr>
</tbody>
</table>
Cataract Post-Surgical Care

Cataracts account for 50% of all vision impairment in the US, affecting approximately one in every six adults over the age of 40. A cataract is an age-related, progressive degradation of the crystalline lens in one or both eyes. Slowly over time, the eye’s lens becomes less flexible, more opaque, and thicker. Certain medical conditions such as hypertension, diabetes, and tobacco abuse accelerate tissue breakdown within the lens. The lens then becomes cloudy leading to impaired vision, or in some cases, blindness. Patients often have difficulty reading small print, impaired nighttime driving, and decreased functional independence.

Three types of cataracts exist: nuclear, cortical, and posterior subcapsular. Currently, no medications are approved for the treatment of any type of cataract. Symptomatic cataracts are managed with surgery. Surgery has been shown to improve quality of life and is more cost-effective than other methods. Medications are often prescribed before and after cataract surgery for symptomatic treatment and prevention of post-operative complications.

Endophthalmitis is an acute eye infection characterized by eye discharge and a white cloudiness on the retina. It occurs after cataract surgery in about one out of every 1000 patients. Patients may experience eye pain, redness, and vision loss. Because endophthalmitis can result in complete blindness, eye surgeons widely prescribed pre-operative antibiotic eye drops in the past. However, povidone eye drops are administered during surgery for additional infection prophylaxis. Recent studies have shown that there is no clinical advantage for patients using topical antibiotics prior to the the procedure over instillation of 5% povidone iodine solution during the procedure. Thus, most physicians have discontinued this preoperative practice in favor of povidone during surgery.

Post-operatively, several medication management strategies exist. Unfortunately, no controlled trials directly compare various post-operative regimens. Topical steroids, NSAIDs and antibiotics, alone or in combination, have been widely recommended. Ketorolac or prednisolone acetate are often prescribed to help with pain and inflammation after their procedure.

### Technician Tutorial

**Calculating days supply for eye drops**

Most eye drop containers hold 5 to 15 mL of product. Verify how many mL are in the container prior to dispensing. One mL of product contains approximately 20 drops.

Example: A patient brings in a prescription for ketotifen fumarate (Zaditor) 0.025% for the treatment of allergic conjunctivitis. The directions read, “Instill 1 drop into both eyes twice daily, every 12 hours.”

You have a 5mL bottle in stock. Calculate the days supply.

- 2 drops per dose x 2 doses per day = 4 drops/day
- 20 drops per ml x 5 ml = 100 drops per bottle
- 100 drops total / 4 drops per day = 25 days supply

### Cataracts

![Healthy Lens](image1)

![Lens with Cataracts](image2)
Conjunctivitis

Conjunctivitis is a common eye disorder, affecting approximately 6 million people each year.  It’s accompanied by systemic viral symptoms, such as fever, pharyngitis, and cough. Bacterial conjunctivitis is caused by Staphylococcus aureus, Streptococcus pneumonia, or Haemophilus influenzae. One can differentiate between bacterial and viral conjunctivitis by evaluating symptoms. In viral conjunctivitis, patients have considerable amounts of thick, purulent discharge throughout the day along with redness. In some instances, clinicians take cultures of eye discharge to determine the cause of conjunctival infection.

Viral and bacterial conjunctivitis are both infectious in nature. Viral conjunctivitis is the most commonly diagnosed form of the disease—accounting for 80% of cases—and is often caused by adenovirus. It’s accompanied by systemic viral symptoms, such as fever, pharyngitis, and cough. Bacterial conjunctivitis is caused by Staphylococcus aureus, Streptococcus pneumonia, or Haemophilus influenzae. One can differentiate between bacterial and viral conjunctivitis by evaluating symptoms. In viral conjunctivitis, patients have considerable amounts of thick, purulent discharge throughout the day along with redness. In some instances, clinicians take cultures of eye discharge to determine the cause of conjunctival infection.

Viral conjunctivitis may persist for two to three weeks, but does not require any medical treatment. Although self-limiting, viral conjunctivitis is contagious and easily transmitted via contaminated hands, medical instruments, doorknobs, swimming pools, etc. Patients should engage supportive measures similar to any other viral infection such as drinking plenty of fluids, resting, using OTC decongestants (when appropriate), and applying warm compresses to the eye. Some patients may also benefit from OTC eye treatments, such as artificial tears and topical antihistamines.

Bacterial conjunctivitis is also a highly contagious. Many assume that bacterial conjunctivitis must be treated with a topical antibiotic, but this is not necessary in all cases. Some studies have shown that there is no difference in clinical improvement between patients treated with antibiotics and those treated with supportive measures only. However, antibiotic use is associated with faster symptom resolution. It is recommended that patients wait to use topical antibiotics because of the increase in antibiotic resistance. If a patient has a positive bacterial culture, he or she should be treated with topical antibiotics.

A recent study assessed the overprescribing of topical antibiotics for acute conjunctivitis. Of note, 60% of patients with conjunctivitis were prescribed and filled prescriptions for topical antibiotics or combination steroid/antibiotic agents. This prescribing practice is of great concern since combination steroid/antibiotic products are not recommended due to growing concern about bacterial resistance.

