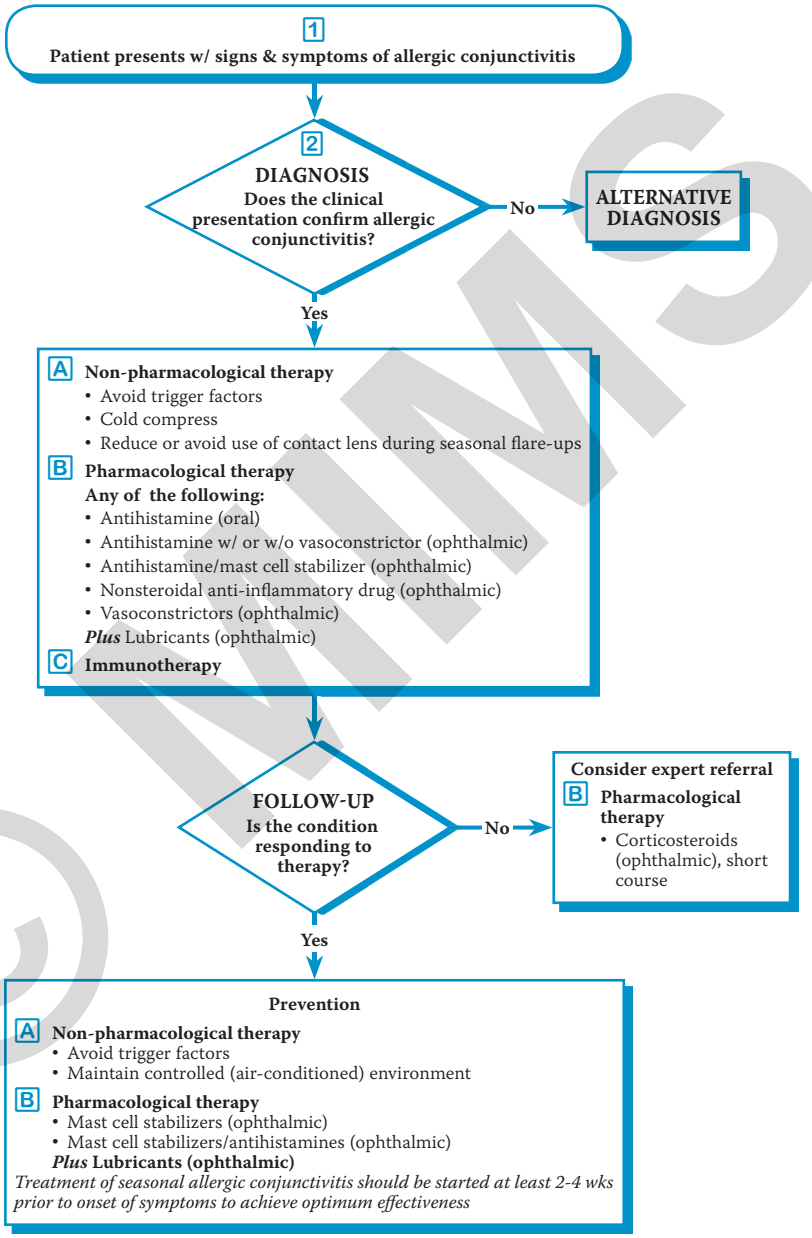
Conjunctivitis - Allergic, Seasonal & Perennial (1 of 9)



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1 ALLERGIC CONJUNCTIVITIS

- Direct exposure of ocular mucosal surfaces to the environment that causes an immediate hypersensitivity reaction in which triggering antigens couple to reaginic antibodies (IgE) on the cell surface of mast cells & basophils, leading to the release of histamines that causes capillary dilation & increased permeability &, thus, conjunctival injection & swelling
  - Nerve endings are also stimulated causing pain & itching

Seasonal Allergic Conjunctivitis (SAC)
- Most common form of allergic conjunctivitis in temperate climates
- Usually occurs & recurs at a certain period of the year (eg summer)
- Subjectively more severe than PAC

Perennial Allergic Conjunctivitis (PAC)
- Manifests & recurs throughout the year w/ no seasonal predilection
- Most common in tropical climates

Vernal Keratoconjunctivitis (VKC)
- Most commonly affects young male individuals residing in hot, dry tropical places (eg Middle East, India, North/South America)

Atopic Keratoconjunctivitis (AKC)
- Attributed to a positive family history of atopy
- Most often triggered by environmental factors

