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Drugs for Allergic Disorders .............................................................. p 71

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Second-generation H1-antihistamines are less effective for nasal congestion. They characterize mild-to-moderate allergic rhinitis. They for relief of the itching, sneezing, and rhinorrhea that sedation.3,4 Fexofenadine is nonsedating and free of CNS-system (CNS) and are signi

First-generation H1-antihistamines such as diphenhydramine (Benadryl, and generics) can cause CNS impairment with or without sedation. They can interfere with learning and memory, impair performance on school examinations, decrease work productivity, and increase the risk of on-the-job injuries, car accidents,
Cumulative exposure to drugs with anticholinergic effects such as first-generation antihistamines has been associated with dementia.\(^7\)

**Intranasal** - Intranasal H\(_1\)-antihistamines have a rapid onset of action. Their clinical efficacy in allergic rhinitis, including relief of nasal congestion, is equal or superior to that of oral H\(_1\)-antihistamines. An intranasal combination of the H\(_1\)-antihistamine azelastine and the corticosteroid fluticasone propionate has improved symptoms more than either drug alone in patients with seasonal allergic rhinitis.\(^8\) Intranasal antihistamines can cause nasal discomfort, epistaxis and headache, and may cause somnolence.

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**Table 1. Some Oral Drugs for Allergic Rhinitis**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Some Available Formulations</th>
<th>Usual Adult Dosage(^1)</th>
<th>Usual Pediatric Dosage(^1)</th>
<th>Cost(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Second-Generation H(_1)-Antihistamines and Combinations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetirizine(^3) – Zyrtec Allergy, (Johnson &amp; Johnson)</td>
<td>5, 10 mg tabs and caps; 5, 10 mg chewable tabs; 5 mg/5 mL syrup</td>
<td>10 mg once/d</td>
<td>6-11 mos: 2.5 mg once/d(^d)</td>
<td>$15.90</td>
</tr>
<tr>
<td></td>
<td>12-23 mos: 2.5 mg once/d-bid(^d)</td>
<td></td>
<td>2-5 yrs: 2.5 mg or 5 mg once/d</td>
<td>or 2.5 mg bid</td>
</tr>
<tr>
<td></td>
<td>6-11 yrs: 5 or 10 mg once/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetirizine/pseudoephedrine(^3) – Zyrtec-D 12 hour (Johnson &amp; Johnson)</td>
<td>5 mg/120 mg ER tabs</td>
<td>1 tab bid</td>
<td>≥12 yrs: 1 tab bid</td>
<td>$39.80</td>
</tr>
<tr>
<td>Desloratadine – generic</td>
<td>5 mg tabs; 2.5, 5 mg disintegrating tabs; 5 mg tabs; 0.5 mg/mL syrup</td>
<td>5 mg once/d</td>
<td>6-11 mos(^e): 1 tab bid</td>
<td>$51.10</td>
</tr>
<tr>
<td>Clarinex (MSD)</td>
<td>60 mg bid or 180 mg once/d</td>
<td></td>
<td>1-5 yrs(^f): 1.25 mg once/d</td>
<td>$206.70</td>
</tr>
<tr>
<td>Desloratadine/pseudoephedrine – Clarinex-D 12 hour (MSD)</td>
<td>2.5 mg/120 mg ER tabs</td>
<td>1 tab bid</td>
<td>≥12 yrs: 1 tab bid</td>
<td>$284.40</td>
</tr>
<tr>
<td>Fexofenadine(^3) – Allegra Allergy, Children’s Allegra Allergy (Chatter)</td>
<td>60 mg/120 mg ER tabs</td>
<td>1 tab bid</td>
<td>≥12 yrs: 1 tab bid</td>
<td>$40.00</td>
</tr>
<tr>
<td>Fexofenadine/pseudoephedrine – Allegra-D 12 hour (Chatter)</td>
<td>180 mg/240 mg ER tabs</td>
<td>1 tab once/d</td>
<td>≥12 yrs: 1 tab once/d</td>
<td>$31.20</td>
</tr>
<tr>
<td></td>
<td>Levocetirizine – generic(^5) – Xyzal Allergy 24 hour, Children’s Xyzal Allergy (Chatter) (^7)</td>
<td>5 mg tabs; 2.5 mg/5 mL oral soln</td>
<td>5 mg once/d</td>
<td>6 mos-5 yrs: 1.25 mg once/d(^d)</td>
</tr>
<tr>
<td></td>
<td>Loratadine(^3) – Alavert (Pfizer) Claritin, Children’s Claritin (Bayer)</td>
<td>10 mg disintegrating tabs</td>
<td>10 mg once/d</td>
<td>6-11 yrs: 2.5 mg once/d</td>
</tr>
<tr>
<td></td>
<td>10 mg tabs and caps; 10 mg disintegrating tabs; 5 mg chewable tabs; 1 mg/mL syrup</td>
<td>2-5 yrs: 5 mg once/d</td>
<td>≥6 yrs: 10 mg once/d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Loratadine/pseudoephedrine(^3) – Alavert-D 12 hour (Pfizer) Claritin-D 24 hour (Bayer)</td>
<td>5 mg/120 mg ER tabs</td>
<td>1 tab bid</td>
<td>≥12 yrs: 1 tab bid</td>
</tr>
<tr>
<td>Leukotriene Receptor Antagonist</td>
<td>10 mg/240 mg ER tabs</td>
<td>1 tab once/d</td>
<td>≥12 yrs: 1 tab once/d</td>
<td>$39.90</td>
</tr>
<tr>
<td>Montelukast – generic</td>
<td>10 mg tabs; 4, 5 mg chewable tabs; 4 mg granule packets</td>
<td>10 mg once/d</td>
<td>6 mos-5 yrs: 4 mg once/d</td>
<td>$215.40</td>
</tr>
<tr>
<td><strong>Singulair (Merck)</strong></td>
<td>6-14 yrs: 5 mg once/d</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ER = extended-release
1. Dosage adjustment may be needed for renal or hepatic impairment.
2. Approximate WAC for 30 days' treatment at the lowest usual adult dosage. When multiple formulations are listed, price is for the first formulation unless otherwise indicated. WAC = wholesaler acquisition cost or manufacturer’s published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. April 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy.
3. Available without a prescription. Products containing pseudoephedrine are subject to sales restrictions.
4. Individual retailers may have their own OTC generic products.
5. The prescription product is FDA-approved for treatment of perennial allergic rhinitis and chronic urticaria in children ≥6 months old. The OTC product is recommended for children ≥2 years old.
7. The prescription product is FDA-approved for treatment of chronic idiopathic urticaria in children ≥6 months old. The OTC product is recommended for children ≥2 years old.
8. Cost of 30 days' treatment with 180 mg once/d.
9. The generic formulation is available by prescription.

**INTRANASAL CORTICOSTEROIDS** – Intranasal corticosteroids are the most effective drugs available for prevention and relief of allergic rhinitis symptoms, including itching, sneezing, discharge, and congestion. They are the drugs of choice for moderate-to-severe disease. Most of these agents are effective when given once daily. The onset of action typically occurs within 12 hours, but maximal effects may not be achieved for ≥7 days. In patients with seasonal allergic rhinitis, intranasal corticosteroid sprays can decrease ocular as well as nasal symptoms.\(^9\) Several intranasal corticosteroids are now available without a prescription (see Table 2).\(^10\)
### Table 2. Some Nasal Sprays for Allergic Rhinitis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Some Available Formulations</th>
<th>Usual Adult Dosage</th>
<th>Usual Pediatric Dosage</th>
<th>Cost†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H1-Antihistamines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azelastine² – Astelin 0.1% (Meda) generic</td>
<td>Metered-dose pump spray (137 mcg/spray)</td>
<td>1-2 sprays per nostril bid²</td>
<td>5-11 yrs: 1 spray per nostril bid</td>
<td>$142.50†</td>
</tr>
<tr>
<td>Aztepo 0.15% (Meda) generic</td>
<td>Metered-dose pump spray (205.5 mcg/spray)</td>
<td>1-2 sprays per nostril bid or 2 sprays per nostril once/d³</td>
<td>6-11 yrs: 1 spray per nostril bid</td>
<td>148.50</td>
</tr>
<tr>
<td>Olopatadine 0.65% – generic Patanase (Alcon)</td>
<td>Metered-dose pump spray (665 mcg/spray)</td>
<td>2 sprays per nostril bid</td>
<td>6-11 yrs: 1 spray per nostril bid</td>
<td>216.70</td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone dipropionate – Beconase AQ (GSK)⁶</td>
<td>Metered-dose pump spray (42 mcg/spray)</td>
<td>1-2 sprays per nostril bid</td>
<td>6-11 yrs: 1-2 sprays per nostril once/d⁷</td>
<td>279.40</td>
</tr>
<tr>
<td>QNASL (Teva)</td>
<td>HFA metered-dose aerosol (80 mcg/actuation)</td>
<td>2 sprays per nostril once/d</td>
<td>≥12 yrs: 2 sprays per nostril once/d</td>
<td>192.40</td>
</tr>
<tr>
<td>QNASL Childrens</td>
<td>HFA metered-dose aerosol (40 mcg/actuation)</td>
<td></td>
<td>4-11 yrs: 1 spray per nostril once/d</td>
<td>192.40</td>
</tr>
<tr>
<td>Budesonide³¹⁰ – Rhinocort Allergy Children's Rhinocort Allergy (Johnson &amp; Johnson)</td>
<td>Metered-dose pump spray (32 mcg/spray)</td>
<td>2 sprays per nostril once/d¹¹</td>
<td>6-11 yrs: 1-2 sprays per nostril once/d¹²</td>
<td>11.10</td>
</tr>
<tr>
<td>Ciclesonide – Omnaris (Sunovion)</td>
<td>Metered-dose pump spray (50 mcg/spray)</td>
<td>2 sprays per nostril once/d</td>
<td>≥6 yrs¹³; 2 sprays per nostril once/d</td>
<td>234.10</td>
</tr>
<tr>
<td>Zetonna (Sunovion)</td>
<td>HFA metered-dose aerosol (37 mcg/actuation)</td>
<td>1 spray per nostril once/d</td>
<td>≥12 yrs: 1 spray per nostril once/d</td>
<td>234.10</td>
</tr>
<tr>
<td>Flunisolide – generic</td>
<td>Metered-dose pump spray (25 mcg/spray)</td>
<td>2 sprays per nostril bid-tid</td>
<td>6-14 yrs: 1 spray per nostril bid or 2 sprays per nostril bid</td>
<td>55.00</td>
</tr>
<tr>
<td>Fluticasone furoate³ – Flonase Sensistim Allergy Relief (GSK)</td>
<td>Metered-dose pump spray (27.5 mcg/spray)</td>
<td>2 sprays per nostril once/d x 7 days, then 1-2 sprays per nostril once/d¹¹</td>
<td>2-11 yrs: 1 spray per nostril once/d¹²</td>
<td>13.60</td>
</tr>
<tr>
<td>Fluticasone propionate³¹³ – Flonase Allergy Relief, Children's Flonase Allergy Relief (GSK)</td>
<td>Clarispray Nasal Allergy Spray (Bayer)</td>
<td>Metered-dose pump spray (50 mcg/spray)</td>
<td>2 sprays per nostril once/d x 7 days, then 1-2 sprays per nostril once/d¹¹</td>
<td>4-11 yrs: 1 spray per nostril once/d¹²</td>
</tr>
<tr>
<td>Mometasone furoate – generic Nasonex (Merck)¹⁴</td>
<td>Metered-dose pump spray (50 mcg/spray)</td>
<td>2 sprays per nostril once/d</td>
<td>2-11 yrs: 1 spray per nostril once/d</td>
<td>162.40</td>
</tr>
<tr>
<td>Triamcinolone acetonide³¹⁰ – Nasacort Allergy 24 hour, Children's Nasacort Allergy 24 hour (Chattem)</td>
<td>Metered-dose pump spray (55 mcg/spray)</td>
<td>2 sprays per nostril once/d¹¹</td>
<td>2-5 yrs: 1 spray per nostril once/d¹²</td>
<td>11.20</td>
</tr>
<tr>
<td>≥2 yrs: 1-2 sprays per nostril once/d¹²</td>
<td>6-11 yrs: 1-2 sprays per nostril once/d¹²</td>
<td>6-11 yrs: 1 spray per nostril bid or 2 sprays per nostril bid</td>
<td>234.10</td>
<td></td>
</tr>
<tr>
<td><strong>H1-Antihistamine/Corticosteroid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azelastine/fluticasone propionate – Dymista (Meda)⁶</td>
<td>Metered-dose pump spray (137 mcg/50 mcg per spray)</td>
<td>1 spray per nostril bid</td>
<td>≥6 yrs: 1 spray per nostril bid</td>
<td>170.20</td>
</tr>
<tr>
<td>Mast Cell Stabilizer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cromolyn sodium – generic Nasalcon⁵ (Prestige)</td>
<td>Metered-dose pump spray (5.2 mg/spray)</td>
<td>1 spray per nostril tid-qid</td>
<td>≥2 yrs: 1 spray per nostril tid-qid</td>
<td>7.00</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium bromide – generic</td>
<td>Metered-dose pump spray (21 or 42 mcg/spray)</td>
<td>2 sprays per nostril bid-qid¹⁵</td>
<td>≥5 yrs: 2 sprays per nostril bid-qid¹⁵</td>
<td>30.00</td>
</tr>
</tbody>
</table>

