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Drug Class Review: Ophthalmic Medication for Allergies

Date of Review: **End Date of Literature Search:** 10/31/2025

Purpose for Class Review:
Review the evidence for the safety and efficacy of ophthalmic eye preparations used to manage allergic conjunctivitis as a pathway to coverage will be necessary once the Health Evidence Review Committee (HERC) benefit plan update is implemented in January 2027. Currently allergic conjunctivitis is not funded by HERC and over-the-counter versions of ophthalmic allergy medications are currently not covered.

Plain Language Summary:
- Conjunctivitis is an inflammation of the conjunctiva. The conjunctiva is the thin membrane that lines the inner surface of the eyelids and the whites of the eyes. Conjunctivitis can affect children and adults.
- There are many potential causes of conjunctivitis, including bacterial or viral infections and allergies. The most common symptoms of conjunctivitis include red eyes, itching, burning and discharge.
- Treatment of allergic conjunctivitis includes avoiding allergy triggers and lubricating eye drops which are available without a prescription. For symptoms that are bothersome, antihistamine eye drops can relieve itching and redness.
- The Drug Utilization Management and Research team recommends making some eye drops used to treat allergic conjunctivitis available without prior authorization for people with Oregon Health Plan insurance.

Research Questions:
1. What is the comparative efficacy for ophthalmic preparations used to treat allergic conjunctivitis?
2. Do ophthalmic preparations differ in safety when used to treat allergic conjunctivitis?
3. Are there specific subpopulations for which one ophthalmic drop or ointment is better tolerated or more effective than other available ophthalmic preparations when used to manage allergic conjunctivitis?

Conclusions:
- There is limited high-quality comparative evidence to evaluate safety and efficacy of ophthalmic preparations indicated for managed of allergic conjunctivitis.
- Two systematic reviews published in 2015 identified moderate-quality evidence that showed azelastine and olopatadine ophthalmic drops are effective in reducing ocular itch when compared to placebo.[1,2]
    - There were limited data to inform if some treatments are more effective than others.[1]
    - Results from one meta-analysis suggested that olopatadine may be more effective than ketotifen in relieving itching, although there was high statistical heterogeneity between the 4 studies included in the analysis.[1]
    - Moderate-quality evidence showed olopatadine has similar efficacy ketotifen and epinastine in relieving ocular itch.[2]

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- Alcaftadine appears to have a superior effect in reducing ocular itch compared to topical olopatadine (moderate-quality evidence).[2]
- Poor quality of reporting challenged the synthesis of evidence, and there was large variability in reporting outcomes.[1] The overall quality of the studies and reporting was poor, and most studies had small sample sizes.[1] Trials only evaluated short-term effects, with a range of treatment of one to eight weeks.[1]

- No high-quality clinical practice guidelines have been published to guide treatment of allergic conjunctivitis.
- There is insufficient evidence to show that there are subgroups of patients based on demographics (based on age, ethnicity, comorbidities, disease duration or severity), for which one treatment for those with allergic conjunctivitis is more effective or associated with fewer adverse events.

Recommendations:

- Create a new PDL class, "Ophthalmic Medications for Allergies".
- Make at least one prescription product preferred without prior authorization. Defer to costs as clinical evidence does not differentiate products.
- Evaluate costs in executive session to identify which ophthalmic products should be preferred and if over the counter products should be covered.

Background:

Ocular allergies are a heterogeneous collection of immunoglobulin (Ig)E- and non–IgE-mediated conditions.[3] Ocular allergy includes seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), and contact blepharoconjunctivitis (CBC).[3] The pathophysiology of allergic conjunctivitis is mediated by IgE-related mast cell activation, with release of histamine and other mediators promoting further immune cell activation and inflammation.[4] Seasonal allergic conjunctivitis and PAC account for most ocular allergies (95%-98%) and AKC and VKC represent an estimated 2% of all ocular allergies.[3] Classification and clinical features of ocular allergic conditions are presented in **Table 1**. Allergic conjunctivitis or conjunctival symptoms are present in 30-71% of patients with allergic rhinitis.[5] Seasonal allergic conjunctivitis and PAC can affect between 14% to 45% of the general population, depending on geographical region.[6] Ocular allergy is often underdiagnosed because only 10% of patients with ocular allergy symptoms seek medical attention, as most patients manage with over-the-counter medications and nonpharmacological remedies.[7]

Table 1. Classification and Clinical Features of Ocular Allergic Conditions[3]

Feature	Seasonal Allergic Conjunctivitis	Perennial Allergic Conjunctivitis	Vernal Keratoconjunctivitis	Atopic Keratoconjunctivitis	Contact Blepharoconjunctivitis
Pattern and Frequency	Intermittent, usually spring	Persistent	Persistent, worse in spring and summer	Persistent with exacerbations	Intermittent or persistent
Comorbid Conditions	Allergic rhinitis, allergic asthma	Allergic rhinitis, allergic asthma	Allergic rhinitis	Atopic dermatitis, allergic rhinitis, asthma	Contact dermatitis of other skin sites, remote from the eyes
Age and Sex	Childhood and young adult onset	Childhood and young adult onset	Childhood: ends by age 20 years. Male prevalence greater than female.	Usually, adults aged 30 to 50 years, can start in childhood. Male prevalence greater than female.	Middle-aged or older. Female prevalence greater than male.

Trigger	Pollen	Dust mite, animal dander, other perennial allergens	Grass pollen, tree pollen, hot and humid environment	Spring and summer seasonal or perennial allergens may worsen	Cosmetics, metals, or medications near the eye
Pathophysiology	IgE	IgE	IgE or non-IgE	IgE	Non-IgE
Abbreviations: IgE = Immunoglobulin E					

Four symptoms characterize ocular allergies: redness, itchiness, swelling, and watering (tearing).[3] Many ocular allergy symptoms overlap with those of dry eye, with more than 50% of patients with ocular allergy also having dry eyes.[3] A detailed history is essential to prevent misdiagnosis of serious conditions that have potential consequences such as vision loss.[3] In particular, VKC and AKC require an ophthalmological evaluation for diagnosis and a close follow-up.[5] Evaluation should not only focus on eliciting symptoms but should also include laterality, duration, triggers, previous treatments, contact lens use, family history, comorbid asthma, comorbid allergic rhinitis, exposures (occupational, environmental, and topical such as cosmetics), and history of ocular surgery, as these are important considerations in making a diagnosis.[3]

The 4 symptom domains of redness, itchiness, swelling, and watering (tearing) constitute an unvalidated questionnaire called the Total Ocular Symptom Score (TOSS) which can be used for describing symptom severity and monitoring treatment response.[3] Scoring is based upon frequency of symptoms as: 4) all of the time; 3) most of the time; 2) half of the time; 1) some of the time; and 0) none of the time.[3] The only Quality of Life (QoL) questionnaire available for ocular allergy pertains specifically to VKC. The QoL in VKC children (QUICK) questionnaire grades frequency of ocular allergy on a 3-point scale (1 = never, 2 = sometimes, and 3 = always) to assess disease status.[3]

The recommended management approach for acute and chronic forms of ocular allergies starts with allergen identification, followed by non-pharmacological treatments (allergen avoidance and hygiene measures), progressing to pharmacological treatment.[7] Early detection of allergic triggers by skin testing and simple allergen avoidance measures, such as eyewear barrier protection, frequent washing of clothes, hypoallergenic bedding and bathing or showering before bedtime, may all help to stop disease progression.[3] Avoidance of eye rubbing, cold compresses, and refrigerated artificial tears may also provide symptomatic relief.[3] Contact lens wearers sensitized to pollen may be better served by switching to glasses during peak pollen seasons.[3] Contact lenses must be removed during the administration of topical medications because of potential interaction between contact lenses and preservatives in ophthalmic medications but may be replaced after 10 minutes after administration.[3]