If antibiotics are indeed indicated, several options exist. Studies have failed to demonstrate that one broad-spectrum topical antibiotic is superior to another. Providers choose an appropriate topical antibiotic based on patient allergies, preference, and cost. If a bacterial culture has been taken, the results can guide decision-making. Common antibiotics include erythromycin, tobramycin, moxifloxacin, ofloxacin, etc. (See Table 5) Treatment with topical antibiotics ranges from five to 14 days depending on the chosen agent and severity of disease.

Unlike infectious conjunctivitis, allergic conjunctivitis affects 40% of the population. The conjunctiva becomes inflamed in response to allergens in the environment. Ninety percent of all cases of allergic conjunctivitis are seasonal. Common symptoms include redness, photophobia and itchiness; purulent discharge occurs less frequently with allergic conjunctivitis compared with infectious conjunctivitis. Symptoms are usually bilateral. Patients can also exhibit systemic symptoms of allergies such as rhinitis, atopic dermatitis, asthma, and itching. For most, allergic conjunctivitis is a self-limiting and self-treatable condition and does not require provider referral. Patients may resort to provider intervention if their allergic conjunctivitis does not resolve with the use of OTC products.

If conjunctivitis is deemed to be allergic, patients are encouraged to avoid their personal allergens—pollen, trees, dust—when possible. Patients experiencing symptoms can try oral first or second-generation antihistamines (loratidine, fexofenadine, etc.). Persistent symptoms can also be managed with appropriate OTC ocular products such as topical antihistamines and/or mast cell stabilizers (See Table 3). OTC ketotifen provides excellent relief of symptoms. Olopatadine is a mixed antihistamine and mast cell stabilizer, and often works well for patients who have failed all OTC therapies.
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drugs in Class Generic (Brand)</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
<th>Clinical Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides</td>
<td>Gentamicin 0.3% ointment and solution (Gentak)</td>
<td>Disruption of bacterial cell protein synthesis leading to cell death</td>
<td>Irritation</td>
<td>Tobramycin is also available in combination with dexamethasone (TobraDex)</td>
</tr>
<tr>
<td></td>
<td>Tobramycin 0.3% ointment and solution (Tobrex)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Ciprofloxacin 0.3% ointment and solution (Ciloxan)</td>
<td>Interferes with DNA gyrase, stopping the synthesis of bacterial DNA</td>
<td>Retinal detachment, burning sensation, eye pain, dry eye, reduced visual acuity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin 0.5% solution (Vigamox)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ofloxacin 0.3% solution (Ocuflox)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Levofloxacin 1.5% solution (Iquix)</td>
<td></td>
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<tr>
<td></td>
<td>Gatifloxacin 0.3% solution (Zymar)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macrolides</td>
<td>Azithromycin 1% solution (Azasite)</td>
<td>Inhibition of protein synthesis via binding to ribosomal 50S subunit in bacteria</td>
<td>Abnormal vision</td>
<td>Azithromycin rarely prescribed, but used in place of erythromycin due to drug shortages</td>
</tr>
<tr>
<td></td>
<td>Erythromycin 0.5% ointment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>Sulfacetamide 10% solution and ointment (Bleph-10)</td>
<td>Bacteriostatic to prevent synthesis of bacterial dihydrofolic acid</td>
<td>Application site irritation</td>
<td></td>
</tr>
<tr>
<td>Polypeptides</td>
<td>Bacitracin 500units/gram ointment</td>
<td>Inhibition of cell wall synthesis</td>
<td>Contact dermatitis</td>
<td>Difficult dosing as patients often given instructions in grams rather than easier dosing formats</td>
</tr>
<tr>
<td>Combination products</td>
<td>Trimethoprim/ polymyxin B (Polytrim)</td>
<td>Polymyxin is bactericidal- increase bacterial cell membrane permeability. Trimethoprim interferes with bacterial biosynthesis</td>
<td>Eye irritation</td>
<td></td>
</tr>
</tbody>
</table>
Dry Eye
Tears play an important role keeping the cornea moist. Made of a mixture of oil, water, and mucous, tears nourish and protect the eye. Dry eye occurs when tear production decreases, tear evaporation increases, and/or the composition of tears is imbalanced. Dry eye can occur at any age, but is more common in older adults as tear production naturally declines with age. Common symptoms of dry eye include blurred vision, feeling that something is stuck in the eye, and sensations of stinging, burning, or scratching. Excessive watering of the eyes can also occur as they try to compensate for irritation and inflammation. More severe cases may cause ocular damage and visual impairment.

Many factors contribute to the development of dry eye. Postmenopausal women, contact lens wearers, those diagnosed with select endocrine and inflammatory disorders (i.e. diabetes, thyroid, vitamin A deficiency, rheumatoid arthritis), and those engaging in prolonged screen time appear at highest risk. Tear evaporation can also occur when a person is exposed to allergens or dry, windy climates. Transient cases of dry eye are often reported after eye injuries and surgery secondary to inflammation.