**Notes:**
- HFA = hydrofluoroalkane
- †Approximate WAC for 30 days' treatment at the lowest recommended adult dosage (using smallest size available). WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. April 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy.
- 1. Approved for seasonal allergic rhinitis (≥5 years old) and vasomotor rhinitis (≥12 years old).
- 2. Approved for seasonal allergic rhinitis, dosage for seasonal allergic rhinitis is 2 sprays per nostril bid.
- 3. Dosage for seasonal allergic rhinitis. Dosage for vasomotor rhinitis is 2 sprays per nostril bid.
- 4. Dosage for seasonal allergic rhinitis. Dosage for perennial allergic rhinitis is 2 sprays per nostril bid.
- 6. FDA-approved only for treatment of seasonal allergic rhinitis.
- 7. Also FDA-approved for treatment of vasomotor rhinitis.
- 8. A dose of 2 sprays/nostril should only be used until symptoms improve; then the dose should be reduced to 1 spray/nostril.
- 10. Individual retailers may have their own OTC generic products.
- 11. OTC intranasal corticosteroids should not be used daily for ≥6 months without consulting a physician.
- 12. OTC intranasal corticosteroids should not be used daily for ≥2 months/year in children ≥12 years old without consulting a physician.
- 14. Also FDA-approved for prophylaxis of seasonal allergic rhinitis in patients ≥12 years old.
- 15. Dosage of 0.03% formulation is 2 sprays (84 mcg) per nostril bid in patients ≥6 years old with allergic or nonallergic perennial rhinitis; dosage of 0.06% formulation is 2 sprays (84 mcg) per nostril qid in patients ≥5 years old with seasonal allergic rhinitis.
Adverse Effects – Intranasal corticosteroids can cause mild dryness, irritation, burning and bleeding of the nasal mucosa, sore throat, epistaxis, and headache. Ulceration, mucosal atrophy, and septal perforation can occur; patients should be examined periodically to detect changes in the nasal mucosa. Increased intraocular pressure has been reported. Use of intranasal corticosteroids for ≥12 months in children has been associated with small decreases in growth velocity.

MONTELUKAST – Release of cysteinyl leukotrienes in the nasal mucosa during allergic inflammation leads to nasal congestion. The leukotriene receptor antagonist montelukast is FDA-approved for treatment of seasonal and perennial allergic rhinitis. It provides modest relief of sneezing, itching, discharge, and congestion, but it is less effective than an intranasal corticosteroid. Montelukast is generally considered safe.

DECONGESTANTS – Oral – Oral decongestants such as phenylephrine and pseudoephedrine act as vasoconstrictors in the nasal mucosa, primarily through stimulation of alpha-1 adrenergic receptors on venous sinusoids. They only relieve congestion, not sneezing, itching, or discharge. They are often used in combination with an H1-antihistamine. Tolerance to the decongestant effect can occur. Phenylephrine has replaced pseudoephedrine in many oral decongestant products because illicit pseudoephedrine use has resulted in sales restrictions. In an open-label, randomized, dose-ranging study, phenylephrine was no more effective than placebo for relief of nasal congestion in 539 patients with seasonal allergic rhinitis who took up to 4 times the typical dose of 10 mg.

Potential adverse effects of oral decongestants include insomnia, excitability, headache, nervousness, anorexia, palpitations, tachycardia, arrhythmias, hypertension, nausea, vomiting, and urinary retention. These drugs should be used cautiously in patients with cardiovascular disease, hypertension, diabetes, hyperthyroidism, closed-angle glaucoma, or bladder neck obstruction.

Intranasal – Intranasal decongestants such as oxymetazoline (Afrin, and generics) are less likely than oral decongestants to cause systemic adverse effects, but they can cause stinging, burning, sneezing, and dryness of the nose and throat. In order to avoid rhinitis medicamentosa (rebound congestion), they should not be used for more than 3-5 consecutive days. Rhinitis medicamentosa associated with prolonged use is treated by discontinuing the intranasal decongestant and using an intranasal corticosteroid instead. In a cross-sectional, observational study, nasal congestion was the predominant symptom in 895 patients who self-medicated for moderate-to-severe persistent rhinitis. The prevalence of intranasal decongestant overuse was high, and was inversely related to intranasal corticosteroid use.

CROMOLYN – Use of intranasal cromolyn sodium before allergen exposure inhibits mast cell degranulation and mediator release, preventing allergic rhinitis symptoms. It is relatively free from adverse effects, but must be used 3-4 times daily and is considerably less effective than an intranasal corticosteroid.

IPRATROPIUM – Ipratropium bromide, a quaternary amine antimuscarinic agent, is poorly absorbed systemically and does not readily cross the blood-brain barrier. Intranasal ipratropium can be useful in patients whose primary symptom is nasal discharge. It does not relieve sneezing, itching, or congestion.

Adverse Effects – Ipratropium can cause dry nose and mouth, epistaxis, and pharyngeal irritation. After inadvertent instillation in the eye, it can increase intraocular pressure and should be used with caution in patients with glaucoma.

OMALIZUMAB – Omalizumab (Xolair), a monoclonal antibody approved by the FDA for treatment of allergic asthma and chronic urticaria, has a dose-dependent beneficial effect in seasonal allergic rhinitis. Injected subcutaneously every 2-4 weeks, it decreases free IgE levels in serum and the number of IgE receptors on mast cells and basophils. In a systematic review and meta-analysis of 11 studies that included 2870 patients with inadequately controlled allergic rhinitis, injection of omalizumab significantly reduced daily nasal symptom severity scores and rescue medication use and improved quality of life. Adverse effects did not differ from placebo. Omalizumab is generally well tolerated, but it has caused anaphylaxis in about 0.1% of patients with asthma.

ORAL CORTICOSTEROIDS – A short course of an oral corticosteroid can be effective in patients with severe allergic rhinitis or rhinitis medicamentosa who cannot tolerate or do not respond to other drugs.

ALLERGEN-SPECIFIC IMMUNOTHERAPY – Immunotherapy can alter the natural history of allergic respiratory disease (see page 79).
PREGNANCY — In a systematic review and meta-analysis of 37 studies that included >50,000 women exposed to H1-antihistamines during the first trimester of pregnancy, use of these drugs was not associated with an increased risk of major malformations, spontaneous abortions, prematurity, or low birth weight. Nasal saline irrigations, cromolyn sodium, and intranasal corticosteroids are also considered safe for pregnant women with allergic rhinitis.

Allergic Conjunctivitis

Allergic conjunctivitis, although underreported, probably occurs in the majority of patients with allergic rhinitis. Symptoms such as itching, redness, tearing, and photophobia are frequently seasonal. Nonpharmacologic management includes allergen identification and avoidance, use of cool compresses, and avoidance of eye rubbing and contact lens wearing during symptomatic periods. Optimal management of allergic rhinitis with an oral second-generation H1-antihistamine and an intranasal corticosteroid can benefit concomitant allergic conjunctivitis as well.

OPHTHALMIC DRUGS — Ophthalmic antihistamines are at least as effective as oral H1-antihistamines for treatment of allergic conjunctivitis. Onset of action occurs within a few minutes. Starting treatment before the pollen season may be more beneficial in controlling symptoms than waiting for them to occur. Alcaftadine, azelastine, bepotastine, epinastine, and olopatadine are marketed as having both H1-antihistamine and mast-cell-stabilizing activity, as is ketotifen, which is available over the counter. A meta-analysis of four studies in a total of 204 patients has suggested that olopatadine may be more effective than ketotifen in improving some ocular symptoms.

The ophthalmic mast cell stabilizers cromolyn, lodoxamide, and nedocromil have a slower onset of action than ophthalmic H1-antihistamines and are mostly used for treatment of mild-to-moderate symptoms.
The topical nonsteroidal anti-inflammatory drug ketorolac is less effective than ophthalmic H₁-antihistamines.

Ophthalmic decongestants such as naphazoline reduce erythema, congestion, itching, and eyelid edema, but they have a short duration of action and can cause burning, stinging, rebound hyperemia, and conjunctivitis medicamentosa. Ophthalmic antihistamine/decongestant combinations available over the counter such as pheniramine/naphazoline (Visine A, and generics) and antazoline/naphazoline (Vasocon-A) have similar adverse effects.

Ophthalmic corticosteroids can be considered for use in allergic conjunctivitis that fails to respond to other medications. Loteprednol is inactivated rapidly in the anterior chamber of the eye and has been associated with significantly lower rates of intraocular pressure elevation than ophthalmic administration of prednisolone or dexamethasone. Treatment with ophthalmic corticosteroids should be limited to two weeks, and even during this brief exposure, patients should be monitored for exacerbations of conjunctival or corneal viral infections and for increased intraocular pressure. With longer treatment, cataract formation is a concern.

STIRRING AND BURNING — Patients who find that application of any topical ophthalmic preparation leads to stinging or burning should try refrigerating the drug before use. Compounding pharmacies can prepare preservative-free formulations for patients with ocular hypersensitivity to preservatives in ophthalmic drugs. A novel filter device has been developed for removal of benzalkonium chloride, the most common offender.

TOPICAL DRUGS — Corticosteroids — A medium- or high-potency topical corticosteroid may be needed to achieve control of skin inflammation in atopic dermatitis. For maintenance treatment, the lowest potency topical corticosteroid that is effective in a given patient should be used. High-potency corticosteroids such as betamethasone dipropionate 0.05% ointment or cream should only be applied to the trunk and extremities for short periods of time and should never be applied to the face or intertriginous areas such as the axillae and groin. Low-potency corticosteroids such as hydrocortisone cream are safe for use on the face and intertriginous areas.

Use of topical corticosteroids can lead to development of striae and skin atrophy. When applied to the eyelids for prolonged periods, they can potentially cause glaucoma and cataracts. The risks of systemic adverse effects, including adrenal suppression and possibly lymphoma, increase with corticosteroid potency, percentage of body surface covered, and duration of treatment. The risks are greatest when high-potency corticosteroids are applied under occlusive dressings in infants and young children with widespread skin involvement who require long-term treatment.

Calcineurin Inhibitors — Topically applied tacrolimus and pimecrolimus can reduce inflammation and itching associated with atopic dermatitis within a few days. Topical tacrolimus 0.1% is similar in efficacy to a medium-potency topical corticosteroid and may be considered for use in patients with topical corticosteroid-resistant atopic dermatitis, especially on the face or intertriginous areas where corticosteroid adverse effects can be troublesome. It can also be used as maintenance treatment to minimize use of topical corticosteroids. After control of inflammation is achieved, applying tacrolimus ointment 2-3 times weekly increases the number of flare-free days and the time to relapse. Pimecrolimus is not as effective as a medium-potency topical corticosteroid, but it can be useful as steroid-sparing therapy for mild-to-moderate atopic dermatitis.

Tacrolimus and, less often, pimecrolimus can cause mild, transient itching, burning, stinging, and erythema, and both have been associated with an increased risk of viral skin infections such as herpes simplex and varicella zoster, but they do not cause cutaneous atrophy. Rare postmarketing reports of malignancies in patients treated with topical calcineurin inhibitors led the FDA to include a boxed warning in the labels of these drugs about possible risks of lymphoma and other malignancies.
### Table 4. Some Topical Drugs for Atopic Dermatitis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vehicle</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CALCINEURIN INHIBITORS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pimecrolimus 1%</td>
<td>Elidel (Novartis) cream</td>
<td>$517.20②</td>
</tr>
<tr>
<td>Tacrolimus 0.03%, 0.1% generic</td>
<td>Protopic (Astellas) oint</td>
<td>416.70②, 486.20②</td>
</tr>
<tr>
<td><strong>PDE4 INHIBITOR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crisaborole 2%</td>
<td>Eucrisa (Pfizer) oint</td>
<td>580.00②</td>
</tr>
<tr>
<td><strong>CORTICOSTEROIDS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate augmented 0.05% generic</td>
<td>Diprolene</td>
<td>105.70, 170.70</td>
</tr>
<tr>
<td><strong>Clobetasol propionate 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clobex (Galderma) cream, oint, gel lotion, soln foam spray</td>
<td>124.50, 149.00, 292.30</td>
<td></td>
</tr>
<tr>
<td><strong>Fluocinonide 0.1%</strong></td>
<td>Vanos (Valeant) cream</td>
<td>323.80</td>
</tr>
<tr>
<td><strong>Halobetasol propionate 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultravate (Runbax) cream, oint, lotion, soln foam</td>
<td>153.10, 916.00③</td>
<td></td>
</tr>
<tr>
<td><strong>Amcinonide 0.1%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate 0.05% augmented generic</td>
<td>Diprolene AF (Merck) cream</td>
<td>42.40, 170.70</td>
</tr>
<tr>
<td><strong>Betamethasone dipropionate 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Desoximetasone 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluocinolone acetonide 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halcinonide 0.1%</td>
<td>Halog (Runbax) cream, oint</td>
<td>452.80</td>
</tr>
<tr>
<td>Mometasone furoate 0.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medium Potency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate 0.05%</td>
<td>Sernivo (Promius) spray</td>
<td>$780.00②</td>
</tr>
<tr>
<td>Betamethasone valerate 0.12% generic</td>
<td>Luxiq (Premis/Mylan) foam</td>
<td>261.50, 411.60</td>
</tr>
<tr>
<td>Fluocinolone acetonide 0.025%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide 0.05% generic</td>
<td>Cordran (Aqua) oint</td>
<td>523.00②, 581.00②</td>
</tr>
<tr>
<td>Hydrocortisone valerate 0.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate 0.1% generic</td>
<td>cream, soln</td>
<td>35.00</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.1%</td>
<td>oint, cream</td>
<td>9.00</td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.05%</td>
<td>Trianex (Promius) oint</td>
<td>860.00②</td>
</tr>
<tr>
<td><strong>Medium-Low Potency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate 0.05%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Betamethasone valerate 0.1%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Desoximetasone 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluocinolone acetonide 0.025%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide 0.05% generic</td>
<td>Cordran (Aqua) cream, lotion</td>
<td>412.70②, 962.00②</td>
</tr>
<tr>
<td>Hydrocortisone butyrate 0.1% generic</td>
<td>Cultivate (PharmaDerm) cream, oint, lotion, soln spray</td>
<td>100.20, 191.20</td>
</tr>
<tr>
<td><strong>Locoid (Onset)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Locoid Lipocream</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hydrocortisone probutate 0.1%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pandel (Sandoz) cream</td>
<td>984.10②</td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone valerate 0.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednicarbarte 0.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Triamcinolone acetonide 0.025%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide 0.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low Potency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alclometasone dipropionate 0.05%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone valerate 0.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clocortolone pivalate 0.1%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Desoximetasone 0.05%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluocinolone acetonide 0.01%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halcinonide 0.1%</td>
<td>Halog (Runbax) cream, oint, lotion, soln foam</td>
<td>523.00②</td>
</tr>
<tr>
<td>Mometasone furoate 0.1%</td>
<td>oint, cream</td>
<td>114.30</td>
</tr>
<tr>
<td><strong>Lowest Potency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone 2.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone 1.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone 0.5%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer’s published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. April 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy. When multiple formulations are listed, the price of the first formulation is provided (30 g of cream, ointment, or gel, 50 or 60 mL of lotion, solution, or spray, 118 mL of shampoo, and 50 g of foam).

2. Cost of 60 g.

3. Cost of 50 g.

4. Cost of 120 g.

5. Cost of 120 mL.

6. Cost of a 430-g jar.

7. Cost of 45 g.

8. Cost of 80 g.


10. Price according to walgreens.com (0.5% cream, 1% cream and lotion). Accessed April 27, 2017.
other cancers with prolonged treatment. A causal relationship has not been established.24

**Crisaborole** – Crisaborole (Eucrisa), a topical phosphodiesterase type-4 (PDE4) inhibitor, has been approved by the FDA for treatment of atopic dermatitis in patients ≥2 years old. It acts in part by increasing levels of cyclic adenosine monophosphate (cAMP) to suppress production of proinflammatory cytokines in the skin. Systemic absorption is minimal.25 In two randomized controlled trials in patients with mild-to-moderate atopic dermatitis, crisaborole 2% ointment applied twice daily to affected areas of skin was compared to its vehicle alone. A significantly higher percentage of patients using crisaborole achieved clear or almost-clear skin in both trials (33% vs 25% and 31% vs 18%).26 Adverse effects have been mainly stinging and burning at the application site. The drug’s long-term adverse effects are unknown. How crisaborole compares to topical corticosteroids or calcineurin inhibitors remains to be established.

**Coal Tar** – Coal tar preparations have antipruritic and anti-inflammatory effects, but they are messy and odoriferous and are now seldom used except in shampoo formulations. Adverse effects include skin irritation, folliculitis, and photosensitivity.

**Antipruritic Therapy** – Pruritus is optimally controlled by regular applications of topical anti-inflammatory medications to the skin. Although the efficacy of oral H1-antihistamines in atopic dermatitis has not been confirmed in randomized controlled trials, some physicians recommend a first-generation sedating H1-antihistamine such as diphenhydramine or hydroxyzine (Vistaril, and generics) at bedtime. Topical H1-antihistamines are potentially sensitizing and are therefore contraindicated for use in atopic dermatitis.27

**SYSTEMIC DRUGS** – Dupilumab (Dupixent), a subcutaneously-injected, fully human monoclonal antibody that inhibits the signaling of the inflammatory cytokines interleukin (IL)-4 and IL-13, has been approved by the FDA for treatment of adults with moderate-to-severe atopic dermatitis that has not responded to topical therapies.28 In two randomized, double-blind, 16-week trials in 1379 adults, dupilumab monotherapy significantly improved measures of skin clearing, overall extent and severity of disease, and pruritus compared to placebo. A score of 4 or almost clear on the Investigator’s Global Assessment scale and a reduction of ≥2 points on that score from baseline, the primary endpoint, occurred in 38% and 36% of patients treated with dupilumab every other week in the two trials versus 10% and 8% of those who received placebo.29 Administration of dupilumab in combination with topical corticosteroids for 52 weeks significantly improved skin clearing and overall disease severity compared to use of topical corticosteroids alone.30 Adverse effects have included injection-site reactions, conjunctivitis, blepharitis, keratitis, and oral herpes and other herpes simplex virus infections.

**Cyclosporine** (Neoral, and generics) is not FDA-approved for use in atopic dermatitis, but it has been recommended for short-term treatment of moderate-to-severe atopic dermatitis that is refractory to topical therapy.31 In multiple randomized controlled trials, it significantly decreased disease activity within 2 to 6 weeks.32 The usual dosage is 3-6 mg/kg/day (150-300 mg/day in adults). Cyclosporine can cause hypertension, nephrotoxicity, GI disturbances, hirsutism, headache, paresthesias, hypertriglycerideremia, and musculoskeletal or joint pain. It also increases the risks of infection and cutaneous and lymphoproliferative malignancies, and it interacts with many other drugs.

Short courses of an oral corticosteroid such as prednisone can be helpful in severe acute exacerbations of atopic dermatitis, but the drug should be tapered quickly and intensified treatment with topical corticosteroids and calcineurin inhibitors should be started.

**PHOTOTHERAPY** – Phototherapy in moderation has been effective in some patients after failure of topical drugs. It can be used alone or in combination with emollients and topical corticosteroids.31

**Urticaria**

**Acute urticaria** is a self-limited condition that responds well to treatment with an oral H1-antihistamine. **Chronic urticaria** (≥6 weeks) can last for months, years, or decades.

**H1-ANTIHISTAMINES** – Randomized controlled trials have shown that oral second-generation H1-antihistamines consistently decrease itching and reduce the number, size, and duration of wheals in acute and chronic urticaria.33 Taken regularly, they can prevent new wheals from appearing. Cetirizine and levocetirizine are more potent in suppressing histamine-induced wheals than fexofenadine, and fexofenadine is more potent than loratadine and desloratadine. High doses (up to 4 times the usual dose) of a second-generation H1-antihistamine are recommended (off-label) for treatment of chronic urticaria that does not
Sublingual immunotherapy (SLIT) has been approved by the FDA for treatment of allergic rhinitis induced by grass pollen, ragweed pollen, and dust mites. Both subcutaneous immunotherapy (SCIT) and SLIT are effective in altering the natural history of allergic respiratory disease and inducing long-term remission, but SCIT has been used much longer, and has been highly effective in preventing future anaphylactic reactions to insect stings. Both SCIT and SLIT may be beneficial in decreasing symptoms and rescue medication use in patients with allergic rhinitis. Definitive randomized controlled trials comparing SCIT with SLIT are needed.

Local adverse effects of SCIT include pain and swelling at injection sites. Anaphylaxis and, very rarely, death can occur. SCIT should only be administered under medical supervision. After dose buildup, maintenance injections are typically continued at monthly intervals for 4-5 years.

SLIT can cause local adverse effects such as mouth and ear pruritus, mouth edema, and throat irritation. Systemic adverse effects include nausea and mild abdominal pain. Anaphylaxis is rare and fatalities have not been reported. Maintenance treatment is self-administered at home.

Advances have been made in immunotherapy for prevention of allergic reactions to peanuts and other foods. Oral, sublingual, and epicutaneous routes of administration are being investigated. No immunotherapy is currently approved by the FDA for treatment of food allergy.