According to guidelines, topical medications are recommended treatments for the management of SAC and PAC.[7] These medications are presented in **Table 2**. When symptoms of allergic rhinitis are present, treatment options usually include systemic antihistamines and intranasal corticosteroids in addition to topical ophthalmic treatment.[7] Topical antihistamines (pheniramine, cetirizine) relieve itching and redness.[3] Ocular decongestants (naphazoline, tetrahydrozoline) reduce ocular erythema through vasoconstriction but have little effect on alleviating itching.[3] Ocular decongestants may be combined with antihistamines to relieve redness and itching, and these combination products are available over the counter without a prescription. The long-term use of ocular decongestants is limited by adverse effects such as ocular burning, mydriasis, worsening of narrow angle glaucoma, rebound hyperemia, conjunctivitis medicamentosa, and tachyphylaxis.[3] Caution should be used with ocular decongestants in patients with cardiovascular disease, hyperthyroidism, and diabetes, and they should be avoided altogether in patients with angle closure glaucoma.[3] Mast cell stabilizers inhibit degranulation of mast cells and prevent the release of mast cell mediators associated with the late phase of the allergic response.[3] The mast cell stabilizer, cromolyn, requires a preloading period before exposure to allergens, generally 3 to 5 days but up to 2 weeks for full benefits of therapy, and frequent instillation, often leading to poor adherence to therapy.[3]

Dual-action drugs have antihistamine and mast cell stabilizing properties and are currently the most commonly prescribed group of agents for SAC.[7] This combination of two mechanisms rapidly affects the early, as well as the late, phase of allergic conjunctivitis signs and symptoms.[4] These agents block the histamine receptor, regulate mast cell reaction, and suppress the inflammatory mediator secretions.[4] The antihistaminic effect reduces the early phase of ocular allergic response action such as itching, whereas the stabilization of mast cell inhibits the release of inflammatory mediators such as cytokines and lipid mediators, which is associated with the late-phase response of ocular allergic conjunctivitis.[4] Side effects are generally mild and include headache, cold-like symptoms, burning, stinging, and possible transient dysgeusia (bitter taste).[7]

Table 2. Ocular Medications by Pharmacologic Classification[8,9]

Medication (BRAND NAME)	OTC or Rx	Dosing	Minimum Age
Decongestants (Vasoconstrictors)			
Naphazoline	OTC	1-2 drops 4 times a day	6 years
Tetrahydrozoline	OTC	1-2 drops 4 times a day	6 years
Decongestant/Antihistamine			
Naphazoline/Pheniramine (NAPHCON A, OPCON-A, VISINE-A)	OTC	1-2 drops 4 times a day	6 years
Antihistamine			
Cetirizine (ZERVIATE)	Rx	1 drop twice a day	2 years
Dual Action: Antihistamine/Mast Cell Stabilizers			
Alcaftadine (LASTACAFT)	OTC	1 drop once daily	2 years
Azelastine (OPTIVAR)	Rx	1 drop twice a day	3 years
Bepotastine (BEPREVE)	Rx	1 drop twice a day	2 years
Epinastine (ELESTAT)	Rx	1 drop twice a day	2 years
Ketotifen (ALAWAY, ZATIDOR)	OTC	1 drop twice a day	3 years
Olopatadine 0.1% (PATANOL)	OTC	1 drop twice a day	2 years
Olopatadine 0.2% (PATADAY)	OTC	1 drops once a day	2 years
Olopatadine 0.7% (PATADAY)	OTC	1 drops once a day	2 years
Mast Cell Stabilizer			
Cromolyn (OPTICROM)	OTC	1-2 drops 4 to 6 times a day	4 years
Abbreviations: OTC = over the counter; Rx = prescription			

A summary of relevant drug information is available in **Appendix 2**, which includes pharmacology and pharmacokinetic characteristics of these drugs, contraindications, warnings and precautions.

Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 2**, which includes dates, search terms and limits

used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Canada's Drug Agency (CDA-AMA), Scottish Intercollegiate Guidelines Network (SIGN), and Oregon Mental Health Clinical Advisory Group (MHCAG) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:

Cochrane: Treatments for Allergic Conjunctivitis[1]

A 2015 Cochrane review assessed the efficacy of topical antihistamines and mast cell stabilizers, alone or in combination, in treating seasonal allergic conjunctivitis.[1] Literature was searched through July 14, 2014.[1] Thirty trials (n=4344) with 17 different drugs or treatment comparisons met inclusion criteria.[1] The primary outcome was any participant-reported evaluation (by questionnaire) of severity of 4 main ocular symptoms: itching, irritation, watering eye, and photophobia, both separately and, if possible, by an overall symptom score.[1] The following antihistamines and mast cell stabilizers marketed in the United States were evaluated in at least one RCT: olopatadine, ketotifen, azelastine, bepotastine, and combination of levocabastine and pemirolast.[1] The most common comparison was azelastine versus placebo (9 studies).[1] The quality of the studies and reporting was variable, but overall, the risk of bias was low.[1] Trials evaluated only short-term effects, with a range of treatment of one to eight weeks.[1] Meta-analysis was only possible in one comparison (olopatadine versus ketotifen).[1]