Treatments for dry eyes aim to restore or maintain normal tear production, minimize irritation and prevent further ocular damage. Most cases of occasional, mild dry eye are suitable for self-treatment. The primary treatment approach for dry eye is use of OTC ocular lubricants, including artificial tears and non-medicated gels and ointments. (See Table 6) Most popular are artificial tears. Artificial tears are specially formulated with water-soluble polymers, inorganic electrolytes, and preservatives. All artificial tears provide moisture. However, the product’s ability to reduce evaporation, heal wounds, and protect the eye will differ depending on its composition. Products can also vary in viscosity. Solutions with higher viscosities will allow longer surface contact time and are less susceptible to tear dilution. Combining artificial tears with non-medicated gels and ointments can further enhance the product’s retention time. Preservative-free formulations may cause less irritation but expire shortly after opening. Patients should be counseled about the risk of contamination and infection with preservative-free formulas.

More severe cases of dry eye are treated with prescription medications or ocular inserts. Immune-suppressing corticosteroids and cyclosporine (Restasis and Cequa) help control inflammation. Corticosteroids are recommended for short-term use only given their side effect profile. Cyclosporine decreases corneal damage, increases basic tear production, and reduces symptoms. Drops should be administered in the affected eye(s) twice a day, every 12 hours. Each bottle is for single-use only. If artificial tears are used concomitantly, 15 minutes should elapse between product applications. Common side effects include burning, redness, tearing, discharge, pain, itching, and stinging. Pharmacy staff should remind patients that cyclosporine’s therapeutic effects may take several months.

An artificial tear insert such as Lacrisert may be an option for individuals with moderate to severe dry eye symptoms. Made of hydroxypropyl cellulose, the patient places the insert between the lower eyelid and eyeball once daily. As it dissolves, it releases lubricants that stabilize and thicken tear film to prolong tear film breakup. If used improperly, corneal abrasion can occur. Common side effects include blurred vision, discomfort, eyelid edema, and photophobia.

Patients may ask if supplementation with omega-3 fatty acids relieves symptoms of dry eye. Findings from the 2018 Dry Eye Assessment and Management Study (DREAM) call this recommendation into question. Participants with moderate to severe dry eye disease were randomly assigned to 3000 mg fish-derived n-3 eicosapentaenoic and docosahexaenoic acids or olive oil placebo daily. After 12 months of supplementation, no statistically significant differences in dry eye symptom severity scores were observed between the groups.

Pharmacists can provide additional non-pharmacologic recommendations for the management of dry eye. When appropriate, patients should be advised to break up prolonged periods of screen time. Wearing sunglasses with wrap around frames can help reduce exposure to wind and dust. Use of a humidifier will help reduce dry air.

Patients who self-treat mild, occasional dry eye should follow-up with their healthcare provider for further evaluation if symptoms do not improve, or worsen, after 72 hours.
Table 6. Over-the-Counter Ophthalmic Lubricants³

<table>
<thead>
<tr>
<th>Artificial Tears</th>
<th>Ingredients</th>
<th>Suggested Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TheraTears</strong></td>
<td>Sodium carboxymethylcellulose (0.25%)</td>
<td>Instill 1 to 2 drops in affected eye(s) as needed</td>
</tr>
<tr>
<td><strong>Refresh Tears</strong></td>
<td>Carboxymethylcellulose Sodium (0.5%)</td>
<td>Instill 1 to 2 drops in affected eye(s) as needed</td>
</tr>
<tr>
<td><strong>Systane Ultra</strong></td>
<td>Polyethylene Glycol 400 (0.4%), Propylene Glycol (0.3%)</td>
<td>Shake well before using. Instill 1 to 2 drops in affected eye(s) as needed</td>
</tr>
<tr>
<td><strong>GenTeal Tears</strong></td>
<td>Dextran (70 0.1%), Hyppromellose 2910 (0.3%)</td>
<td>Instill 1 to 2 drops in affected eye(s) as needed. Make sure container is intact before use.</td>
</tr>
<tr>
<td><strong>Soothe</strong></td>
<td>Glycerin (0.6%), Propylene Glycol (0.6%)</td>
<td>Instill 1 to 2 drops in affected eye(s) as needed</td>
</tr>
<tr>
<td><strong>Blink tears</strong></td>
<td>Polyethylene Glycol 400 (0.25%)</td>
<td>Instill 1 to 2 drops in affected eye(s) as needed or as directed by your eye care professional</td>
</tr>
</tbody>
</table>

**Non-Medicated Gels**

| **Systane Gel Nighttime Protection**     | Hyppromellose (0.3%)                             | Instill 1 or 2 drops in the affected eye(s) as needed     |
| **Refresh Liquigel**                     | Carboxymethylcellulose Sodium (1%)               | Instill 1 or 2 drops in the affected eye(s) as needed     |

**Non-Medicated Ointments**

| **GenTeal Nighttime PM ointment**        | Mineral oil (3%), white petrolatum (94%), inactive ingredient anhydrous liquid lanolin 3% | Apply 1 or more times per day as directed                  |
| **Systane Nighttime**                    | Mineral oil (3%), white petrolatum (94%), inactive ingredient anhydrous liquid lanolin 3% | Pull down the lower lid of the affected eye and apply a small amount (one-fourth inch) of ointment to the inside of the eyelid |