OMALIZUMAB — Omalizumab is FDA-approved for treatment of chronic idiopathic urticaria refractory to H1-antihistamines. In randomized placebo-controlled trials, subcutaneous injections of omalizumab every 4 weeks significantly reduced itch and wheal scores and significantly increased rates of complete response; the highest response rates occurred with a 300-mg dose. Omalizumab also significantly reduced the angioedema that was associated with urticaria in some patients. Adverse events were similar to those with placebo. No patients developed anaphylaxis, which has occurred with use of omalizumab in patients with asthma.

OTHER DRUGS — A short course (3-7 days) of an oral corticosteroid such as prednisone 1 mg/kg (maximum dose 50 mg) can be helpful in relieving severe exacerbations of itching and whealing in chronic urticaria. Topical corticosteroids are not effective. Cyclosporine is recommended in guidelines as a low-cost alternative to omalizumab in H1-antihistamine-refractory chronic urticaria. Although not FDA-approved for this indication, it has been effective in randomized controlled trials. Patients taking cyclosporine require monitoring of blood pressure and renal function. In one small randomized controlled trial, use of dapsone 100 mg/day to treat antihistamine-refractory chronic urticaria led to a significant improvement in symptoms; monitoring of complete blood counts and hepatic function is required, and dapsone should not be used in G6PD-deficient patients.

In some randomized controlled trials, the leukotriene receptor antagonist montelukast had a beneficial effect in H1-antihistamine-refractory chronic urticaria, but results have been inconsistent. Montelukast is not FDA-approved for treatment of urticaria, but it has been recommended in some guidelines as an alternative when other treatments have failed.

Other immunomodulators such as systemic tacrolimus, mycophenolate mofetil, and hydroxychloroquine have been recommended for treatment of urticaria based on anecdotal experience.

Anaphylaxis

Anaphylaxis, a multi-system allergic reaction that is rapid in onset and may cause death, often occurs in community settings where it is typically triggered by a food, insect sting, or medication. The incidence of anaphylaxis is increasing in the US population. The greatest increase has been reported in food-related anaphylaxis, which occurs most commonly in the pediatric population. Vaccine-triggered anaphylaxis remains rare. Patients at risk for anaphylaxis in community settings should receive printed information about how to avoid their relevant triggers. Those who have had an anaphylactic reaction triggered...
by stinging insects should be instructed in insect avoidance measures and referred to an allergy/immunology specialist for immunotherapy with standardized extracts of insect venom or whole-body extract from fire ants.50

**EPINEPHRINE** — All patients at risk for anaphylaxis recurrence in community settings and caregivers of children at risk should be equipped with one or more epinephrine auto-injectors such as EpiPen or Auvi-Q (or generic epinephrine for injection) and trained to recognize anaphylaxis and use the auto-injector correctly and safely. There are no absolute contraindications to epinephrine injection in anaphylaxis. Concerns about potential adverse effects in the elderly and in patients with cardiovascular disease need to be weighed against the possibility of death from anaphylaxis.51

Injection of epinephrine 0.3 mg from either Auvi-Q or EpiPen results in similar peak epinephrine levels and total epinephrine exposure.52 Auvi-Q, reintroduced in the US in 2017, has a compact rectangular shape and provides visual signals and step-by-step audio instructions for use. Compared with pen-type auto-injectors, it is more convenient to carry and easier to use, has additional safety features including an automatic fully retractable needle, and is less likely to cause unintentional injuries.53,54

The recommended dose of epinephrine is 0.01 mg/kg (0.5 mg maximum) intramuscularly. Until recently, epinephrine auto-injectors provided epinephrine only in fixed doses of 0.15 or 0.3 mg. The FDA has now approved Auvi-Q 0.1 mg for use in infants and small children weighing 7.5-15 kg. Auto-injectors containing 0.15 mg are labeled for children weighing 15-30 kg, and those containing 0.3 mg are labeled for adults and children weighing ≥30 kg. No auto-injector provides an optimal dose for children weighing between 15 and 30 kg; some clinicians prescribe an auto-injector containing 0.3 mg for children who weigh ≥25 kg.55

After injection of epinephrine, patients should be taken to the nearest emergency department for observation because anaphylaxis symptoms recur within hours in up to 20% of patients. Intravenous fluids and oxygen may be required in cases of severe anaphylaxis. H1-antihistamines and corticosteroids are not recommended for treatment of anaphylaxis in community settings; they do not prevent or relieve airway obstruction, hypotension or shock, or prevent death.

### Insect Stings and Bites

Small local allergic reactions to insect stings and bites (itchy red swellings) are self-limited. Large local reactions that occur at the sites of stings from honeybees, yellowjackets, wasps, and fire ants, or bites from mosquitoes, deer flies, and other insects, can involve a large portion of the face or an entire extremity and cause extreme discomfort. For prevention and treatment of large local reactions, an oral second-generation H1-antihistamine such as cetirizine should be used as soon as possible after the sting or bite. For mild or moderate large local reactions, a topical corticosteroid cream can be applied to the affected area for 5–7 days. Oral prednisone 1 mg/kg once daily (maximum daily dose 50 mg) for 5–7 days may be needed for severe large local reactions. Although the risk of anaphylaxis in patients with large local reactions to stinging insects is <5%, epinephrine auto-injectors are often prescribed for these patients. Venom immunotherapy is effective in preventing large local reactions and can be considered for those with occupational or other unavoidable exposure to stinging insects who frequently require treatment for reactions to stings.56

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**Table 5. Epinephrine Auto-Injectors**