Nine studies compared azelastine against placebo, conducted over 2 to 6 weeks.[1] All studies reported less itching with azelastine compared to placebo, but in some studies, it was not possible to confirm whether the results were statistically significant.[1] It was not possible to perform formal meta-analyses for this treatment comparison due to variations of outcomes reported and the lack of suitable data.[1]

Four eligible studies compared olopatadine 0.1% and ketotifen 0.25% or 0.5%.[1] Studies were conducted over 2 to 4 weeks.[1] In all studies, the sample size was relatively small (n=32 to 92).[1] All four studies collected data on participant-reported itching using a 0-3 scale.[1] Two studies did not find any differences between olopatadine and ketotifen in itching reporting while two studies found a greater reduction in itching with olopatadine than with ketotifen after 2 weeks of treatment.[1] A random-effects meta-analysis of these 4 studies showed evidence of a statistically significant difference in favor of olopatadine in the reduction of itching at 14 days (mean difference [MD] -0.32, 95% confidence interval [CI],-0.59 to -0.06).[1] However, there was high statistical heterogeneity (I^2 = 83%).[1]

One study, at high risk of bias, compared bepotastine to olopatadine 0.2% in an investigator-masked, single-center, cross-over study that randomized 30 participants.[1] Participants were not masked.[1] The duration of treatment was 2 weeks, followed by a 7-day washout period.[1] After the washout period, participants were crossed-over to the alternative treatment for 2 additional weeks.[1] From the participants' diary responses, bepotastine was significantly more effective at relieving morning and evening ocular allergy symptoms (P=0.032 and P<0.0001, respectively) compared to olopatadine.[1]

In summary, there is some evidence to support the ability of azelastine to reduce symptoms and signs of seasonal allergic conjunctivitis when compared with placebo.[1] There were limited data to evaluate whether some treatments are more effective than others for short-term symptom relief.[1] Results from a meta-analysis suggested that olopatadine may be more effective than ketotifen in relieving itching, although there was high statistical heterogeneity between the 4

studies.[1] The overall quality of the studies and reporting was poor, and most studies had small sample sizes.[1] Trials only evaluated short-term effects, with a range of treatment of one to eight weeks.[1]

Topical Olopatadine in the Treatment of Allergic Conjunctivitis

A 2105 systematic review and meta-analysis assessed the safety and efficacy of topical olopatadine versus placebo and other topical medications in treating allergic conjunctivitis.[2] Literature was searched through January 4, 2015 and 23 RCTs met inclusion criteria.[2] Seventeen studies compared topical olopatadine with placebo, of which 11 included only adults and 6 included both adults and children.[2] Five studies compared the efficacy of topical olopatadine versus topical ketotifen, 5 compared topical olopatadine with epinastine, and 3 compared topical olopatadine with alcaftadine.[2] Overall, there was low risk of bias in the RCTs.[2] Ocular itching ratings were made on a scale of 0 (none) to 4 (severe), allowing half-unit increments.[2]

In the meta-analysis of olopatadine 0.1% or 0.2% versus placebo RCTs, olopatadine use was associated with a significantly lower ocular itch, with a pooled mean difference of –1.33 (95% CI, –1.43 to –1.23; p<0.00001; I^2 = 85%; 17 RCTs).[2] In the meta-analysis of olopatadine versus epinastine RCTs, no significant differences were identified between treatments in terms of ocular itch (MD -0.23; 95% CI, -0.50 to 0.03; p=0.08; I^2 = 91%; 5 RCTs).[2] Similar results were observed in the meta-analysis of olopatadine versus ketotifen 0.1% (MD -0.25; 95% CI, -0.64 to 0.15; p=0.22; I^2 = 91%; 5 RCTs).[10] In the meta-analysis of olopatadine versus alcaftadine RCTs, alcaftadine use was associated with a significantly lower ocular itch, with a pooled MD of 0.39 (95% CI, 0.28 to 0.50; p<0.00001; I^2 = 0%; 3 RCTs).[2]