Giant Papillary Conjunctivitis (GPC)
- An inflammatory reaction by the eyelids to a foreign object
- Most commonly associated w/ use of contact lenses; other causes include exposed post-operative sutures, ocular prostheses, glaucoma filtering blebs

2 DIAGNOSIS

- Allergic conjunctivitis are usually diagnosed by history & clinical presentation

History

Symptoms
- Ocular/periocular itching w/ redness, tearing, burning, stinging, photophobia, watery discharge, &/or ecchymosis ("allergic shiner"), foreign body sensation; characterized by exacerbations & remissions
  - Itching is considered the cardinal symptom
  - Identify the date & timing of onset, & progress of symptoms
  - Symptoms tend to decrease w/ age

Medical history
- Personal or family history of other allergic conditions (eg atopic dermatitis, allergic rhinitis, asthma)

Determine Possible Trigger Factors
- Review history w/ regards to:
  - History of exposure to allergens
    - House dust mites, animal dander, & feathers are the major allergens implicated in PAC & AKC
  - Occupational exposure
  - Travel
  - Use of eye care products, topical medications, or solutions
  - Use of contact lenses (lens hygiene, duration of use, frequency of lens replacement)

Physical Exam
- Clinical signs are usually bilateral & vary based on patient's age, mediating cell type & association w/ other conditions
- Conjunctival chemosis, hyperemia & a predominantly papillary conjunctival reaction

Lab Tests
- Rarely needed to make diagnosis-
- Usually done for academic or confirmatory purposes

Conjunctival Scrapings
- If positive for eosinophils it is strongly suggestive of allergy
- Negative scraping is inconclusive

Confocal Microscopy
- A non-invasive procedure used to evaluate for AKC & other ocular disease w/ underlying conditions

Cytological Exam of Tear Fluid
- Collect tear sample w/ capillary tube, spread on slide & stain
- Allergic response is indicated by presence of eosinophils, neutrophils &/or lymphocytes
  - Tear histamine or tryptase levels can also be measured

Immunoassay Testing of Tear Fluid
- Measure mast cell's activity by determining the level of tryptase using immunoassay testing

Alternative Diagnosis
- Bacterial or viral conjunctivitis
- Blepharoconjunctivitis
- Keratitis sicca/dysfunctional tear syndrome (dry eye)
- Superior limbic keratoconjunctivitis

A NON-PHARMACOLOGICAL THERAPY

Identification of Trigger Factors

- Trial of avoidance may identify antigens
- Skin testing or allergen challenge (serum antigen specific IgE antibody measurements) may be useful for identifying specific problematic antigens but are rarely needed

Avoidance of Trigger Factors

- Eg closing windows, filtering air, removing pets & stuffed toys, vacuuming & dusting regularly, etc
- Mainstay of managing allergic conjunctivitis
- Use of goggle-type glasses are recommended during pollen-flying period
- Reduce or avoid use of contact lens during seasonal flare-ups
- House mites are a common allergen & can be reduced by using dust mite-proof encasings on pillows & mattresses, & washing sheets in hot water
- Sensitive patients should attempt to limit exposure to outdoors during times of high pollen count or other allergen counts

Cold Compress

- Causes vasoconstriction which can improve patient comfort by reducing itching

B PHARMACOLOGICAL THERAPY

Antihistamines (Ophthalmic)

- Eg Emedastine, Levocabastine, Nedocromil
- Compete for the histamine receptor sites
  - In human conjunctiva, stimulation of H_1 receptor mediates symptoms of pruritus while H_2 receptor is involved in vasodilation
- Reduce itching & vasodilation
  - Emedastine was shown to be more effective than Levocabastine in decreasing chemosis, eyelid swelling, & other signs & symptoms of seasonal allergic conjunctivitis
    - A selective H_1 antagonist w/ no adrenergic, dopaminergic or serotonergic effect
- Provides immediate ocular relief as compared to oral antihistamines
- May be used as monotherapy or in combination w/ decongestants/vasoconstrictors in treating signs & symptoms of allergic conjunctivitis
  - Antihistamine w/ decongestant/vasoconstrictor should not be used for >2 weeks without medical advice
- Should not be used for >6 weeks without medical advice
  - Prolonged use of antihistamines that are nonselective may cause ciliary muscle paralysis, mydriasis, & photophobia, especially when used by patients w/ lighter irides
  - May also cause angle-closure glaucoma particularly in patients who are at risk (ie history of narrow-angle glaucoma, patients w/ narrow angles)

Antihistamines (Oral)

- Eg Cetirizine, Chlorpheniramine, Hydroxyzine, Loratadine
- May be used as adjunctive therapy for moderate to severe allergic conjunctivitis
- Useful in cases accompanied by non-ocular allergies (eg allergic rhinitis)
- Inferior to ophthalmic antihistamines primarily due to 1- to 2- hours delay from systemic administration to delivery to ocular tissues but has longer duration of action
- More likely than topical antihistamines to cause side effects
  - May be associated w/ drying of mucosal membranes & decreased tear production, especially in patients w/ concomitant dry eye

Antihistamines/Mast Cell Stabilizers (Ophthalmic)

- Eg Alcaftadine, Azelastine, Bepotastine besilate, Epinastine, Ketotifen, Olopatadine
- Have both mast-cell stabilizing & antihistaminic activity
  - Binds to H_1 & H_2 receptors, stabilizes mast cell, & down-regulates inflammatory markers that affects early & late phases of the conjunctival allergic response
- May be used for either acute or chronic diseases
  - Relieve acute symptoms (eg ocular itchiness & redness) & prevent recurrence of allergic conjunctivitis
- Fast-acting, effective & generally well tolerated

B PHARMACOLOGICAL THERAPY (CONT'D)

Corticosteroids (Ophthalmic)

- Used for the treatment of severe & chronic ocular allergy
  - Block inflammatory pathways that perpetuate the persistent & chronic forms of ocular allergy
- Used when patient's symptoms have not responded to other agents
  - 1-2 weeks course can be added to antihistamine/mast cell stabilizers if symptoms were not controlled
  - Lowest potency & frequency that relieves the patient's symptoms should be given
- Relieve symptoms fast
- Should only be used for a short period of time (≤2 weeks) & under the guidance of an experienced ophthalmologist
  - Chronic use of topical steroids is associated w/ glaucoma, cataract formation, & corneal/conjunctival infection
  - Lowest potency & frequency that relieves patient's symptoms should be given

Lubricants (Ophthalmic)[1]

- Consist of saline solution combined w/ wetting & viscosity agents, which is used 2-6x/day as needed
  - Non-preserved formulations are recommended if will be used frequently to prevent allergic reactions secondary to preservatives
- Assist in the removal & dilution of allergens that come in contact w/ the eye surface
  - Do not alter the pathophysiology of the disease but treat co-existing tear deficiency
- Numerous lubricants that differ by class, osmolarity & electrolyte composition are available

Mast Cell Stabilizers (Ophthalmic)

- Eg Cromoglicic acid, Lodoxamide, Nedocromil, Pemirolast
- Inhibit degranulation of mast cells which limits the release of inflammatory mediators & platelet-activating factor
- Used for prevention of symptoms & for conditions that are recurrent or persistent
  - Have slower onset of action as compared to antihistamines
    - Effects of Cromoglicic acid are evident 2-5 days after the initiation of the therapy w/ maximum improvement of ocular symptoms after 15 days
  - Requires multiple applications everyday to show effects
  - Most useful in the seasonal management of chronic allergic diseases of the eye
- Usually given to patients w/ moderate symptoms, after an ophthalmic decongestant have been administered to provide immediate relief
- Studies have shown that Lodoxamide is more effective than Cromoglicic acid in reducing eosinophil activation, & clinical signs & symptoms
- Pemirolast was shown to specifically inhibit mast cell degranulation, preventing the release of chemical mediators like histamine
- May also help in improving symptoms of allergic rhinitis
- Generally well tolerated & may be used as long as needed

Nonsteroidal Anti-inflammatory Drugs (Ophthalmic)

- Eg Ketorolac
  - Inhibits the activity of cyclooxygenase blocking the production of prostaglandins
  - Helps reduce ocular signs & symptoms like itching or conjunctival hyperemia
  - Does not mask ocular infections, affect wound healing or intraocular pressure, nor contribute to cataract formation

Vasoconstrictors (Ophthalmic)

- Eg Naphazoline, Phenylephrine, Tetrahydrozoline
- Sympathomimetic agents
- Decreases vascular congestion & eyelid edema but do not affect allergic response
- Usually used in combination w/ ophthalmic antihistamines
  - Have been shown to have synergistic effect
    - Based on studies, Naphazoline *plus* Antazolin or Pheniramine were comparable in decreasing the signs & symptoms of allergic conjunctivitis
- Chronic use (>10 days) may cause conjunctivitis medicamentosa

[1]Many ophthalmic lubricants are available. Please see the latest MIMS for specific formulations.

C IMMUNOTHERAPY

Principles of Therapy

- Repeated administration of specific allergens in patients w/ IgE-mediated conditions to provide protection against allergic symptoms associated w/ exposure to these allergens
- Only intervention that alters the natural history of allergic rhinoconjunctivitis
- Activates regulatory T cells, thereby altering humoral response to allergens by increasing CD8+ T cells & IL-10, & reducing IL-13 production
- Indicated for patients w/ the following:
  - Evidence of specific IgE antibody to allergen (positive allergy test results)
  - Any of the following:
    - Clinically diagnosed w/ both allergic rhinoconjunctivitis & asthma
    - Required medications
    - Poor response to avoidance measures
    - Adverse effects to medications
- Initial dose should be performed in a medical facility by a trained personnel
- Recommended course is usually 4-5 years

Subcutaneous Immunotherapy (SCIT)

- Efficacy is comparable to that of nasal glucocorticoids
- Limited by frequent injection on regular basis & small risk of anaphylactic reactions

Sublingual immunotherapy (SLIT)

- A more viable treatment compared to SCIT as self-administration is encouraged w/ this form
- Use should be limited to those who can tolerate systemic reactions & its treatment
- Auto/self-injectable Epinephrine should be prescribed to all patients receiving SLIT
- Has been associated w/ mild oral & GI symptoms & less risk for anaphylaxis compared to SCIT

FOLLOW-UP

- Frequency depends on the severity of the disease, etiology, & treatment
- Visual acuity should be measured & slit-lamp biomicroscopy should be performed
  - Intraocular pressure measurement & pupillary dilation should be done if corticosteroids have been used in treating patient's chronic or recurrent conjunctivitis
    - Assesses possible side effect such as cataract & glaucoma
    - Baseline & periodic measurement is advised

Dosage Guidelines

ANTIHISTAMINES & ANTIALLERGICS (ALLERGEN EXTRACTS)

Drug	Available Strength	Dosage	Remarks
House-dust mite allergen extract (*D pteronyssinus & D farinae*)	10 IR/mL 300 IR/mL	**Initial dose:** **Day 1-6 (10 IR/mL):** Spray under the tongue w/ increasing doses/day: 1, 2, 4, 6, 8, 10 sprays consecutively 24 hrly until Day 6 **Day 7-9 (300 IR/mL):** Spray under the tongue w/ increasing doses/day: 1, 2, 4 sprays consecutively 24 hrly **Maintenance dose** **Day 10 onwards (300 IR/mL):** Spray 4x under the tongue 24 hrly	**Adverse Reactions** • Nasopharyngeal effects (oromucosal blistering, throat irritation, nasal congestion, tonsillitis); CNS effects (headache, dizziness); Resp effects (bronchitis, asthma, dyspnea); Other effects (chest pain, GI upset, pruritus) **Special Instructions** • Use w/ caution in patients w/ fungal infection, oral cavity inflammation, recent tooth extraction, oral lesions, oral surgery, modified diet (strict low sodium diet) • Maintain sublingually for 2 min before swallowing

ANTIHISTAMINES & ANTIALLERGICS (ORAL)[1]

Drug	Dosage	Remarks
First Generation		
Chlorpheniramine	**1-2 yr:** 1 mg PO 12 hrly **2-5 yr:** 1 mg PO 4-6 hrly **Max dose:** 6 mg/day **6-12 yr:** 2 mg PO 4-6 hrly **Max dose:** 12 mg/day	**Adverse Reactions** • CNS effects (drowsiness, dizziness, headache, somnolence, lassitude, incoordination; paradoxical stimulation may occur esp at high doses); GI effects (N/V, diarrhea, epigastric pain, anorexia or increased appetite); Dermatologic effects (hypersensitivity reactions, rashes); Antimuscarinic effects (dry mouth, viscous secretions, urinary retention, blurred vision); CV effects (palpitations, arrhythmias, rarely hazardous ventricular arrhythmias) **Special Instructions** • Use w/ caution in patients w/ breathing problems (eg asthma, chronic bronchitis), liver disease, seizure disorder
Clemastine	**1-3 yr:** 0.25-0.5 mg PO 12 hrly **3-6 yr:** 0.5 mg PO 12 hrly **6-12 yr:** 0.5-1 mg PO 12 hrly **>12 yr:** 1 mg PO 12 hrly	
Diphenhydramine	6.25-25 mg PO 6-8 hrly **Max dose:** 300 mg/day	
Promethazine	**2-5 yr:** 5-15 mg/day PO divided 12-24 hrly **5-10 yr: 10-25 mg/day PO** divided 12-24 hrly	
Second Generation		
Bilastine	**>12 yr:** 20 mg PO 24 hrly	**Adverse Reactions** • CNS effects (drowsiness, sleepiness, headache, dizziness); GI effects (N/V, dry mouth, stomach pain, diarrhea); Resp effects (cough, epistaxis, bronchospasm,); Other effects (excessive tiredness) **Special Instructions** • Use w/ caution in patients w/ renal/hepatic disease
Cetirizine	**<6 mth:** 2.5 mg PO 24 hrly **6 mth-<2 yr:** 2.5 mg PO 12-24 hrly **2-5 yr:** 2.5 mg PO 12 hrly or 5 mg PO 24 hrly **6-11 yr:** 5 mg PO 12 hrly or 10 mg PO 24 hrly **≥12 yr:** 10 mg PO 24 hrly	
Loratadine	**2-12 yr:** **>30 kg:** 10 mg PO 24 hrly **<30 kg:** 5 mg PO 24 hrly	
Mequitazine	5 mg PO 12 hrly	

[1]Combination preparations are available. Please see the latest MIMS for specific formulations.

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Dosage Guidelines

EYE CORTICOSTEROIDS[1]

Drug	Available Strength	Dosage	Remarks
Dexamethasone	0.1% ophth drops, susp	Instill 1-2 drops 1-6 hrly	**Adverse Reactions** • Increased intraocular pressure that is dependent on concentration, frequency & duration of use • Can lead to secondary open angle glaucoma (irreversible optic nerve damage & possible irreversible blindness) • May slow corneal wound healing; infection of the cornea/conjunctiva; cataract formation • Rarely: Transient stinging, burning; ocular discharge, potential for systemic side effects **Special Instructions** • Should be used w/ caution & only in severe cases of allergic conjunctivitis • Short course pulse treatment is preferred during the acute symptomatic phase is desirable rather than prolonged chronic treatment • Should be monitored by a specialist
	0.1% oint	Apply 6 hrly	
Fluorometholone	0.1% ophth drops, susp	Instill 1-2 drops 6-12 hrly	
Loteprednol etabonate	0.2% ophth susp 0.5% ophth drops	Instill 1-2 drops 6 hrly	
Prednisolone	0.12%, 0.5%, 1% ophth drops, susp	Instill 1-2 drops 4-12 hrly or as required	

[1]Corticosteroids combined w/ vasoconstrictors are available. Please see the latest MIMS for specific formulations.

OPHTHALMIC DECONGESTANTS[1]

Drug	Available Strength	Dosage	Remarks
Antihistamine			
Emedastine	0.05% ophth soln	Instill 1 drop 6-12 hrly	**Adverse Reactions** • Local effects (transient ocular burning/stinging, blurred vision, dry eye, tearing); Other effects (headache, asthenia, rhinitis, abnormal dreams) **Special Instructions** • Use w/ caution in patients w/ renal or hepatic impairment • Remove contact lens prior to administration then reinsert after 10 mins
Antihistamine/Mast Cell Stabilizers			
Alcaftadine	0.25% ophth soln	Instill 1 drop 24 hrly	**Adverse Reactions** • Local effects (burning sensation, hyperemia, discharge, visual disturbance); Other effects (headache, rhinitis) - Ketotifen may cause somnolence, allergic reactions **Special Instructions** • Use w/ caution in patients who will drive or operate machineries • Remove contact lens prior to administration then reinsert after 10 mins
Epinastine	0.05% ophth soln	Instill 1 drop 12 hrly	
Ketotifen	0.025% ophth soln	**≥3 yr:** Instill 1 drop 12 hrly	
Olopatadine	0.1% ophth soln	Instill 1-2 drops 12 hrly	
	0.2% ophth soln	Instill 1 drop 24 hrly	

