OVERVIEW

Eye and ear infections are among the most common reasons for patient self-referral. A wide variety of conditions can lead to ocular and ophthalmic inflammation. Inflammation of the eye is mostly caused by allergens, bacteria, and viral infections. On the other hand, ear infections are mostly caused by bacterial infections, although viral infections are also possible. Most infections are mild. However, severe cases can rapidly progress to permanent visual/hearing loss if not cared for properly. This review will examine the recommended use of topical anti-inflammatory agents and their coverage criteria.

Available Agents: (Current as of 11/2015)

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Generic Name (Brand Name)</th>
<th>Available Strengths</th>
<th>FML Limits</th>
<th>Avg Cost/Rx</th>
<th>Notes/Restriction Language</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular Corticosteroids</td>
<td>Dexamethasone (Maxidex)</td>
<td>0.1% Drops, Suspension</td>
<td>-</td>
<td>$16.39</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Fluorometholone (FML SOP)</td>
<td>0.1% Ointment</td>
<td>-</td>
<td>$92.29</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Fluorometholone (FML Forte)</td>
<td>0.25% Drops, Suspension</td>
<td>-</td>
<td>$113.29</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Prednisolone Acetate</td>
<td>0.12%, 1% Drops, Suspension</td>
<td>-</td>
<td>$70.98</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Prednisolone Sodium Phosphate</td>
<td>1% Drops</td>
<td>-</td>
<td>$44.38</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Rimexolone (Vexol)</td>
<td>1% Drops, Suspension</td>
<td>-</td>
<td>$112.63</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Loteprednol (Lotemax, Alrex)</td>
<td>0.5% Gel, Oint, Drops</td>
<td>PA</td>
<td>$213.78</td>
<td>Reserved for pts with glaucoma.</td>
</tr>
<tr>
<td>Topical NSAIDs</td>
<td>Diclofenac</td>
<td>0.1% Drops</td>
<td>-</td>
<td>$20.42</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Flurbiprofen (Ocufen)</td>
<td>0.03% Drops</td>
<td>-</td>
<td>$7.18</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Ketorolac (Acular LS, Acular)</td>
<td>0.4%, 0.5% Drops</td>
<td>-</td>
<td>$36.02</td>
<td>No restrictions.</td>
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<tr>
<td>Antibiotics</td>
<td>Gentamicin/Prednisolone</td>
<td>0.3%-1% Drops, Suspension 0.3%-0.6% Ointment</td>
<td>-</td>
<td>$129.57</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Neomycin/Polyoxymyxin/Dexamethasone</td>
<td>3.5mg-10,000 U/G-0.1% Ointment 3.5-10,000 U/ml</td>
<td>-</td>
<td>$17.38</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Neomycin/Bacitracin/Polyoxymyxin/HC</td>
<td>3.5mg-400-10,000 U/G-1% Ointment</td>
<td>-</td>
<td>$37.08</td>
<td>No restrictions.</td>
</tr>
<tr>
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<td>Neomycin/Polyoxymyxin/HC</td>
<td>3.5mg-400-10,000 U-10mg/ml Drops</td>
<td>-</td>
<td>$104.54</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Tobramycin/ Dexamethasone (Tobradex)</td>
<td>0.3%-0.1% Drops, Ointment</td>
<td>-</td>
<td>$86.29</td>
<td>No restrictions.</td>
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<td></td>
<td>Sulfacetamide Sodium</td>
<td>10% Drops, Ointment</td>
<td>-</td>
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<td>Sulfacetamide/Prednisolone</td>
<td>10%-0.23% Drops</td>
<td>-</td>
<td>$11.25</td>
<td>No restrictions.</td>
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<td>Sulfacetamide/Prednisolone Acetate (Blephamide SOP, Blephamide)</td>
<td>10-0.2% Ointment, Drops</td>
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<td>Category</td>
<td>Drug Name</td>
<td>Formulation</td>
<td>Coverage</td>
<td>Price</td>
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<tr>
<td><strong>Antivirals</strong></td>
<td>Trifluridine</td>
<td>1% Drops</td>
<td>-</td>
<td>$116.32</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Ganciclovir</td>
<td>0.15% Gel</td>
<td>NF</td>
<td>$275.46</td>
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<tr>
<td></td>
<td><strong>Ketotifen</strong></td>
<td>0.025% Drops</td>
<td>PA, QL</td>
<td>$9.27</td>
<td>Limit 10 ml per month.</td>
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<tr>
<td></td>
<td><strong>Olopatadine</strong></td>
<td>2.5% Drops</td>
<td>PA, QL</td>
<td>$128.73</td>
<td>Non-Formulary.</td>
</tr>
<tr>
<td></td>
<td><strong>Olopatadine</strong></td>
<td>0.1% Drops</td>
<td>PA, QL</td>
<td>$230.25</td>
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<td></td>
<td>Alkaftadine</td>
<td>0.25% Drops</td>
<td>NF</td>
<td>$162.40</td>
<td>Non-Formulary.</td>
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<tr>
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<td>Azelastine</td>
<td>0.05% Drops</td>
<td>ST</td>
<td>$73.07</td>
<td>ST to Ketotifen.</td>
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<tr>
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<td>Bepotastine</td>
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<td>NF</td>
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<td>Non-Formulary.</td>
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<tr>
<td><strong>Antihistamines</strong></td>
<td><strong>Immunomodulator</strong></td>
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<td></td>
<td>Cyclosporine</td>
<td>0.05% Drops</td>
<td>PA</td>
<td>$361.60</td>
<td>Treatment failure to ophthalmic lubricants.</td>
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<tr>
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<td>Propylene Glycol/Peg 400</td>
<td>0.4%-0.3% Drops</td>
<td>-</td>
<td>-</td>
<td>No restrictions.</td>
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<td>Glycerin/Propylene Glycol</td>
<td>0.1%-0.3% Drops</td>
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<td>-</td>
<td>No restrictions.</td>
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<td>Petrolatum/Mineral Oil/Sodium Chloride</td>
<td>Ointment</td>
<td>-</td>
<td>-</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Carboxymethylcellulose</td>
<td>1% Gel Drops</td>
<td>-</td>
<td>-</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td><strong>Dextran 70/Hypromellose</strong></td>
<td>Drops</td>
<td>-</td>
<td>-</td>
<td>No restrictions.</td>
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<tr>
<td></td>
<td>Polyvinyl Alcohol</td>
<td>1.4% Drops</td>
<td>-</td>
<td>-</td>
<td>No restrictions.</td>
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<tr>
<td><strong>Artificial Tears</strong></td>
<td><strong>Vasoconstrictors</strong></td>
<td></td>
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<td></td>
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<td>Naphazoline</td>
<td>0.1% Drops</td>
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<td>$5.88</td>
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<td>Naphazoline/Pheniramine</td>
<td>0.025%-0.3% Drops</td>
<td>-</td>
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<td>restrictions</td>
</tr>
<tr>
<td></td>
<td>Phenylephrine</td>
<td>2.5%, 10% Drops</td>
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<td>No restrictions.</td>
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<tr>
<td><strong>Topical Anesthetic</strong></td>
<td><strong>Otic Agents</strong></td>
<td></td>
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</tr>
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<td></td>
<td>Proparacaine</td>
<td>0.5%</td>
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<td>$31.59</td>
<td>No restrictions.</td>
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<td><strong>Antibiotics</strong></td>
<td>Ofloxacin</td>
<td>0.3% Drops</td>
<td>-</td>
<td>$15.44</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Neomycin/Polymyxin B/HC</td>
<td>3.5mg-10,000 U/ml-1% Suspension</td>
<td>-</td>
<td>$17.20-20.26</td>
<td>No restrictions.</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin/HC</td>
<td>0.2%-1% Suspension</td>
<td>NF</td>
<td>$215.39</td>
<td>Non-Formulary.</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin/Dexamethasone</td>
<td>0.3%-1.7% Suspension</td>
<td>PA</td>
<td>$181.17</td>
<td>Treatment failure to Ofloxacin and Neomycin/Polymyxin/HC in the last 30 days.</td>
</tr>
</tbody>
</table>
EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

### Ocular Corticosteroids

**Loteprednol (Lotemax)**
- **Coverage Criteria:** Reserved for use in patients with glaucoma or for use in children <10 years. Must be prescribed by an ophthalmologist.
- **Limits:** None
- **Required Information for Approval:**
  - Growth charts documenting patient has glaucoma or request is for patients 10 years or younger.
  - Medication is requested by an ophthalmologist.
- **Other Notes:** N/A

All other formulary ocular corticosteroids
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

### Ocular NSAIDs

**Diclofenac, Flurbiprofen (Ocufen), Ketorolac (Acular LS, Acular)**
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

### Ocular Antibiotics

**Gentamicin/Prednisolone, Neomycin/Polymyxin/Dexamethasone, Neomycin/Bacitracin/Polymyxin/HC, Neomycin/Polymyxin/HC, Tobramycin/ Dexamethasone (Tobradex), Sulfacetamide Sodium, Sulfacetamide/Prednisolone, Sulfacetamide/Prednisolone Acetate (Blephamide SOP, Blephamide)**
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

### Ocular Antiviral

**Trifluridine (Viroptic)**
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A
## Ocular Antihistamine

- **Ketotifen (Alaway, Refresh, Allergy Eye, Itchy Eye, Children’s Alaway), Olopatadine (Patanol), Azelastine (Optivar)**

### Ketotifen
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

### Azelastine (Optivar)
- **Coverage Criteria:** Step therapy to previous treatment with Ketotifen in the last 30 days.
- **Limits:** None
- **Required Information for Approval:** Fill history of Ketotifen in the last 30 days.
- **Other Notes:** N/A

### Olopatadine (Patanol)
- **Coverage Criteria:** Reserved for treatment failure or intolerance to Azelastine and 1 of the following: Ketotifen (Alaway, Zaditor), Naphazoline/Pheniramine (Visine-A).
- **Limits:** Limit 5ml (1 bottle) per 30 days.
- **Required Information for Approval:** Fill history of Azelastine and either Ketotifen or Naphazoline/Pheniramine.
- **Other Notes:** Pataday is non-formulary.

## Ocular Lubricants

- **Propylene Glycol/Peg 400, Glycerin/Propylene Glycol (Artificial Tears), Petrolatum/Mineral Oil/Sodium Chloride (Artificial Tears, Nighttime Relief), Carboxymethylcellulose (Refresh Liquigel), Dextran 70/Hypromellose (Artificial Tears, Tears Naturale, Tears pure), Polyvinyl Alcohol (Liquitears, Lubricant Eye)**

### Ocular Lubricants
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

## Topical Immunomodulators

- **Topical Cyclosporine (Restasis)**

### Topical Immunomodulators
- **Coverage Criteria:** Reserved for treatment failure to ophthalmic lubricants (e.g., Systane, Artificial Tears, Refresh) in the last 6 months.
- **Limits:** None
- **Required Information for Approval:**
  - Fill history or clinic notes documenting trials with ophthalmic lubricants.
  - Medication is requested by an ophthalmologist.
- **Other Notes:** Must be prescribed by ophthalmologists.

## Ocular Vasoconstrictors

- **Naphazoline/Pheniramine (Visine-A), Naphazoline, Phenylephrine**

### Ocular Vasoconstrictors
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

## Ocular Anesthetics

- **Proparacaine**

### Ocular Anesthetics
- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A
Otic Antibiotics

**Ofloxacin, Neomycin/Polymyxin B/HC, Ciprofloxacin/ Dexamethasone (Ciprodex)**

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

- **Ciprofloxacin/Dexamethasone (Ciprodex)**
  - **Coverage Criteria:** Reserved for treatment failure to Ofloxacin and Neomycin/Polymyxin/HC in the last 30 days.
  - **Limits:** None
  - **Required Information for Approval:** Fill history of Ofloxacin and Neomycin/Polymyxin/HC in the last 30 days or clinical documentation of intolerance to Ofloxacin and/or Neomycin/Polymyxin/HC.
  - **Other Notes:** N/A

Otic Anti-Infectives

**Acetic Acid, Acetic Acid/Hydrocortisone, Acetic Acid/Aluminum Acetate**

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

Local Anesthetics

**Antipyrine/Benzocaine (Aurodex, Aurogard)**

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** N/A

**Clinical Justification**

Most eye and ear inflammatory conditions are self-limiting. However, the use of medications can quicken the time to recovery. Topical corticosteroids will help reduce local inflammation while antibiotics clear the infection. Chronic or recurrent infections may be indicative of an underlining malignancy and should be further examined.

Ocular inflammatory treatment recommendations are based on the 2013 American Academy of Ophthalmology are summarized below:

**Management of Ocular Inflammatory Disorders**

<table>
<thead>
<tr>
<th>Type</th>
<th>Condition</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctiontis</td>
<td>Allergic Conjunctivitis</td>
<td>• Remove source of irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• OTC topical antihistamine/vasoconstrictor eye drops</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 2nd generation topical antihistamine eye drops</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Antihistamine + mast-cell stabilizers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If symptoms not resolved, may utilize 1-2 weeks of topical corticosteroid +/- topical NSAIDs</td>
</tr>
<tr>
<td>Vernal/Atopic</td>
<td>Conjunctivitis</td>
<td>• Remove source of irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cool compresses and ocular lubricants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Topical and oral antihistamines +/- topical mast cell stabilizers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• For acute exacerbations, topical corticosteroids are used to control severe symptoms +/- topical cyclosporine</td>
</tr>
</tbody>
</table>
Adenoviral Conjunctivitis
- Usually self-limiting and do not require treatment
- Artificial tears, antihistamine, and cold compresses may help relieve symptoms

Herpes Simplex Virus Conjunctivitis
- Topical trifluridine 1% solution 5-8x per day, ganciclovir 0.15% gel 3-5x per day, or acyclovir 200-400mg 5x per day
- Alternative oral tx include: oral valacyclovir 500mg 2-3x per day or famciclovir 250mg twice a day
- Avoid topical corticosteroids as they can worsen HSV infection

Bacterial Conjunctivitis
- Treatment not necessary but can shorten time to remission (5 days vs. 7 days)
- Topical antibiotic therapy x 5-7 days
  - Choice of therapy is empiric

Gonococcal/Chlamydial Conjunctivitis
- Treatment is with systemic therapy. No evidence that topical therapy will confer additional benefit.
- Gonococcal:
  - Adults: Ceftriaxone 250mg IM or Azithromycin 1Gm PO or Doxycycline 100mg PO BID x 7 days
  - Children: Ceftriaxone 250mg IM
- Chlamydia:
  - Adults: Azithromycin 1Gm PO or Doxycycline 100mg PO BID x 7 days
  - Children: Azithromycin 1Gm PO

Keratitis Bacterial Keratitis
- Treatment with empiric topical therapy—usually fluoroquinolones (e.g. Tobramycin, Neomycin, Gentamicin, etc) +/- topical corticosteroid therapy

Dry Eyes
- Mild: Artificial tears
- Moderate: Artificial tears + topical cyclosporine
- Severe: Artificial tears + topical cyclosporine + pilocarpine

Management of Acute Otic Inflammatory Disorders

Acute Otitis Externa
Topical antimicrobials or antibiotics such as acetic acid, aminoglycosides, polymyxin B, and quinolones are the treatment of choice in uncomplicated acute otitis externa. There is no literature that suggests any one antimicrobial or antibiotic preparation is clinically superior to another. If the tympanic membrane is intact (hypersensitivity to aminoglycosides is not a concern), neomycin/polymyxin B/hydrocortisone otic preparation would be a first-line therapy because of its cost-effectiveness. Ofloxacin and ciprofloxacin/dexamethasone (Ciprodex) are approved for middle ear use and should be used if the tympanic membrane is not intact or its status cannot be determined visually. The addition of corticosteroids may help resolve symptoms more quickly. Systemic antibiotics should only be used when the infection has spread beyond the ear canal.2

Acute Otitis Media (AOM)
Systemic high-dose amoxicillin is first-line therapy unless amoxicillin was given within the last 30 days or patient is allergic to amoxicillin. Alternative regimens to patients with penicillin allergy includes: cefdinir, cefuroxime, or cefpodoxime. In patients who’ve tried and failed amoxicillin, amoxicillin/clavulanate or ceftriaxone is recommended.3

NEWLY APPROVED MEDICATIONS NOT ON FORMULARY
None

GUIDELINE & LITERATURE REVIEW
2013 American Academy of Ophthalmology—Conjunctivitis

CRITERIA REVIEW FOR UNNECESSARY BARRIERS
Current requirements are appropriate
**RECOMMENDATIONS**

See Ophthalmic & Otic Anti-Inflammatory Class Review for more details.

**REFERENCES**

1. 2013 American Academy of Ophthalmology—Conjunctivitis
5. HPSJ Policy UM26 – Pharmacy & Therapeutics Committee

**REVIEW & EDIT HISTORY**

<table>
<thead>
<tr>
<th>Document Changes</th>
<th>Reference</th>
<th>Date</th>
<th>P&amp;T Chairman</th>
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<tr>
<td>Creation of Policy</td>
<td>Ophthalmics Feb 08.docx</td>
<td>02/2008</td>
<td>Allen Shek PharmD</td>
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<tr>
<td>Update Policy</td>
<td>Ophthalmic Corticosteroids Class Review 9-21-10.docx</td>
<td>09/2010</td>
<td>Allen Shek PharmD</td>
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<td>Update Policy</td>
<td>Ophthalmic ABX Class Review REVISED 9-21-10.docx</td>
<td>09/2010</td>
<td>Allen Shek PharmD</td>
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<td>Update Policy</td>
<td>Drug Class Review - Ophthalmic &amp; Otic - Anti-Inflammatory Agents 2015-11.docx</td>
<td>11/2015</td>
<td>Johnathan Yeh, PharmD</td>
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*Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy*