Ophthalmic Antihistamine Step Therapy Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace and KeyRx.

This is a FlexRx standard and GenRx standard step therapy program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Indication(s)</th>
<th>Administration and Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bepreve®</strong></td>
<td>Treatment of itching associated with allergic conjunctivitis.</td>
<td>Instill one drop into the affected eye(s) twice a day.</td>
</tr>
<tr>
<td>(bepotastine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Elestat®</strong></td>
<td>Prevention of itching associated with allergic conjunctivitis.</td>
<td>One drop in each eye twice a day.</td>
</tr>
<tr>
<td>(epinastine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.05% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Emadine®</strong></td>
<td>Temporary relief of the signs and symptoms of allergic conjunctivitis.</td>
<td>One drop in the effected eye up to four times daily.</td>
</tr>
<tr>
<td>(emedastine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.05% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lastacaft®</strong></td>
<td>Prevention of itching associated with allergic conjunctivitis.</td>
<td>Instill one drop in each eye once daily.</td>
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<tr>
<td>(alcaftadine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>azelastine³</td>
<td>Treatment of itching of the eye associated with allergic conjunctivitis.</td>
<td>One drop instilled into each affected eye twice a day.</td>
</tr>
<tr>
<td>0.05% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patanol™</strong></td>
<td>Treatment of the signs and symptoms of allergic conjunctivitis.</td>
<td>One drop in each affected eye two times per day at an interval of 6 to 8 hours.</td>
</tr>
<tr>
<td>(olopatadine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a³ available as generic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pataday™</strong></td>
<td>Treatment of ocular itching associated with allergic conjunctivitis.</td>
<td>One drop in each affected eye once a day.</td>
</tr>
<tr>
<td>(olopatadine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a³ available as generic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.2% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pazeo™</strong></td>
<td>Treatment of ocular itching associated with allergic conjunctivitis.</td>
<td>One drop in each affected eye once a day.</td>
</tr>
<tr>
<td>(olopatadine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.07% ophthalmic solution</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**CLINICAL RATIONALE**
An algorithm on treatment of allergic conjunctivitis (2013) uses a step wise approach, suggesting cold compresses, artificial tears, and OTC ophthalmic agents (e.g., pheniramine/naphazoline, ketotifen) as first line treatments for mild cases. Then if symptoms continue, or if OTC agents are not effective or not tolerated, prescription agents are recommended. Topical ophthalmic agents for the treatment of ocular allergy have a more rapid onset of action vs. oral antihistamines and are generally better tolerated. Topical antihistamines do not cause significant systemic side effects and generally do not contribute to ocular dryness. In clinical trials, dual-acting agents (e.g., ketotifen) have been shown to effectively reduce itching associated with allergic conjunctivitis with longer duration of effect and better tolerability than single-action antihistamines.9

For seasonal allergic conjunctivitis, the American Academy of Ophthalmology (AAO, 2013) suggests mild cases may be treated with an over-the-counter (OTC) antihistamine/vasoconstrictor (e.g., naphazoline/pheniramine), or with a more effective second-generation topical histamine H1-receptor antagonist (e.g., emedastine, alcaftadine). If the condition is frequently recurrent or persistent, mast cell stabilizers (e.g., cromolyn, lodoxamide, nedocromil) may be used to maintain comfort. Ophthalmic allergy preparations with dual antihistamine and mast-cell stabilizing properties, (e.g., ketotifen [OTC], azelastine, bepotastine, epinastine, olopatadine) may be used for either acute or chronic disease. There is no preference for one particular product in each class over the others.10

Numerous comparative trials using allergic conjunctivitis agents have been conducted. From the results of the trials, it is difficult to declare one agent superior to another.11,12,13 A meta-analysis of 8 studies compared the efficacy of the treatment of allergic conjunctivitis with topical antihistamines versus topical mast cell stabilizers, Results showed no significant differences being recorded in favor of any of the interventions.14 Cochrane review authors concluded all reported topical antihistamines and mast cell stabilisers reduce symptoms/signs of seasonal allergic conjunctivitis vs. placebo in the short term.15

REFERENCES

14. Cochrane Data System Review. 2015 June 1;(6): CD009566
Ophthalmic Antihistamine Step Therapy

OBJECTIVE
The intent of the Ophthalmic Antihistamine Step Therapy (ST) program is to encourage use of cost-effective generic products over the more expensive brand products. This program will accommodate for use of brand products when generic prerequisites cannot be used due to previous trial and failure; or the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a generic product. Requests for brand products will be reviewed when patient-specific documentation is provided.

TARGET AGENTS
- Bepreve® (bepotastine)
- Elestat® (epinastine)\(^a\)
- Emadine® (emedastine)
- Lastacaft® (alcaftadine)
- Patanol™ (olopatadine)\(^a\)
- Pataday™ (olopatadine)\(^a\)
- Pazeo™ (olopatadine)
\(^a\) – generic available

azelastine available as generic only and is a prerequisite

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Brand Ophthalmic Antihistamines will be approved when ONE of the following is met:
1. The patient’s medication history indicates previous use of a generic ophthalmic antihistamine product in the past 90 days
   OR
2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a generic ophthalmic antihistamine product

Length of approval: 12 months
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria