Allergic Rhinitis Intranasal Steroids
Drug Class Monograph

Line of Business: Medi-Cal
Effective Date: May 17, 2017
Revision Date: May 17, 2017

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutic Subcommittee.

Drugs: Beconase AQ (beclomethasone), Budesonide, Clarispray (fluticasone propionate), Flonase Allergy RLF (fluticasone propionate), Flonase Sensimist (fluticasone furoate), Fluticasone Propionate, Flunisolide, Mometasone Furoate, Nasacort Allergy (triamcinolone), Nasonex (mometasone), Omnaris (ciclesonide), Qnasl (Beclomethasone), Rhinocort Allergy (budesonide), Triamcinolone, Veramyst (fluticasone furoate), Zetonna (Ciclesonide)

Policy/Criteria:

A. Non-Formulary Intranasal Corticosteroid Agents

Diagnosis:
   a. Allergic rhinitis
      OR
   b. Nasal polyps

Specialist: No restriction

Criteria:
   a. Allergic rhinitis:
      i. Failure or clinically significant adverse effects to ONE of the formulary oral anti-histamines: cetirizine or loratadine
      ii. Failure or clinically significant adverse effects to TWO formulary intranasal steroid sprays: fluticasone spray and triamcinolone spray
c. Nasal polyps:
i. Beconase AQ (beclomethasone), Nasonex (mometasone) and Rhinocort (budesonide) will be approved as medically necessary for nasal polyps.

**Clinical Justification:**

**American Academy of Otolaryngology: Clinical Practice Guideline 2015**

1) The treatment goal for allergic rhinitis is relief of symptoms. The first line treatment of allergic rhinitis involves the avoidance of relevant allergens and irritants.
2) Clinicians to recommend oral second generation/less sedating antihistamines for patients with allergic rhinitis.
3) Clinicians to recommend intranasal steroids for patients with allergic rhinitis.
4) Clinicians should make the clinical diagnosis of allergic rhinitis when patients present with a history and physical examination consistent with an allergic cause and one or more of the following: nasal congestion, runny nose, itchy nose, or sneezing.
5) Clinicians should perform and interpret, or refer to a clinician who can perform and interpret, specific IgE allergy testing for patients with a clinical diagnosis of allergic rhinitis who do not respond to empiric treatment.
6) Clinicians should assess patients with a clinical diagnosis of allergic rhinitis for the presence of associated conditions such as asthma, atopic dermatitis, sleep disordered breathing, conjunctivitis, rhinosinusitis, and otitis media.
7) Clinicians should offer, or refer to a clinician who can offer, immunotherapy for patients with allergic rhinitis who have inadequate response to symptoms with pharmacologic therapy with or without environmental controls.

**American Academy of Allergy Asthma and Immunology: Diagnosis and management of rhinitis 2008**

1) The most common allergic triggers for rhinitis include pollens, fungi, dust mites, furry animals, and insect emanations.
2) Second generation oral antihistamines are generally preferred over first generations antihistamines for treatment of allergic rhinitis.
3) Intranasal antihistamines have demonstrated efficacy that is equal to or superior to oral second generation antihistamines.
4) Oral decongestants are effective at relieving nasal congestion in patients with allergic rhinitis but can result in insomnia, loss of appetite, irritability, and palpitations.
5) Intranasal corticosteroids are the most effective mediations for treating allergic rhinitis.
6) Oral corticosteroids (few days) may be required for the treatment of very severe intractable rhinitis.
7) Nasal cromolyn is effective in the prevention of symptoms and in the treatment of rhinitis.
8) The nasal anticholinergic ipratropium is effective in reducing rhinorrhea caused by allergic rhinitis.
9) Leukotriene receptor antagonists are effective in the treatment of allergic rhinitis.

<table>
<thead>
<tr>
<th>MOA</th>
<th>Fluticasone propionate (Flonase, GoodSense Nasoflow)</th>
<th>Fluticasone Furoate (Flonase Sensimist)</th>
<th>Flunisolide</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>A glucocorticoid that is an extremely potent vasoconstrictor and has anti-inflammatory activity</td>
<td>Decreases inflammation by suppression of migration of polymorphonuclear leukocytes and reversal of increased capillary permeability; does not depress hypothalamus</td>
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<table>
<thead>
<tr>
<th>Usual Dosing</th>
<th>1 spray (50 mcg/spray) per nostril once daily</th>
<th>1 or 2 sprays per nostril per day (55-110 mcg/day)</th>
<th>2 sprays (50 mcg) in each nostril BID</th>
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<table>
<thead>
<tr>
<th>FDA Indication</th>
<th>Nonallergic Rhinitis, Upper respiratory allergies</th>
<th>Upper Respiratory Allergies</th>
<th>Rhinitis (seasonal/perennial)</th>
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<table>
<thead>
<tr>
<th>Pediatric Indication</th>
<th>Children 4 years and older</th>
<th>Children 2 years and older</th>
<th>Children 6 years and older</th>
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<table>
<thead>
<tr>
<th>Administration</th>
<th>For use in nostril only</th>
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<table>
<thead>
<tr>
<th>PK/PD</th>
<th>Fluticasone propionate (Flonase, GoodSense Nasoflow)</th>
<th>Fluticasone Furoate (Flonase Sensimist)</th>
<th>Flunisolide</th>
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<tbody>
<tr>
<td></td>
<td>Onset of Action: Maximal benefit may take several days</td>
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<td>Absorption: well absorbed</td>
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<tr>
<td></td>
<td>Distribution: 4.2 L/kg</td>
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<td>Bioavailability: 50%</td>
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<td></td>
<td>Protein binding: 99%</td>
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<td>Half-life elimination: 1-2 hours</td>
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<td></td>
<td>Metabolism: Hepatic via CYP3A4 to 17 beta-carboxylic acid (negligible activity)</td>
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<tr>
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<td>Bioavailability: &lt;2%</td>
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<tr>
<th>Contraindications</th>
<th>Hypersensitivity to fluticasone, use for asthma or with current injury or surgery to nose that is not fully healed, children &lt;4 years (Flonase, GoodSense Nasoflow) or &lt;2 years (Flonase Sensimist)</th>
<th>Hypersensitivity to flunisolide</th>
</tr>
</thead>
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| Warnings | Adrenal suppression, delayed wound healing, hypersensitivity, immunosuppression, local nasal effects, use with caution in patients with cataracts or glaucoma | Delayed wound healing, avoid using higher doses than recommended in pediatric populations |

<table>
<thead>
<tr>
<th>Drug-drug interaction</th>
<th>Cobicistat, CYP3A4 inhibitors (strong), Ritonavir, Telaprevir, Tipranavir,</th>
<th>Ceritinib</th>
</tr>
</thead>
</table>
### Common Side effects
- Headache, pharyngitis, epistaxis, fever, nausea and vomiting, pharyngolaryngeal pain
- Burning/stinging sensation of the nose, nasal congestion, anosmia, dry nose, nasal mucosa irritation

### Monitoring
- Growth (adolescents and children), Signs/symptoms of HPA axis suppression/adrenal insufficiency, ocular changes, signs/symptoms of Candida infection

### Pregnancy
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### Lactation
- Use with caution in nursing women

### Storage and stability
- **Triamcinolone OTC** (Nasacort Allergy)
  - Suspension, Nasal
    - 50 mcg/actuation
- **Beclomethasone** (Beconase AQ, Qnasl)
  - Suspension, Nasal
    - 27.5 mcg/spray (9.9 mL, 5.8 mL)
- **Budesonide** (Rhinocort Allergy, Rhinocort Aqua)
  - Solution, Nasal
    - 25 mcg/actuation (0.025%)

### How supplied
- **Triamcinolone OTC** (Nasacort Allergy)
- **Beclomethasone** (Beconase AQ, Qnasl)
- **Budesonide** (Rhinocort Allergy, Rhinocort Aqua)

### MOA
- **Triamcinolone OTC** (Nasacort Allergy)
  - Controls the rate of protein synthesis, depresses the migration of polymorphonuclear leukocytes and fibroblasts, reverses capillary permeability, and stabilizes lysosomal membranes at the cellular level to prevent or control inflammation
- **Beclomethasone** (Beconase AQ, Qnasl)
  - Controls the rate of protein synthesis; depresses the migration of polymorphonuclear leukocytes, fibroblasts; reverses capillary permeability and lysosomal stabilization at the cellular level to prevent or control inflammation. Budesonide: potent glucocorticoid activity, weak mineralocorticoid activity

### Usual Dosing
- **Triamcinolone OTC** (Nasacort Allergy)
  - 1-2 (55 mcg) sprays in each nostril once daily
- **Beclomethasone** (Beconase AQ, Qnasl)
  - 2 sprays in each nostril 1-2 times daily
- **Budesonide** (Rhinocort Allergy, Rhinocort Aqua)
  - 1 spray in each nostril once daily

### FDA Indication
- **Triamcinolone OTC** (Nasacort Allergy)
  - Allergic rhinitis, upper respiratory symptoms
- **Beclomethasone** (Beconase AQ, Qnasl)
  - Nasal polyps, rhinitis
- **Budesonide** (Rhinocort Allergy, Rhinocort Aqua)
  - Allergic rhinitis, upper respiratory symptoms

### Pediatric Indication
- **Triamcinolone OTC** (Nasacort Allergy)
  - Children 2 years and older
- **Beclomethasone** (Beconase AQ, Qnasl)
  - Children 6 years and older
- **Budesonide** (Rhinocort Allergy, Rhinocort Aqua)
  - Children 6 years and older

### Administration
- Intranasal use only
### PK/PD
- Absorption: systemic absorption may occur following intranasal administration
- Half-life elimination: 3.1 hrs
- Excretion: urine (~40%), feces (~60%)
- Onset of action: few days up to 2 weeks
- Distribution: 20 L
- Protein binding: 87%
- Metabolism: Beclomethasone dipropionate is a prodrug converted to beclomethasone-17-monopropionate
  - Followed by extensive through CYP3A4
- Half-life elimination: 0.5 hrs
- Excretion: feces (60%); urine (<10%)
- Onset of action: within 10 hrs
- Distribution: 2-3 L/kg
- Protein binding: 85-90%
- Metabolism: hepatic, CYP3A4 to 16 alpha-hydroxyxyprednisolone and 6 beta-hydroxybudesonide
- Bioavailability: 34%
- Half-life elimination: 2-3 hrs
- Time to peak, plasma: 30 min
- Excretion: urine (66%) and feces as metabolites

### Contraindications
- Hypersensitivity to triamcinolone, use in children <2 years old
- Hypersensitivity to beclomethasone
- Hypersensitivity to budesonide, OTC use in children < 6 years old

### Warnings
- Adrenal suppression, delayed wound healing, immunosuppression, local nasal effects, caution in patients with infections or ocular disease
- Adrenal suppression, delayed wound healing, immunosuppression and local nasal effects may occur, use with caution in patients with glaucoma and/or cataracts and infections

### Drug-drug interaction
- Ceritinib
- Ceritinib
- Ceritinib, Cobicistat, CYP3A4 Inhibitors (Strong), Telaprevir

### Common Side effects
- Headache, pharyngitis, dysgeusia, back pain, flu-like symptoms, sinusitis, cough, epistaxis
- Dizziness, headache, nausea, intraocular pressure increased, epistaxis, sneezing, upper respiratory tract infection
- Epistaxis, pharyngitis, bronchospasm, cough, nasal mucosa irritation

### Monitoring
- Growth (adolescents and children), signs/symptoms of HPA axis suppression/adrenal insufficiency, ocular changes, signs/symptoms of Candida infection

### Pregnancy
- C
- C
- B

### Lactation
- Use with caution in nursing women
- Use only when clinically appropriate at lowest effective dose and administer after breast feeding to minimize potential exposure to infant

### Storage and stability
- Store at 20°C to 25°C; do not freeze
- Beconase AQ: store between 15°C to 30°C (59°F to 86°F)
- Qnasl: Store at 25°C (77°F), excursions permitted to 15°C to 30°C (59°F to 86°F), do not freeze. Protect from light.
### Ciclesonide (Omnaris, Zetonna) vs. Mometasone (Nasonex)

<table>
<thead>
<tr>
<th></th>
<th>Ciclesonide (Omnaris, Zetonna)</th>
<th>Mometasone (Nasonex)</th>
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<tr>
<td><strong>MOA</strong></td>
<td>Controls the rate of protein synthesis; depresses the migration of polymorphonuclear leukocytes, fibroblasts; reverses capillary permeability and lysosomal stabilization at the cellular level to prevent or control inflammation.</td>
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<td><strong>Usual Dosing</strong></td>
<td>Omnaris: 2 sprays per nostril/day</td>
<td>2 sprays in each nostril 1-2 times per day</td>
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<td></td>
<td>Zetonna: 1 spray per nostril/day</td>
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<tr>
<td><strong>FDA Indication</strong></td>
<td>Seasonal and perennial allergic rhinitis</td>
<td>Allergic rhinitis (seasonal and perennial), nasal congestion associated with seasonal rhinitis, nasal polyps, seasonal allergic rhinitis (prophylaxis)</td>
</tr>
<tr>
<td><strong>Pediatric Indication</strong></td>
<td>Children 6 years and older</td>
<td>Children 2 years and older</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Intranasal use only</td>
<td></td>
</tr>
<tr>
<td><strong>PK/PD</strong></td>
<td>- Onset of action: 24-48 hrs</td>
<td>- Onset of action: 11 hrs, maximum effect within 1-2 weeks</td>
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<td>- Absorption: minimal systemic absorption</td>
<td>- Absorption: undetectable in plasma</td>
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<td>- Metabolism: ciclesonide is hydrolyzed into its active metabolite – des-ciclesonide – via esterases in nasal mucosa and lungs</td>
<td>- Protein binding: 98-99%</td>
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<td>- Further metabolism via CYP3A4 and 2D6</td>
<td>- Metabolism: hepatic, multiple metabolites via CYP3A4</td>
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<tr>
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<td>- Bioavailability: &lt; 1%</td>
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<td></td>
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<td>- Excretion: bile (primary), urine (limited)</td>
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<td><strong>Contraindications</strong></td>
<td>Hypersensitivity to ciclesonide</td>
<td>Hypersensitivity to mometasone</td>
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<td><strong>Warnings</strong></td>
<td>Adrenal suppression, delayed wound healing, immunosuppression and local nasal effects may occur, use with caution in patients with glaucoma and/or cataracts and infections</td>
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<td>Certinib</td>
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<td><strong>Common Side effects</strong></td>
<td>Epistaxis, headache, nausea, UTI, influenza, back pain, strain, otalgia, nasal discomfort, pharyngolaryngeal pain</td>
<td>Headache, viral infection, pharyngitis, cough, epistaxis</td>
</tr>
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<td><strong>Monitoring</strong></td>
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<td><strong>Storage and stability</strong></td>
<td>- Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F)</td>
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</tr>
<tr>
<td></td>
<td>- Omnisas: do not freeze, use within 4</td>
<td>- Excursions permitted to 15°C to 30°C (59°F to 86°F).</td>
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<td>- Protect from light.</td>
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months of opening aluminum pouch
• Zetonna: protect from heat or open flame, do not puncture

| How supplied | Aerosol Solution, nasal
• Zetonna: 37 mcg/actuation
Suspension, nasal
• Omnaris: 50 mcg/actuation | Suspension, nasal
• 50 mcg/actuation |

References:


<table>
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<tr>
<th>Date</th>
<th>Change</th>
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</table>
| 05/17/2017 | • Removed flunisolide from Medi-Cal formulary
• Revised criteria for non-formulary intranasal steroid agents:
  o Failure or clinically significant adverse effects to TWO formulary intranasal steroid sprays |