Learning Objectives

- Identify current pharmacologic agents that are appropriate for each condition/diagnosis.
- Recommend optimal pharmacologic interventions based on patient-specific characteristics.
- Provide appropriate patient-specific counseling points and optimal overall medication management.

Key Terms: antihistamines, histamine, first-generation antihistamines (ethanolamine derivatives, ethylenediamine derivatives, phenothiazine derivatives, piperazine derivatives, propylamine derivatives, miscellaneous), second-generation antihistamines, allergy, anaphylaxis, antibody, anticholinergic, antigen, anxiolytic, central nervous system, congestion, conjunctivitis, dermatoses, drowsiness, gastric acid, hay fever, insomnia, motion sickness, nausea, rhinitis, rhinorrhea, sedating, somnolence, urticaria, vomiting

Overview of Antihistamines

Antihistamines are commonly utilized, predominantly over-the-counter (OTC) medications for treatment of allergic conditions. Histamine is found throughout the body, including within the vesicles of mast cells or basophils, and is abundant in the mast cells in areas particularly susceptible to tissue injury, such as the nose, mouth, feet, internal body surfaces, and blood vessels. While intracellular histamine is inert, it is released and becomes activated when a noxious antigen is detected by sensitized antibodies. Histamine that is not found within mast cells functions as a neurotransmitter in the brain and is involved with neuroendocrine control, cardiovascular functions, thermal and weight regulation, and sleep and arousal balance. The enterochromaffin-like (ECL) cells of the stomach release histamine, which is one of the main factors that stimulates the stomach mucosal parietal cells to produce gastric acid for digestion.

Four different histamine receptors have been identified. Each of these receptors is distributed in a different area of the body and elicits a different response to histamine agonism or antagonism. H1 receptors are found on smooth muscle cells, the endothelium, and the brain; H2 receptors are distributed in the gastric mucosa, cardiac muscle, mast cells, and the brain; H3 receptors are located in the brain; and H4 receptors are predominantly found on eosinophils, neutrophils, and T cells. When histamine stimulates the H1 receptor, the reaction produces the allergic response commonly observed with insect stings and contact with other allergens, including symptoms such as bronchoconstriction, pain, and itching. H2 receptors, when exposed to histamine, cause the contraction of gastrointestinal smooth muscles and the release of gastric acid. H3 receptors in the brain are responsible for the release of many neurotransmitters and may also have an effect on satiety. H4 receptors on blood cells produce inflammation and other allergic responses.
when histamine is present. Currently available antihistamine agents affect the H₁ and H₂ receptors; no antihistamines are approved for use that affect the H₃ and H₄ receptors, but there is a potential for these receptors to be drug targets in treatments for sleeping disorders, attention-deficit/hyperactivity disorder (ADHD), and obesity, to name a few conditions.

H₁ antihistamines are typically the first drugs used to treat the symptoms of an allergic reaction or allergic rhinitis, but when used intranasally they are considered secondary agents, to be used after glucocorticoids. These antihistamines are also the drugs of choice for managing urticaria (itching) associated with an allergic response; they are effective in this indication even if given prior to an anticipated exposure. If allergic rhinitis (hay fever) presents with nasal congestion, antihistamines are not as efficacious as nasal decongestants, such as pseudoephedrine, or combination antihistamine-decongestants (frequently named with a “D” added after the drug name, such as loratidine-D). H₁ antihistamines are not effective for bronchial asthma and antihistamines are used only as adjuvant treatment for patients experiencing systemic anaphylaxis (epinephrine is the mainstay of treatment).

Many antihistamine formulations are also available for topical administration in the eye and nose. When ophthalmic preparations are used, contact lenses should be removed prior to application, and can be reinserted 10–15 minutes after administration, unless otherwise specified. Do not reinsert the lenses if the eyes are red, and separate administration of other ophthalmic topical agents by 5 minutes. With nasal preparations, the nasal spray must be primed prior to first use until a fine mist appears. Repriming is necessary when the product is unused for a number of days specified by the certain manufacturer.

1.1 First-Generation Antihistamines

First-generation antihistamines are H₁ antagonists and are known for their strong sedating properties due to the easy penetration of the central nervous system (CNS). Since the sedating effect is so powerful with some agents, they are commonly used as sleep aids. However, children and some adults (though rare) may experience an excitation effect. Some medications in this class have antinausea and antiemetic effects and can be used to prevent motion sickness (though they are not as effective if used to treat an active episode). Some H₁ antagonists—predominantly diphenhydramine—can suppress extrapyramidal symptoms caused by antipsychotic use. The ethanolamine and ethylenediamine agent subgroups have antimuscarinic actions, which may help patients with non-allergic rhinorrhea, but also cause undesirable side effects of urinary retention and blurred vision.

First-generation antihistamines are largely anticholinergic and can cause dry mouth, dry eyes, urinary retention, constipation, and cognitive disturbances. Patients with a diagnosis of closed-angle glaucoma, urinary retention, peptic ulcer disease, or uncontrolled asthma should not use first-generation antihistamines. Anticholinergic side effects can be further exacerbated by other anticholinergic medications, such as tricyclic antidepressants (TCAs). Because monoamine oxidase inhibitors (MAOIs) can also exacerbate anticholinergic side effects, first-generation antihistamines should not be used during treatment or within 2 weeks of MAOI discontinuation.

Toxicities of the first-generation antihistamines include convulsions, postural hypotension (increasing the risk of falls in patients, especially the elderly), and cardiac arrhythmias. Central nervous system depression can be additive if first-generation antihistamines are combined with other medications with sedative properties or alcohol. Patients should be cautioned about driving and operating machinery while using these medications. There is also a potential for sedative properties to still be present the following morning if these agents are used for sleep. First-generation antihistamines are on the Beers list and are considered potentially harmful in elderly patients; other medication options should be explored if possible.

First-Generation Antihistamines

- Brompheniramine
- Carbinoxamine
- Chlorpheniramine
- Clemastine
- Cyproheptadine
Diphenhydramine
Doxylamine
Promethazine
Triprolidine
Dimenhydrinate (See also the Antiemetics section in the Gastrointestinal Agents chapter)
Hydroxyzine (See also the Anxiolytics, Sedatives, and Hypnotics section in the Central Nervous System chapter)
Meclizine (See also the Antiemetics section in the Gastrointestinal Agents chapter)

Case Studies and Conclusions

Joanne was doing yard work over the weekend and is now covered in an itchy rash on both arms. She states she has not been able to sleep at night because she cannot stop scratching.

1. Which of the following would be the best option to manage Joanne’s allergic reaction?
   a. Fexofenadine
   b. Epinephrine
   c. Diphenhydramine
   d. Ranitidine

   Answer C is correct. Fexofenadine is a nonsedating second-generation antihistamine; this patient would benefit from a first-generation antihistamine to increase sedation at night. Epinephrine is used in cases of anaphylaxis, but this patient presents with a local rash. Ranitidine is an H₂ antihistamine that is used for gastrointestinal disorders, not allergies.

   It has been a few days, and Joanne’s rash has improved and has almost disappeared. She states that she is going on a cruise next week and is afraid she will get motion sickness. She wants a recommendation for an OTC product.

2. What is an OTC formulation of an antihistamine that can be used to prevent nausea?
   a. Doxylamine
   b. Promethazine
   c. Diphenhydramine
   d. Cetirizine

   Answer C is correct. Doxylamine and cetirizine are not indicated for the treatment of nausea. Promethazine is a prescription-only medication. Diphenhydramine is OTC and has indications for nausea and vomiting as well as helping with the urticaria and insomnia.

   Joanne returned from her cruise and came home just in time for allergy season. She states that she would like to take a first-generation antihistamine to manage her seasonal allergies.