<table>
<thead>
<tr>
<th>Epinephrine Injection, USP</th>
<th>Formulations†</th>
<th>Cost‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>generic (Mylan)†</td>
<td>0.15 mg/0.3 mL, 0.3 mg/0.3 mL</td>
<td>$300.00*</td>
</tr>
<tr>
<td>EpiPen Jr (Mylan)</td>
<td>0.15 mg/0.3 mL</td>
<td>608.60*</td>
</tr>
<tr>
<td>EpiPen</td>
<td>0.3 mg/0.3 mL</td>
<td>608.60*</td>
</tr>
<tr>
<td>generic (Impax)‡</td>
<td>0.15 mg/0.15 mL, 0.3 mg/0.3 mL</td>
<td>395.20*</td>
</tr>
<tr>
<td>Auvi-Q (Kaléo)§</td>
<td>0.1 mg/0.1 mL, 0.15 mg/0.15 mL, 0.3 mg/0.3 mL</td>
<td>4900.00*</td>
</tr>
<tr>
<td>Symjepi (Adamis)®</td>
<td>0.3 mg/0.3 mL</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

† N.A. = not available at time of publication.
‡ Cost is out-of-pocket cost.
1. The dose of epinephrine is 0.1 mg for patients who weigh 7.5-15 kg, 0.15 mg for those who weigh 15-30 kg, and 0.3 mg for those who weigh ≥30 kg.
2. Approximate WAC for one package containing two auto-injectors. WAC = wholesaler acquisition cost or manufacturer’s published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. May 5, 2018. Reprinted with permission by First Databank, Inc. All rights reserved. ©2018. www.fdbhealth.com/policies/drug-pricing-policy.
3. Interchangeable with EpiPen and EpiPen Jr.
4. The manufacturer provides free epinephrine auto-injectors to eligible uninsured or underinsured patients who are from families earning up to 400% of the federal poverty level (https://aspe.hhs.gov/poverty-guidelines).
5. All strengths cost the same.
6. Authorized generic of Adrenaclick, which has been discontinued. Similar to EpiPen and EpiPen Jr in size and functionality, but not considered interchangeable due to differences in device design and instructions for use.
7. Both strengths are available at discounted prices at some pharmacies (at CVS pharmacies, the cash price is $110.00 for a package containing two auto-injectors).
8. Auvi-Q is not interchangeable with other currently available epinephrine auto-injectors.
9. According to the manufacturer, the out-of-pocket cost is $0 for all commercially insured patients, whether or not their insurer covers the $4900 for the device. The cash price for patients without government or commercial insurance is $360 for those with a household income <$100,000/year and $0 for those with a household income ≥$100,000/year.
10. Approved by the FDA, but not yet marketed as of May 2018.


10. OTC fluticasone furoate nasal spray (Flonase Sensimist) for allergic rhinitis. Med Lett Drugs Ther 2017; 59:e70.


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**LEARNING OBJECTIVES:**

Activity participants will read and assimilate unbiased reviews of FDA-approved and off-label uses of drugs and other treatment modalities. Activity participants will be able to select and prescribe, or confirm the appropriateness of the prescribed usage of, the drugs and other therapeutic modalities discussed in The Medical Letter with specific attention to clinical trials, pathophysiology, dosage and administration, drug metabolism and interactions, and patient management. Activity participants will make independent and informed therapeutic choices in their practice.

Upon completion of this program, the participant will be able to:

1. Explain the current approach to the management of a patient with an allergic disorder.
2. Discuss the pharmacologic options and treatment regimens available for patients with an allergic disorder and compare them based on their efficacy, dosage and administration, potential adverse effects, and drug interactions.
3. Determine the most appropriate therapy given the clinical presentation of an individual patient.

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Questions start on next page
Drugs for Allergic Disorders

1. Which of the following is the preferred first-line treatment for mild-to-moderate allergic rhinitis?
   a. oral first-generation H₁-antihistamines
   b. oral second-generation H₁-antihistamines
   c. intranasal corticosteroids
   d. intranasal H₁-antihistamines

2. The most effective drugs for treatment of allergic rhinitis are:
   a. oral first-generation H₁-antihistamines
   b. oral second-generation H₁-antihistamines
   c. intranasal corticosteroids
   d. intranasal H₁-antihistamines

3. Intranasal corticosteroids can cause:
   a. nasal irritation
   b. septal perforation
   c. reduced growth velocity in children
   d. all of the above

4. Which of the following is the most effective for monotherapy of allergic conjunctivitis?
   a. an ophthalmic antibiotic
   b. an ophthalmic H₁-antihistamine
   c. an opthalmic mast cell stabilizer
   d. an ophthalmic nonsteroidal anti-inflammatory drug

5. Which of the following statements about calcineurin inhibitors is true?
   a. pimecrolimus is more effective than a medium-potency topical corticosteroid for atopic dermatitis
   b. they should not be applied to the face
   c. they do not cause cutaneous atrophy
   d. all of the above

6. Prolonged use of topical corticosteroids can lead to:
   a. development of striae
   b. skin atrophy
   c. adrenal suppression
   d. all of the above

7. A 27-year-old woman with a history of atopic dermatitis presents with severe disease that has not responded to a super-high potency topical corticosteroid or topical tacrolimus. She has heard that Dupixent (dupilumab) may be a game changer for patients like her. You could tell her that:
   a. it must be injected every 2 weeks
   b. it produced complete or near-complete clearing in about 40% of patients in clinical trials
   c. side effects reported with its use included conjunctivitis and oral herpes
   d. all of the above

8. For treatment of urticaria, which of the following oral second-generation H₁-antihistamines is the most potent in suppressing histamine-induced wheals?
   a. cetirizine
   b. fexofenadine
   c. loratadine
   d. desloratadine

9. Which of the following is FDA-approved for treatment of chronic idiopathic urticaria refractory to H₁-antihistamines?
   a. omalizumab
   b. cyclosporine
   c. montelukast
   d. all of the above

10. Which of the following statements about subcutaneous and sublingual immunotherapy is true?
    a. both can induce long-term remission in allergic respiratory disease
    b. controlled trials comparing them are not available
    c. subcutaneous immunotherapy has been used much longer than sublingual immunotherapy
    d. all of the above