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Dosage Guidelines

OPHTHALMIC DECONGESTANTS[1] (CONT'D)			
Drug	**Available Strength**	**Dosage**	**Remarks**
Antihistamine/Vasoconstrictors			
Antazoline/ naphazoline	0.5/0.05% ophth soln	Instill 1 drop 3-4 hrly	**Adverse Reactions** • Local effects (conjunctival irritation, hyperemia) **Special Instructions** • Avoid use in patients w/ narrow-angle glaucoma • Use w/ caution in patients w/ CV disease, DM, hypertension, hyperthyroidism, serious eye disease or infection
Antazoline/ tetryzoline (Antazoline/ tetrahydroline)	0.05%/0.04% ophth drops	**Acute treatment:** Instill 1 drop 3 hrly **Maintenance therapy:** Instill 1 drop 8-12 hrly **>2 yr:** 1-2 drops 24 hrly	**Adverse Reactions** • Local effects (transient burning sensation, mydriasis, hyperemia); Other effects (headache, drowsiness) **Special Instructions** • Avoid use in patients w/ narrow-angle glaucoma or dry eye syndrome • Use w/ caution in patients w/ DM, hypertension, severe heart disease, hyperthyroidism, pheochromocytoma, rhinitis sicca, chronic & recurring allergies • Remove contact lens prior to administration then reinsert after 15 mins
Mast Cell Stabilizers			
Cromoglicic acid (Cromolyn Na, Disodium cromoglycate, Na cromoglycate)	2% ophth drops	**≥4 yr:** Instill 1-2 drops 4-6 hrly	**Adverse Reactions** • Local effects (transient ocular burning/stinging, pruritus, erythema) - Permirolast may cause blepharitis, palpebral dermatitis **Special Instructions** • Avoid use w/ contact lens • Use w/ caution in patients w/ renal or hepatic disorders • Discontinue Pemirolast if irritation occurs
Lodoxamide	0.1% ophth drops	Instill 1-2 drops 6 hrly	
Pemirolast	0.1% ophth drops	Instill 1 drop 12 hrly	
Nonsteroidal Anti-inflammatory Drug			
Ketorolac	0.5% ophth drops	Instill 1 drop 6 hrly	**Adverse Reactions** • Local effects (transient ocular burning/stinging, irritation, allergic reactions, ocular infection, superficial keratitis) **Special Instructions** • Avoid use w/ contact lens • Use w/ caution in patients w/ bleeding tendencies or receiving medication that prolongs bleeding time, w/ known sensitivity to acetylsalicylic acid or other NSAIDs

[1]Combination preparations are available. Please see the latest MIMS for specific formulations.

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Dosage Guidelines

OPHTHALMIC DECONGESTANTS[1] (CONT'D)

Drug	Available Strength	Dosage	Remarks
Other Ophthalmologic Antiallergics			
Isospaglumic acid	4.9% ophth drops	Instill 1 drop 4-12 hrly	**Adverse Reactions** • Local effects (mild burning & prickling sensation) **Special Instructions** • Remove contact lens prior to administration
Vasoconstrictors			
Naphazoline	0.05%, 0.01%, 0.1% ophth soln/drops	Instill 1-2 drops 3-4 hrly	**Adverse Reactions** • Local effects (pupillary dilation, increase in IOP, hyperemia, irritation); Other effects (sensitivity reactions, hypertension, hyperglycemia, drowsiness) - Tetryzoline may also cause N/V, headache, rebound congestion **Special Instructions** • Avoid use in patients w/ narrow-angle glaucoma • Use w/ caution in patients w/ hypertension, DM, cardiac irregularities, hyperthyroidism • Remove contact lens prior to administration
	0.012% ophth drops	Instill 1-2 drops up to 6 hrly	
Tetryzoline (Tetrahydrozoline)	0.05% ophth drops	Instill 1-2 drops 6-12 hrly	

[1]Combination preparations are available. Please see the latest MIMS for specific formulations.

OTHER EYE PREPARATIONS

Drug	Available Strength	Dosage	Remarks
Azelastine	0.05% ophth soln	Instill 1-2 drops 12 hrly	**Adverse Reactions** • Local effects (transient ocular burning/ stinging, blurred vision, dry eye, tearing); Other effects (somnolence, taste disturbances, headache, nausea, dry mouth) **Special Instructions** • Dip tip of bottle in boiling water, dry then cover after every use
Nedocromil sodium	2% ophth soln	**≥3 yr:** Instill 1-2 drops 12 hrly	**Adverse Reactions** • Local effects (ocular burning/stinging/ irritation, conjunctivitis, eye redness, photophobia); CNS effects (headache, somnolence); Other effects (rhinitis, asthma, nasal congestion, taste disturbance) **Special Instructions** • Dip tip of bottle in boiling water, dry then cover after every use • Avoid use w/ contact lens

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