3. Which of the following statements is FALSE?
   a. Counsel the patient about the morning “hangover” that may occur if she takes a first-generation antihistamine at bedtime.
   b. A common side effect with frequent use of a first-generation antihistamine is diarrhea.
   c. Many of the first-generation antihistamines should be used with caution in geriatric patients.
   d. First-generation antihistamines should not be used within 2 weeks of use of an MAOI.

   Answer B is correct. First-generation antihistamines can cause daytime sleepiness, so patients should be warned about driving or operating machinery. The most common side effects with these drugs are anticholinergic, such as constipation, urinary retention, dry eyes, and dry mouth. First-generation antihistamines are on the Beers list, so second-generation antihistamines should be used instead if possible. The combination of MAOIs and first-generation antihistamines has the potential to cause hypertensive crisis due to the antihistamine’s concurrent effects on neurotransmitters.
George is a 68-year-old patient being seen for his annual physical examination appointment. He mentions that he experiences seasonal allergies and in the past had success with diphenhydramine. His medical history includes depression, hypertension, dyslipidemia, and type 2 diabetes mellitus.

1. **What is a concern with using a first-generation antihistamine in George?**
   a. Many first-generation antihistamines are Beers list medications and may not be safe for all patients.
   b. First-generation antihistamines may cause excitation in geriatric patients instead of sedation.
   c. Use of antihistamines may exacerbate George’s diabetes.
   d. All of the above are true.

   Answer A is correct. First-generation antihistamines are on the Beers list, and alternative options for therapy should be explored if possible. In George’s case, it would be appropriate to try a second-generation antihistamine first. Excitation—as opposed to sedation—is a possible side effect when first-generation antihistamines are used in pediatric patients. These antihistamines have anticholinergic properties and could exacerbate closed-angle glaucoma, urinary retention, and prostatic hypertrophy.

Despite your suggestion that a first-generation antihistamine may not be the best option, George says that he is used to these products and would rather take something with which he has had prior experience. George is currently being treated with fluoxetine (a selective serotonin reuptake inhibitor [SSRI]) for his depression.

2. **Which of the following statements is true regarding possible drug interactions between the SSRI and first-generation antihistamines?**
   a. George must wait 2 weeks between his last dose of fluoxetine and brompheniramine.
   b. Fluoxetine will exacerbate the anticholinergic side effects of the first-generation antihistamines.
   c. Fluoxetine may worsen the drowsiness/sedative effects of the first-generation antihistamines.
   d. Use of antidepressants is contraindicated with the first-generation antihistamines.

   Answer C is correct. Use of MAOIs should be avoided when a patient is taking brompheniramine, with a 2-week washout period being recommended. TCAs have the potential to exacerbate anticholinergic side effects of the first-generation antihistamines; some SSRIs have the potential to cause anticholinergic effects, although this is not a common side effect of fluoxetine. Medications that have the potential to lead to CNS depression (including antidepressants) may also worsen the drowsiness and sedative effects of the first-generation antihistamines. Although use of antidepressants is not contraindicated with the first-generation antihistamines, MAOIs, TCAs, and other antidepressants with anticholinergic side effects should be used with caution.

   George states that his biggest complaint about his allergies occurs when he is working in his garden. On top of the typical “hay fever”-like symptoms, he says that he almost always manages to come in contact with poison ivy or poison oak and breaks out in a rash.

3. **Which product would be best to manage this patient’s allergic rhinitis and the contact allergic reaction?**
   a. Meclizine
   b. Chlorpheniramine
   c. Doxylamine
   d. Diphenhydramine

   Answer D is correct. Meclizine is approved as an antiemetic drug. Chlorpheniramine will treat the allergic rhinitis but does not have contact allergic reactions as a labeled indication. Doxylamine is used for insomnia or allergic rhinitis. Diphenhydramine would manage both allergic rhinitis and the contact allergic reaction.