In summary, moderate-quality evidence confirms topical olopatadine 0.1% or 0.2% ophthalmic solution to be a safe and effective medication for allergic conjunctivitis in reducing ocular itch compared to placebo.[2] Moderate-quality evidence showed olopatadine has similar efficacy ketotifen and epinastine in relieving ocular itch.[2] Alcaftadine appears to have a superior effect in reducing ocular itch compared to topical olopatadine (moderate-quality evidence).[2] There was wide variation in study designs, inclusion criteria, baseline symptoms and signs, which made the meta-analysis difficult to interpret due to the heterogeneities across studies.[2]

After review, 8 systematic reviews were excluded due to poor quality (e.g., network meta-analyses), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).[10-17]

Guidelines:

High Quality Guidelines: None identified.

After review, 2 guidelines were excluded due to poor quality.[18,19]

Randomized Controlled Trials:

A total of 98 citations were manually reviewed from the initial literature search. After further review, 98 citations were excluded because of wrong study design (e.g, observational), comparator (e.g, no control or placebo-controlled), or outcome studied (e.g, non-clinical).

References:

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Appendix 1: PDL Status

Generic	Brand	Route	Form	PDL	OTC
alcaftadine	LASTACAFT ONCE DAILY RELIEF	OPHTHALMIC	DROPS	N	O
azelastine HCl	AZELASTINE HCL	OPHTHALMIC	DROPS		F
bepotastine besilate	BEPOTASTINE BESILATE	OPHTHALMIC	DROPS		F
bepotastine besilate	BEPREVE	OPHTHALMIC	DROPS		F
brimonidine tartrate	LUMIFY	OPHTHALMIC	DROPS		O
brimonidine tartrate/PF	LUMIFY	OPHTHALMIC	DROPERETTE		O
cetirizine HCl	ZERVIATE	OPHTHALMIC	DROPERETTE		F
cromolyn sodium	CROMOLYN SODIUM	OPHTHALMIC	DROPS		F
epinastine HCl	EPINASTINE HCL	OPHTHALMIC	DROPS		F
ketotifen fumarate	ALAWAY	OPHTHALMIC	DROPS		O
ketotifen fumarate	CHILDREN'S ALAWAY	OPHTHALMIC	DROPS		O
ketotifen fumarate	EYE ITCH RELIEF	OPHTHALMIC	DROPS		O
ketotifen fumarate	KETOTIFEN FUMARATE	OPHTHALMIC	DROPS		O
ketotifen fumarate	ZADITOR	OPHTHALMIC	DROPS		O
naphazoline HCl/glycerin	MAX REDNESS RELIEF	OPHTHALMIC	DROPS		O
naphazoline HCl/glycerin	REDNESS RELIEF	OPHTHALMIC	DROPS		O
naphazoline HCl/zinc sulfate	CLEAR EYES ACR	OPHTHALMIC	DROPS		O
olopatadine HCl	ADVANCED EYE RELIEF	OPHTHALMIC	DROPS		O
olopatadine HCl	EYE ALLERGY ITCH RELIEF	OPHTHALMIC	DROPS		O
olopatadine HCl	EYE ALLERGY ITCH-REDNESS RLF	OPHTHALMIC	DROPS		O
olopatadine HCl	OLOPATADINE HCL	OPHTHALMIC	DROPS		F
olopatadine HCl	OLOPATADINE HCL	OPHTHALMIC	DROPS		O
olopatadine HCl	PATADAY ONCE DAILY RELIEF	OPHTHALMIC	DROPS		O
olopatadine HCl	PATADAY TWICE DAILY RELIEF	OPHTHALMIC	DROPS		O
tetrahydroz/dext 70/peg 400/pv	EYE DROPS	OPHTHALMIC	DROPS		O
tetrahydroz/dext 70/peg 400/pv	EYE DROPS ADVANCED RELIEF	OPHTHALMIC	DROPS		O
tetrahydroz/dext 70/peg 400/pv	EYE DROPS MOISTURIZING RELIEF	OPHTHALMIC	DROPS		O
tetrahydrozoline HCl	EYE DROPS	OPHTHALMIC	DROPS		O
tetrahydrozoline HCl	MURINE PLUS	OPHTHALMIC	DROPS		O
tetrahydrozoline HCl/zinc sulf	EYE DROPS IRRITATION RELIEF	OPHTHALMIC	DROPS		O
tetrahydrozoline HCl/zinc sulf	EYE DROPS SEASONAL RELIEF	OPHTHALMIC	DROPS		O
tetrahydrozoline/polyethyl gly	EYE DROPS	OPHTHALMIC	DROPS		O
tetrahydrozoline/zinc/peg 400	MULTI-SYMPTOM RELIEF EYE	OPHTHALMIC	DROPS		O

Appendix 2: Specific Drug Information

Table 1. Clinical Pharmacology and Pharmacokinetics[8,9]

Drug Name	Mechanism of Action	Absorption	Metabolism/Excretion	Pharmacokinetics (mean)
Naphazoline	Alpha$_1$ Agonist, Vasoconstrictor	N/A	N/A	Onset of action: 10 minutes Duration: 2-6 hours
Tetrahydrozoline		N/A	N/A	Onset of action: 10 minutes Duration: 4-8 hours
Cetirizine	Histamine H_1 Antagonist	N/A	N/A	Half-life: 8 hours Onset of action and Duration: N/A
Alcaftadine	Direct H_1-receptor antagonist and inhibitor of histamine release from mast cells	Minimal systemic absorption following ophthalmic administration	Metabolism: Primarily via aldehyde oxidation to the active major metabolite, carboxylic acid	Half-life: 2 hours (carboxylic acid) Onset of action: 15 minutes Duration: 3 hours
Azelastine			Metabolism: Primarily by CYP enzymes	Half-life: 2 hours Onset of action: 3 minutes Duration: 8 hours
Bepotastine			Metabolism: Minimal via CYP enzymes Excretion: Urine (75% to 90% unchanged drug)	Half-life: hours Onset of action: 3 minutes Duration: 16 hours
Epinastine			Protein Binding: 64% Metabolism <10% metabolized Excretion: IV: Urine (55% as unchanged drug; 30% feces	Half-life: 12 hours Onset of action: 3-5 minutes Duration: 8 hours
Olopatadine			Excretion: Urine (60% to 70% unchanged drug)	Half-life: 3 hours Onset of action: N/A Duration: N/A
Cromolyn	Mast Cell Stabilizer	Minimal systemic absorption following ophthalmic administration	Not known	Half-life: N/A Onset of action: N/A Duration: N/A
Abbreviations: CYP = cytochrome P450; N/A: Not Available				

Use in Specific Populations:

Contact lens wearers: Some products may contain benzalkonium chloride which may be absorbed by contact lenses; do not wear contact lenses during treatment.[8]

Table 2. Summary of Warnings and Precautions[8,9]

Warning/Precaution	Naphazoline	Tetrahydrozoline
Use with caution in diabetes	X	X
Use with caution in narrow angle glaucoma	X	X
Use with caution in hyperthyroidism	X	X
Use with caution in cardiovascular disease	X	X

Other ophthalmic products used to treat allergic conjunctivitis do not have warnings or precautions.

Appendix 3: Medline Search Strategy

Ovid MEDLINE(R) ALL <1946 to October 30, 2025>

1	Conjunctivitis, Allergic/ or alcaftadine.mp. or Olopatadine Hydrochloride/	4100
2	azelastine.mp.	853
3	Ophthalmic Solutions/ or bepotastine.mp.	16480
4	Brimonidine Tartrate/	1637
5	Cetirizine/ or cetirizine.mp.	2267
6	Cromolyn Sodium/	4144
7	Cromolyn Sodium/	4144
8	Anti-Allergic Agents/ or Conjunctivitis, Allergic/ or epinastine.mp.	12705
9	Ketotifen/	1197
10	Naphazoline/	400
11	Olopatadine Hydrochloride/	318
12	Ophthalmic Solutions/ or tetrahydrozoline.mp.	16518
13	Conjunctivitis, Allergic/	3883
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	37492
15	13 and 14	3883
16	limit 15 to (english language and humans)	3052
17	limit 16 to (clinical trial, phase iii or guideline or meta-analysis or practice guideline or "systematic review")	98