*Not inclusive list*

**Color of Bottle Cap**

<table>
<thead>
<tr>
<th>Color of Bottle Cap</th>
<th>Medication Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pink</td>
<td>Anti-inflammatories/steroids</td>
</tr>
<tr>
<td>Red</td>
<td>Mydriatics and cycloplegics</td>
</tr>
<tr>
<td>Orange</td>
<td>Carbonic anhydrase inhibitors</td>
</tr>
<tr>
<td>Yellow</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Light green</td>
<td>Adrenergic agonist combinations</td>
</tr>
<tr>
<td>Olive green</td>
<td>Anti-inflammatory, immunomodulators</td>
</tr>
<tr>
<td>Dark green</td>
<td>Miotics</td>
</tr>
<tr>
<td>Turquoise</td>
<td>Prostaglandin analogues</td>
</tr>
<tr>
<td>Dark blue</td>
<td>Beta-blocker combination</td>
</tr>
<tr>
<td>Purple</td>
<td>Adrenergic agonists</td>
</tr>
<tr>
<td>Tan</td>
<td>Anti-infectives</td>
</tr>
<tr>
<td>Gray</td>
<td>Nonsteroidal anti-inflammatories</td>
</tr>
<tr>
<td>Black</td>
<td>Cytotoxics</td>
</tr>
</tbody>
</table>

**An Eye-Opening Fact**

Did you know that manufacturers voluntarily use a color-coding system for topical ocular medications’ caps and labels?

Since 1983, manufacturers have used this system to increase patient safety. The American Academy of Ophthalmology (AAO) proposed the system after many patients who had trouble distinguishing among various ocular medications experienced serious adverse events.

The AAO selected specific Pantone colors (which are standardized and reproducible) for each drug class according to the nature of the disease being treated, the product’s side-effect profile, and the risk of serious sequelae if a product is inadvertently switched with another.

Glaucoma

Glaucoma is the second leading cause of blindness in the world. Approximately 8.4 million are blind from the disease.\textsuperscript{34} It is a complicated medical condition characterized by increased IOP and disc abnormalities that can lead to optic neuropathy and field vision loss. Two forms of glaucoma are widely recognized: open angle and angle-closure glaucoma (i.e. closed angle).

Open angle glaucoma (OAG), the more common type, affects 45 million adults worldwide.\textsuperscript{34} It primarily affects adults over the age of 40. The pathogenesis is poorly understood, but retinal cell death is believed to contribute to increased IOP. IOP depends on the balance between production of aqueous humor and its outflow through the trabecular meshwork. In OAG, aqueous humor outflow is diminished. Patients do not often complain of symptoms when they have OAG largely because symptoms do not occur until later stages. This can delay diagnosis and as a result, treatment. OAG is usually discovered during routine eye exams.\textsuperscript{35}

IOP can be elevated (> 21 mmHg) or within the normal range, so a diagnosis of OAG must include visual field loss and optic nerve damage; IOP is not a diagnostic factor.

The primary goal of treatment for OAG is to lower IOP to prevent vision loss. Lowering the IOP has proven to decrease disease progression.\textsuperscript{35} Eye drops are the treatment of choice. They reduce IOP by either decreasing the aqueous humor production (beta-blockers, carbonic anhydrase inhibitors), increasing aqueous outflow (prostaglandins), or both (alpha-agonists). (See Table 7) Combination therapy should be considered when monotherapy fails to reach the IOP target. Prostaglandins are the preferred first-line treatment. Prostaglandins are dosed once a day, offering an advantage for patients with adherence problems. They also have minimal systemic side effects compared to other agents. The most frequently prescribed prostaglandin is latanoprost.\textsuperscript{34} Patients using prostaglandins should be advised of side effects including eyelash growth and iris pigmentation changes.

A second line agent can be added if IOP goals are not met. Some providers may choose to discontinue the prostaglandin altogether in favor of a second line medication. Second line options include beta-blockers, topical carbonic anhydrase inhibitors, and alpha-adrenergic agonists. Topical beta-blockers, including timolol and betaxolol, lower IOP and have few ocular side effects. These medications should however be used with caution because of the possibility of systemic side effects such as hypotension, decreased heart rate, and increased airway resistance.\textsuperscript{34} Carbonic anhydrase inhibitors such as dorzolamide or brinzolamide are commonly used as adjunctive therapies but rarely as initial therapy. Currently, the only commercially available alpha-adrenergic agonist is brimonidine. Brimonidine has been found to lower rates of visual field disturbances more than topical beta-blockers.\textsuperscript{36} Although it effectively slows OAG’s progression, many patients discontinue brimonidine because of ocular allergy. This chronic itchy eye associated with brimonidine often leads poor adherence.\textsuperscript{36}

If patients do not respond to topical medications, surgery is an option. This procedure is called laser trabeculoplasty and involves the trabecular network, releasing pressure from the eye. Some patients who have the procedure still require topical treatment after the fact.\textsuperscript{37}

Unlike OAG, angle closure glaucoma usually presents as an acute condition. It is characterized by the blockage of aqueous humor flow caused by the peripheral iris contacting the peripheral cornea. This blockage causes a sharp, dangerous increase in IOP. Patients with acute angle closure glaucoma complain of severe ocular pain, blurred vision, and halos. Patients can also experience general nausea and vomiting. Acute angle closure glaucoma is a medical emergency. Without prompt treatment it could lead to temporary or permanent vision loss.\textsuperscript{37}

Treatment of angle closure glaucoma involves similar medications to OAG but with different administration schedules. One drug commonly used for symptom relief is pilocarpine. Pilocarpine quickly reduces pressure in the eye when administered as one drop every 15 to 60 minutes for two to four doses until IOP drops within the acceptable range. Topical beta-blockers can be used in combination with pilocarpine. Miotic agents are also an option to increase aqueous humor outflow and help to pull the iris into place. This pulling allows for the closed angle in the eye to open and pressure to be released. Following relief of the acute episode, patients will use topical prostaglandins, beta-blockers, etc. in a manner similar to OAG.\textsuperscript{37}
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drugs in Class Generic (Brand)</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
<th>Storage &amp; Administration</th>
</tr>
</thead>
</table>
| **Beta-Blockers** | • Timolol 0.25% or 0.5% solution or gel-forming solution (Timoptic)  
• Betaxolol 0.5% and 0.25% suspension and solution (Kerlone and Betoptic)  
• Levobunolol 0.5% solution (Betagan) | Decrease aqueous humor production        | Allergic conjunctivitis, keratitis.  
Monitor for systemic side effects, such as bradycardia, fatigue | Use with caution in patients with restrictive airway diseases  
Dosed 1-2 times daily                                                                 |
| **Prostaglandins**| • Latanoprost 0.005% solution (Xalatan)  
• Bimatoprost 0.01% solution (Lumigan)  
• Travoprost 0.004% (Travatan Z) | Increase aqueous humor outflow           | Increased eyelash growth, periocular hyperpigmentation, uveitis, flu-like symptoms | Do not use in patients with uveitis or macular edema.  
Latanoprost must be stored in the refrigerator.  
Good for 42 days once at room temperature  
Use in the evening                                                                 |
| **Alpha adrenergic agonists** | • Brimonidine 0.15% and 0.2% solution (Alphagan)                                                                 | Improve outflow of aqueous humor. Decreases aqueous humor production. Decreases venous pressure | Allergic conjunctivitis, dry mouth, dry nose | Do not use with MAOIs  
Usually administered 2-3 times a day                                                                 |
| **Carbonic anhydrase inhibitors ( topical)** | • Dorzolamide 2% solution (Trusopt)  
• Brinzolamide 1% (Azopt)                                                                 | Decrease aqueous humor production        | Corneal edema, allergic conjunctivitis, metallic taste | Do not use in patients with sulfa allergies                                                                 |
| **Combination Therapy** | • Dorzolamide 2%/timolol 0.5% (Cosopt)  
• Brimonidine 0.2%/timolol 0.5% (Combigan)  
• Brinzolamide 1%/brimonidine tartrate 0.2% (Simbrinza)                                                                 | Decrease aqueous humor production        | Burning in the eye, blepharitis, blurred vision, excessive tear production, itchy eye  
Watch for systemic effects of beta blockers |                                                                 |
| **Miotics** | • Pilocarpine 2% solution (Pilor)                                                                 | Increase outflow of aqueous humor. Contracts ciliary muscles in the eye to open the trabecular meshwork | Headache, sweating when absorbed systemically | Do not use with uveitis                                                                 |

*Please see the table on page 12 for a complete list of cap colors by drug class.*
Retinal Detachment Perioperative Care

Retinal detachment is most frequently characterized by a break in the retina, sometimes complete but most often partial. This allows fluid located in the vitreous cavity to leak into the sub-retinal space disrupting vision. Breaks in the retina are caused by various factors and the type of detachment is categorized based on the underlying cause. Rhegmatogenous breaks are associated with age, myopia, ocular surgery, and trauma. Tractional breaks occur when scarring is present on the retinal surface and vitreous cavity caused by proliferative diabetic retinopathy. Additional causes of tractional breaks include eye injury, sickle retinopathy, and retinal vein occlusion. Exudative retinal detachment is associated with inflammatory eye conditions (uveitis), maculopathy, and vascular conditions.

Patients with retinal detachment often experience photopsia, floaters, opacities, black dots, and visual field defects. With a full tear of the retina, the patient loses vision in that eye. Patients with such symptoms should be referred for emergency care. Treatment for retinal detachment is limited to surgical reattachment. The severity of the condition determines how quickly the surgical reattachment should occur. Three types of surgical procedures are available for retinal reattachment: scleral buckling, vitrectomy, and pneumatic retinopexy.

Following surgery, patients will need a variety of treatments including topical antibiotics, pain relievers, steroids, cycloplegic agents, and/or beta-blockers. Antibiotics, such as ofloxacin, are used to prevent post-operative endophthalmitis. Prednisolone or other topical steroids are used to help with inflammation associated with the surgery. Some physicians recommend as few as four days of post-operative medications, while others advise longer regimens. It is currently unknown which treatment combinations and durations of therapy are most effective; therapeutic decisions are at the provider’s discretion.

MEDICATION-INDUCED OCULAR DISEASE

Countless topical and systemic medications can cause undesirable ocular side effects. Some effects can be minor causing transient dryness and irritation, while others can be more serious resulting in vision loss. The extent of such side effects is related to the dose, duration of use, and individual patient characteristics. Prompt discontinuation of the offending drug can often reverse ocular damage. In some cases however, the damage may be irreversible. As medication experts, pharmacists are best suited to assist with the detection and prevention of such side effects. This section highlights several widely used medications known to cause ocular side effects.

Preservatives – Preservatives are commonly added to eye drops to reduce product contamination. Thiomersal and benzalkonium chloride containing preservatives can irritate corneal and conjunctival cells causing local redness and inflammation. Patients with such sensitivity should opt for preservative-free formulations when possible.

Corticosteroids – Use of topical and systemic corticosteroids (e.g. prednisone) causes structural and functional changes within the eye. Steroids reduce aqueous humor outflow resulting in increased IOP. Clinicians should monitor patients with preexisting OAG for worsening disease. Bilateral, posterior subcapsular cataracts have also been linked to long-term (more than 1 year), high-dose (more than 10 mg/day) steroid use. Cataract surgery can successfully restore vision loss from steroids.

Anticholinergics – Various anticholinergic drugs (histamine antagonists, tricyclic antidepressants, paroxetine, tiotropium, etc.) induce photophobia and mydriasis thus increasing the risk for angle-closure glaucoma. Additionally, the drying effects of anticholinergics reduce tear production and may cause or worsen dry eye.

Hydroxychloroquine – Hydroxychloroquine use can result in irreversible, toxic retinopathy. Metabolism of retinal cells is believed to cause the problem, although the mechanism is poorly understood. Factors that increase risk of developing retinopathy include the following:
- Long durations of treatment
- Doses greater than 5 mg/kg/real weight/day
- Comorbid renal disease
- Use of concomitant tamoxifen

A basic fundus exam is recommended prior to the start of therapy. After five years of treatment, yearly exams are recommended.

Amiodarone - Amiodarone can cause reversible optic neuropathy and photophobia. Corneal deposits and degeneration cause blurred vision and the appearance of colored rings or halos around objects. Ocular changes happen gradually over several months. Eye screenings should be done at baseline, and every six months during the first year. Annual follow-up is recommended thereafter.

Tamsulosin – Tamsulosin has high affinity for the α1A receptor found in the smooth muscle and iris dilator. Blocking this receptor triggers iris prolapse (“floppy eye syndrome”) and impairs pupillary dilation, making dilator drops used in cataract surgery ineffective. Patients considering cataract surgery should discuss use of tamsulosin or any alpha-blocker with their surgeon as soon as possible.

Digoxin – Digoxin toxicity can manifest with visual abnormalities of the retina. These include reduced visual acuity, xanthopsia, discoloration of objects, and photophobia. Symptoms are reversible upon discontinuation. Maintaining normal serum levels of digoxin (0.5–2 ng/mL) can minimize ocular side effects.
**TRENDS IN EYE CARE**

**New Technologies**

Eye drops are the mainstay of treatment for most ocular disorders; more than 90% of available ocular products are formulated as eye drops.44 Unfortunately, the cornea hampers most drug absorption.44 New drug delivery systems are needed to overcome these barriers. By doing so, drugs can penetrate the cornea and maintain therapeutic concentrations in the ocular space. New delivery systems have become widely available in recent years. These include ointments, emulsions, gels, suspensions, and nanoparticles. Nanoparticle technology is of particular interest since most products are associated with low rates of ocular irritation. Solubility and bioavailability are also enhanced.44 Common nanoparticle formulations include liposomes, nanomicelles, and nanoparticles.

**New Products**

A handheld stimulator, TrueTear, is the first Food and Drug Administration (FDA) approved device for dry eye. The drug-free device comes with disposable tips that are inserted into the nose to help stimulate tear production. The neurostimulation technology is similar to well known devices like pacemakers and TENS devices used for back pain. It is recommended for those suffering from severe dry eye symptoms.45

In late 2017, the FDA approved a new drug class of eye drops for the treatment of OAG and ocular hypertension. The approved agent, latanoprostene bunod ophthalmic solution 0.024% (Vyzulta) has a novel mechanism of action combining the function of prostaglandins to increase the outflow of aqueous humor and nitric oxide donation to relax the trabecular meshwork for greater humor outflow.46 Safety studies indicate latanoprostene bunod seems have a side effect profile similar to other prostaglandins. Although its exact place in treatment for OAG is unknown at this time, researchers believe that this drug will be useful.

In August 2018, the FDA also approved cyclosporine A ophthalmic solution 0.09% (Cequa) to increase tear production in patients with dry eye. It is purported to provide the highest FDA-approved concentration of cyclosporine A. The product uses nanomicellar technology, to improve solubility and product penetration. The most common side effects include pain upon administration and conjunctival hyperemia.47

**New Uses for Old Products**

Women rely on make-up to enhance their natural beauty. Recently, prostaglandin analogues have been formulated into various cosmetic products, sparking a billion dollar beauty craze.48 Several prostaglandin-containing products are available to assist, both OTC and by prescription. They are marketed to enhance eyelash length, volume, and color. Only bimatoprost 0.03% (Latisse) is FDA-approved to treat hypotrichosis of the eyelashes. Revitalash, LiLash, and MD Lash Factor (among others) are cosmetic options available without a prescription. These serums are co-formulated with vitamins, extracts, and peptides.48 OTC products’ safety and efficacy have not been firmly established.

**BARRIERS TO MEDICATION ADHERENCE: AN OPPORTUNITY FOR PHARMACISTS**

Patients who don’t take their medications as directed have difficulty achieving treatment outcomes. In the case of glaucoma or AMD, poor adherence can lead to progressive vision loss and blindness. For dry eye or allergy sufferers, quality of life may be reduced if symptoms are untreated. Actual rates of medication nonadherence are often underestimated. For patients with glaucoma, adherence to standard eye drops varies from 30% to 80%.49

Medication nonadherence takes many forms. It is not limited to failing to take the medication. Medication nonadherence also includes incorrect administration. A recent study evaluated the eye drop instillation technique of 164 patients with glaucoma or ocular hypertension.50 Patients were asked at baseline to self-assess the degree of difficulty they had with administering their daily eye drops. Study personnel observed participants’ administration technique at baseline and 12 weeks later. Approximately 88% of patients self-reported no difficulty in using eye drops at baseline. However, when researchers observed these patients, they noted errors such as the bottle touches the eye, the eye drop misses the eye, and more than one drop administered were noted.50 Interestingly, a majority of the patients enrolled had been using eye drops for more than a year prior to the start of the study and received counseling on how to properly administer eye drops. These findings reinforce the need to not only ensure patients take their medications, but do so correctly!

Several barriers have been linked to poor adherence with ocular medications. Common reasons include skepticism about the disease and its impact on vision, skepticism that medications are effective, poor understanding of the disease itself, poor self-efficacy, forgetfulness, cost, complexity of the medication regimen, side effects, difficult administration techniques, and life stress.49 The greater number of barriers identified, the more likely a patient will be non-adherent.49

**Complex medication regimens** - Recommend simplification of the dosing regimen when possible. Switch from multiple daily doses to once daily or twice daily regimens. This minimizes the need for patients to carry their drops with them throughout the day and lessens the interference of dosing during work, school, or other important times. Fewer daily doses have been linked with better rates of adherence.51 Alternatively, pharmacists can recommend use of fixed-dose combination products when available. Some examples for the treatment of glaucoma include Cosopt (dorzolamide/timolol), Combigan (brimonidine tartrate/timolol) and Simbrinza (brinzolamide/brimonidine).
Use of combination products may also offer the advantage of reducing ocular exposure to preservatives and lessen the chances of multiple container contaminations.

**Forgetfulness** – Forgetting to take one’s medication is the most frequently cited reason for nonadherence.52 It’s natural to forget things once in a while, especially when things get busy. However, repeated forgetfulness can impact a patient’s ability to reach his or her therapeutic goals. Using mobile applications (apps) can help improve adherence, even for patients who are not technologically savvy.53 Free options include MyMeds Medication Management and Dosecast Medication Reminder. Other strategies to minimize forgetfulness include simplifying the regimen so there is less to forget, providing patients with medication calendars or schedules, and scheduling more frequent follow-up, thus holding patients accountable.

**Side effects** – Many conventional eye drops and ointments can cause local stinging or irritation upon administration. Highly concentrated products or excessive application of such products can enter the circulation through the conjunctival vessels, thus increasing the chance for systemic side effects. Timolol for example can decrease heart rate if it enters the systemic circulation. How a patient perceives or experiences these side effects contributes greatly in his or her decision to take or not take subsequent doses. Fortunately, this behavior is modifiable. When a patient complains of such side effects, pharmacists should verify the patient’s administration technique is correct (See ‘Administration technique’ below); identify any errors; and correct the patient’s technique. If side effects persist, the prescriber should be contacted to see if any alternative medications could be tried. This includes finding preservative free formulas, ingredients with lower concentrations, or an alternative with less frequent dosing.

**Cost** – High co-payments and deductibles can keep patients from filling their prescriptions. If ultimately a patient does pick up a prescription after a cost-related delay, he or she may be more prone to change the frequency of administration to make the supply last longer. Fortunately, information about medication cost is widely available. Most insurance companies publish their preferred drug formulary online. If patients do not have access to a computer, they can call the insurer directly to ask about copayment information and/or less expensive alternatives. Pharmacists can also identify and recommend OTC and prescription generic products, which tend to be less expensive. In some cases, use of fixed-dose combination products may help reduce overall medication costs and number of individual co-payments. Many manufacturers offer patient assistance programs or coupons to offset drug costs for those who cannot afford their medications. Each program has different eligibility criteria. Pharmacists can help patients enroll in such programs. Patients should be discouraged from sharing eye drops in an effort to minimize cost. Shared containers can become contaminated and increase the risk of infection among users, especially if the product is preservative-free.

Since eye drops can be costly, every effort should be made to minimize product waste. If the drops do not fall onto the eye, spillage down the cheek and face can occur. With proper instillation, eye drop waste should be minimal. Most eye drop containers are intended to last more than 30 days when packaged in 5 mL and 10 mL bottles (See Technician Tutorial on page 8). If a patient is running out of medication early, pharmacists should suspect waste and reassess administration technique.

**Skepticism about the disease** – It is important to understand a patient’s beliefs about their disease. Several ocular conditions are largely asymptomatic and progress slowly. Consequently, patients may not be aware of the disease severity or the degree of vision loss that can occur. Rates of nonadherence are higher when patients are symptom free.54 Pharmacists can teach patients about their disease and help correct any educational gaps or misconceptions. Patients can be encouraged to learn more about their disease(s) by visiting the National Eye Institute at https://nei.nih.gov/ or MedlinePlus at https://medlineplus.gov/.

**Skepticism of product effectiveness** – Conventional eye drops are absorbed through the cornea and conjunctival mucosa and vessels. This offers an advantage over systemic medications that cannot easily penetrate the aqueous humor and cornea.55 However, depending on the formulation of the eye drops (pH, buffers, tonicity adjusters, etc.), the product can evaporate from the eye’s surface leaving patients to question whether the product is effective or not. Patients need to be educated that product evaporation is common and does not signify reduced efficacy. Frequent dosing helps overcome the short contact time. However, if a patient remains skeptical, pharmacists can recommend alternative formulations. Ophthalmic ointments and gels prolong ocular contact time and improve drug bioavailability thus reducing the need for multiple doses.55 Such dosage forms are associated with blurred vision. For this reason, nighttime dosing is preferred. As new formulations come to market, patients will have a greater number of options.

**Pause and Ponder:**

What are some of the most common reasons that patients do not take their ophthalmic medications as directed?
Administration technique – To maximize product effectiveness and minimize side effects, proper administration of ocular products is needed. Pharmacists and pharmacy technicians should note that many patients, as they age, develop arthritis in their hands and may have difficulty with the administration technique. For this and many other reasons, ophthalmic products are often used incorrectly; therefore patient education should be a top priority for pharmacy staff. Different dosage forms require different techniques.

Eye drop administration technique
1. Inspect the product. Solutions will be clear. Suspensions will be cloudy.
2. Wash hands thoroughly.
3. Remove contact lenses unless the product is designed for use with contact lenses.
4. Tilt head back.
5. Gently grasp the lower outer eyelid below the lashes and pull the eyelid away from the eye to create a pouch.
6. Place dropper over eye by looking directly at it. The tip of the dropper should NOT touch the eye.
7. Before applying a drop, look up.
8. As soon as the drop is applied, release the eyelid slowly. Close eyes gently for three minutes by placing your head down as though looking at the floor (using gravity to pull the drop onto the cornea). Minimize blinking or squeezing the eyelid.
9. Use a finger to put gentle pressure over the opening of the tear duct.
10. Blot excessive medication from around the eye.
11. If multiple drops are needed, wait five minutes before instilling the next drop.
12. If using a suspension, shake it well before instilling. If using suspensions with other dosage forms, use the suspension drop last since it has the longest retention time in the tear film.
13. If using both drops and ointments, instill the drop at least 10 minutes before the ointment so that the ointment does not become a barrier to the drop’s penetration of the tear film or cornea.

Eye ointment administration technique
1. Wash hands thoroughly.
2. Tilt head back.
3. Remove contact lenses. Contact lenses are not compatible with ointment use.
4. Gently grasp the lower outer eyelid below the lashes and pull the eyelid away.
5. Place ointment tube over eye by looking directly at it.
6. With a sweeping motion, place ¼ to ½ inch of ointment inside the lower eyelid by gently squeezing the tube. AVOID touching the tube tip to any tissue surface.
7. Release the eyelid slowly.
8. Close eye gently for 1-2 minutes.
9. Blot excessive ointment from around the eye.
10. Vision may be temporarily blurred. Avoid activities that require good visual ability until vision clears.
The American Academy of Ophthalmology offers a comprehensive patient education site called Eye Health A-Z. Pharmacy staff can refer patients to the site (https://www.aao.org/eye-health/a-z) when they have questions about any type of ophthalmic condition. In addition to covering age-related macular degeneration, blepharitis, cataracts, corneal conditions, conjunctivitis, dry eye, and glaucoma, it covers dozens of other conditions. The University of Texas Health Science Center at San Antonio also has a patient information page on eye diseases and conditions (http://uthscsa.edu/eye/patientinfo.asp) and it offers the advantage of providing the information in both English and Spanish.

CONCLUSION

Ocular diseases are common and impact patients in many ways. From minor eye irritation to severe vision loss, these consequences can greatly influence a patient’s quality of life. Luckily, pharmacists are widely accessible and can play a critical role in screening appropriate self-care candidates, selecting drug therapy and providing patient education (see Figure 3). Pharmacists can also teach patients about new drug products and technological advancements in eye care. Because adherence to ocular medications is poor, pharmacists and their staff need to be well versed on ways to improve the medication management process. Only then can patients achieve their goals.

Figure 3. Advancing Pharmacists and Pharmacy Technicians Role in Ocular Health

Best

1. **Be COMMUNITY CHAMPIONS** and talk to aging patients about the importance of screening for glaucoma and age-related macular degeneration

2. **Collaborate** with local ocular care specialists to enhance information transfer and improve patient safety

3. **Counsel, counsel, counsel and demonstrate** proper technique for instilling eye drops and ointments. It takes just a few minutes!

Better

1. **Always ask about potential adherence issues** (especially arthritis) when filling prescriptions for ophthalmics

2. **Recognize that cap color means something** when dispensing ophthalmics and make a note of it! This can increase safety.

3. **Know the basic treatment approaches** for common ophthalmic products, especially conjunctivitis and dry eye, which are common

Good

1. **Be familiar with ocular conditions** in general, and the red flags that indicate referral to an ocular specialist

2. **Educate patients** about the differences between eye conditions and eye products

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REFERENCES


45. TrueTear website. https://www.truetear.com/