### 1.2 Second-Generation Antihistamines

Both first and second generations of antihistamines have been found to have equal efficacy in the treatment of allergic responses. Unlike the first-generation antihistamines, however, the second-generation products do not cross the blood–brain barrier to the same extent and, therefore, do not have the same sedative properties; in addition, they have fewer antimuscarinic and anticholinergic effects. Nevertheless, the second-generation antihistamines may still cause drowsiness in some patients, especially if used concurrently with medications that cause CNS depression or...
alcohol. The second-generation products are most commonly used for chronic allergy symptoms due to their lack of sedation and amenability to daily use. This class is the preferred treatment in geriatric patients and children due to the favorable side-effect profile and minimal CNS penetration.

### Second-Generation Antihistamines

- Acrivastine
- Cetirizine
- Desloratadine
- Fexofenadine
- Levocetirizine
- Loratadine
- Azelastine (See also the Antiallergic Agents section in the Eye, Ears, Nose, and Throat Preparations chapter)

### Case Studies and Conclusions

Ray is a construction worker and has complaints of seasonal allergies. He says that whenever the pollen level is high, he gets watery and itchy eyes, a runny nose, and persistent sneezing.

1. Which of the following would be the best first-choice option for managing Ray’s allergies?
   a. Diphenhydramine by mouth
   b. Azelastine intranasally
   c. Loratadine by mouth
   d. Cimetidine by mouth

   Answer C is correct. Ray is a construction worker, so he presumably operates machinery that requires full attention. Thus diphenhydramine would be too sedating for him. Azelastine intranasally is not a first-choice option; instead, intranasal antihistamines are used after the patient has tried an intranasal glucocorticoid. Cimetidine is an H₂ antihistamine and used to treat gastrointestinal upset.

   Ray later adds that he typically is very congested, during especially bad pollen days.

2. What would be the best advice be for the patient?
   a. An antihistamine is sufficient alone to manage nasal congestion.
   b. Use a combination antihistamine and decongestant.
   c. Use a decongestant alone.
   d. Use a combination oral and nasal antihistamine when symptoms are worse.

   Answer B is correct. Antihistamines alone are not sufficient to manage nasal congestion with allergy symptoms; combination products with a decongestant, such as pseudoephedrine, are more effective. A decongestant alone would manage Ray’s nasal symptoms, but the antihistamine would be required to help treat his other symptoms, such as watery eyes. While nasal antihistamines are effective for symptom management in patients with nasal congestion, they are not a first-line option and need to be used regularly to achieve their greatest efficacy.

   Ray asks whether his medications might also be safe for his 72-year old father, who is having similar reactions.

3. Which of the following statements best summarizes the recommended use of antihistamines in older adults?
   a. First-generation antihistamines are a good option for geriatric patients with seasonal allergies because they can cause CNS excitation, which can help give them more energy.
   b. Second-generation antihistamines are the best option for geriatric patients with seasonal allergies because of their minimal CNS penetration.
   c. Geriatric patients should be offered only intranasal or ophthalmic preparations; oral medications are not recommended in older adults.
   d. No antihistamines are safe in geriatric patients under any circumstances.

   Answer B is correct. Second-generation antihistamines have less CNS penetration and a safer side-effect profile for geriatric patients.
Pharmacotherapeutics for Advanced Nursing Practice

Sam presents to his doctor’s appointment with complaints of a runny nose, watery eyes, and nasal congestion. He says that these symptoms occur every year around this time, but he usually just muddles his way through the allergy season without any medications. This year, however, his symptoms are worse than ever, and he would like to explore possible medication options.

1. Which of the following is NOT a benefit of Sam using a second-generation antihistamine as opposed to a first-generation antihistamine?
   a. The risk of sedation is less with the first-generation antihistamines, so using the second-generation products could help him sleep better at night.
   b. Many second-generation products come in combination products with a decongestant.
   c. Most second-generation medications are dosed once a day.
   d. All of the above are true.

Answer A is correct. Second-generation antihistamines are less sedating than the first-generation products. Second-generation antihistamines are available in many different combinations, including with pseudoephedrine, ibuprofen, or acetaminophen. