Conjunctivitis is a condition characterised by conjunctival inflammation.\textsuperscript{1} The conjunctiva is the thin membrane that lines the inside of the eyelids and covers the sclera (the whites of the eyes).\textsuperscript{1} Allergic conjunctivitis is caused by airborne allergens that come in contact with the surface of the eye in a person who is allergic to that specific allergen.\textsuperscript{2,3}

Allergic conjunctivitis usually affects both eyes and typically presents as redness, ocular pruritus (itching of eyes), and watery discharge.\textsuperscript{1,2} Other symptoms may include light sensitivity, burning and swelling of the eyelids.\textsuperscript{1}

### Types of allergic conjunctivitis

Allergic conjunctivitis can be subdivided into acute, seasonal or perennial allergic conjunctivitis.\textsuperscript{1,3}

- **Acute allergic conjunctivitis** has a sudden onset and is characterised by intense episodes of itching, tearing, redness and swelling of the eyelid(s); for example, when a person comes in contact with a known allergen such as cat dander.\textsuperscript{2} The hypersensitivity reaction usually occurs within minutes (within 30 minutes) after exposure and typically resolves quickly (within 24 hours) once the allergen has been removed.\textsuperscript{1,2}

- **Seasonal allergic conjunctivitis (SAC)** symptoms usually develop over days to weeks and occur during a particular pollen season. SAC is often associated with rhinitis and attributable to outdoor seasonal allergens such as tree, grass or weed pollens.\textsuperscript{1,2}

- **Perennial allergic conjunctivitis (PAC)** is related to contact with year-round environmental (usually indoor) allergens such as moulds, animal dander and dust mites.\textsuperscript{1}

Topical (ocular) treatment is preferred for allergic conjunctivitis as they are faster-acting (onset of action is usually faster) and less likely to cause systemic side-effects, when compared with systemic administrations.\textsuperscript{4}

Topical modalities available for the treatment of allergic conjunctivitis include antihistamine/vasoconstrictor combination products, mast cell stabilisers, antihistamines with mast cell stabilising properties and, for refractory symptoms, topical glucocorticosteroids.\textsuperscript{3,4}

### The allergic response and role of antihistamines with mast cell stabilising properties

#### Two phases of the allergic response

Allergic conjunctivitis is considered a classic type I immunoglobulin E (IgE)-mediated hypersensitivity reaction.\textsuperscript{2}

The immediate allergic response is mediated mainly by mast cells. The conjunctival epithelium contains high concentrations of mast cells which are further elevated in individuals with allergic conjunctivitis.\textsuperscript{2,5}

In the early phase allergic reaction, mast cells in the conjunctival epithelium become activated when allergens crosslink allergen-specific IgE molecules on mast cell membranes.\textsuperscript{2,5} This results in mast cell degranulation and the subsequent release of histamine and other mediators.\textsuperscript{5} Histamine causes vasodilatation, vasopermeability and is responsible for the immediate onset of ocular itching.\textsuperscript{2,3,5} H1 and H2-receptors play a role in ocular allergy.\textsuperscript{2}

The late phase of the allergic reaction begins with the influx of neutrophils, basophils and eosinophils into the conjunctiva (approximately 6 to 10 hours after the allergen challenge), followed by lymphocytes and monocytes.\textsuperscript{2} The activity of these cells results in continued inflammation.\textsuperscript{2}

#### Antihistamines with mast cell stabilising properties

Antihistamines with mast cell stabilising properties such as olopatadine, ketotifen and epinastine have two main actions:\textsuperscript{3,4,6-10}

- As antihistamines, they competitively and reversibly block histamine receptors (they are relatively selective histamine H1-receptor antagonists), in the eyelids and conjunctiva.\textsuperscript{4} Thus inhibiting the actions of histamine on human conjunctival epithelial cells.\textsuperscript{6,7}

### Olopatadine in the management of allergic conjunctivitis

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• Furthermore, as mast cell stabilisers, they prevent mast cell
degranulation, limiting the release of histamine, tryptase and
prostaglandin D₂. The first step in the allergic cascade is the
release of these proinflammatory mediators.⁴,⁷,¹⁰
Antihistamines with mast cell stabilising properties:
• Provide immediate relief; the onset of action is usually within
minutes.
• Provide sustained relief during the onset as well as the late-
phase ocular allergic reactions.⁵
• Address both the acute and chronic aspects of SAC and PAC.⁴
• Are considered the first-line agents for the management of SAC
and PAC.³,⁴

Focus on olopatadine
Patanol® contains olopatadine (0,1 mg/ml), a selective topically
active antihistaminic and mast cell stabilising agent.⁶,⁸ It is
indicated for the temporary prevention of itching of the eye in
individuals from 3 years of age and older.⁶

Dosage and directions for use
One drop of olopatadine should be instilled twice a day in the
conjunctival sac of the affected eye(s).⁶
To help with absorption into ocular tissue, the eyelid(s) should
be closed for a few seconds after the drop has been instilled.⁴
Repetitive blinking should, however, be avoided as this may result
in the topical treatments being washed out of the ocular surface
more quickly.⁴
In order to prevent contamination, patients should be advised to:
• Avoid touching the dropper tip.⁶
• Prevent the dropper tip from coming into contact with the
eyelids, surrounding areas or other surfaces.⁶
• Replace the cap and to close the bottle tightly after use.⁶
• Keep the bottle closed when not in use.⁶
Patients wearing contact lenses, should be informed not to wear
contact lenses when olopatadine is instilled; they should wait
at least 10 minutes after instilling olopatadine eye drops before
inserting the contact lenses.⁶

Efficacy
Various studies have demonstrated that topical olopatadine
significantly reduces ocular itch, a hallmark symptom in all forms
of ocular allergy.⁵,⁸,¹¹,¹²
In a systematic review and meta-analysis, Kam KW et al. 2016,
assessed the safety and efficacy of topical olopatadine when
compared with placebo and other topical anti-allergic medications
used in the treatment of allergic conjunctivitis. Results showed that
topical olopatadine was more efficacious in reducing ocular itch
and hyperaemia in allergic conjunctivitis, compared to placebo.⁹
According to Kam KW et al. 2016, topical olopatadine “has a
favourable safety and efficacy profile similar to other commonly
prescribed medications such as ketotifen and epinastine (which are
both antihistamines with mast cell stabilising properties).”⁹
Borazan M et al. 2009, compared the efficacy of olopatadine
(0,1%), ketotifen, epinastine, emedastine and fluorometholone
acetate ophthalmic solutions for seasonal conjunctivitis.¹¹ Their
study included 100 patients with SAC, who where randomly
assigned to one of the five treatments. One eye of each patient
was treated with the study drug and the other eye with placebo.
They evaluated signs and symptoms of SAC (itching, redness,
tearing, chemosis and eyelid swelling) at baseline and again after
one and two weeks of treatment.¹¹
Results from their study showed that:
• All antiallergic agents were significantly more effective than
placebo in alleviating itching, redness, tearing, chemosis and
eyelid swelling in patients with SAC.¹¹
• Olopatadine, ketotifen, epinastine and emedastine were
significantly more effective than fluorometholone acetate in
alleviating ocular itching and conjunctival redness in patients
with SAC.¹¹
Several other studies have compared topical olopatadine to other
treatment modalities:
• Berdy GJ et al. 2002, compared the clinical efficacy and
tolerability of olopatadine 0,1%, loteprednol etabonate 0.2%
and placebo in inhibiting the early-phase allergic reaction after
conjunctival allergen challenge. They found olopatadine to be
“more efficacious than loteprednol etabonate in reducing the
acute signs and symptoms of SAC during the early phase of the
ocular allergic reaction”. In addition, olopatadine appeared to be
better tolerated.¹²
• Studies have found topical olopatadine to be more effective
than oral loratadine or fexofenadine in reducing ocular itching
related to allergic conjunctivitis.¹³,¹⁴
• According to the analysis from the United Kingdom’s National
Health Services olopatadine resulted in sufficiently fewer return
visits compared to cromolyn.¹³,¹⁴
• Results from a study by Yaylali V et al. 2003, showed that 0,1%
olopatadine reduced ocular itching significantly more than
0,5% ketorolac.⁵,¹⁵

Safety of olopatadine
Contraindications, special warnings and precautions for use
Olopatadine eye drops are contraindicated in individuals with
known hypersensitivity to the active ingredient or any of the
excipients.⁶
Olopatadine eye drops contain benzalkonium chloride, a
preservative commonly used in eye drops. Punctate keratopathy
and/or toxic ulcerative keratopathy have been reported with
the use of benzalkonium chloride-containing eye drops.⁶ It is
therefore important to monitor patients with dry eye syndrome or patients with conditions where the cornea is compromised and when frequent or prolonged use of olopatadine eye drops is anticipated.\(^6\)

The use of olopatadine is not recommended in pregnancy and breastfeeding.\(^6\)

**Adverse effects**

Common ocular (incidence 1\% to 10\%) adverse effects include ocular discomfort (burning and stinging).\(^5\)

Individuals who experience blurred vision or other visual disturbances after instilling Patanol\(^6\) should be informed to wait until the vision has cleared before driving or using machinery.\(^6\)

**Drug interactions**

The systemic absorption of olopatadine is minimal following topical ocular administration.\(^4\)

If concomitant topical therapy is indicated, for example, if the patient needs to use a topical medication and artificial tears, the patient should be advised to allow for a five minute interval between consecutive treatments.\(^4\) This is to ensure that the first drop is not washed out by the second drop.\(^4\)

**Important prescribing points**

The management of allergic conjunctivitis involves both non-pharmacological and pharmacological measures.\(^1,4\)

**Non-pharmacological measures**

The initial step for effective management of allergic conjunctivitis is allergen avoidance or reduction of contact with known allergens.\(^4\) For SAC, allergen avoidance measures during peak pollen seasons include the use of air conditioning, limiting outdoor exposures and keeping windows closed (in the house and car).\(^3\) Patients allergic to dust mites should be advised to use dust mite impermeable covers and to replace old pillows, mattresses and blankets.\(^3\)

Patients should also be advised to:

- Avoid rubbing their eye(s), as rubbing may cause mechanical mast cell degranulation and worsening of symptoms.\(^4\)
- Apply cool compresses, this may help to reduce eyelid and periorbital oedema.\(^4\)
- Regularly instil refrigerated artificial tears. Artificial tears can help to dilute and remove allergens and should be instilled throughout the day.\(^4\)
- Not wear contact lenses during symptomatic periods, as allergens tend to adhere to contact lens surfaces.\(^3\)

**Pharmacological measures**

Olopatadine was discovered in the late 1990s and was the “first dual-acting topical agent to change the therapeutic paradigm”.\(^5,9\)

Results from a systematic review and meta-analysis showed that topical olopatadine was associated with a statistically significant reduction in ocular itch, a hallmark symptom in all forms of ocular allergy.\(^5\) In addition, they found that topical olopatadine had a favourable safety profile, similar to ketotifen and epinastine.\(^9\)

Most antihistamines with mast cell stabilising properties start working within minutes and decreased itching should be evident within 24 to 72 hours.\(^1,5\) However, it may be prudent to allow for at least two weeks of treatment, in order to assess the full efficacy of therapy.\(^4\)

Patients who do not respond to two or three weeks of consistent therapy with an antihistamine with mast cell stabilising properties should be referred to an ophthalmologist.\(^6\) Differential diagnosis includes infective conjunctivitis, blepharitis, more severe forms of allergic ocular disease (vernal keratoconjunctivitis, giant papillary conjunctivitis and atopic keratoconjunctivitis), drug-induced conjunctivitis and keratoconjunctivitis sicca.\(^3\)

**References**


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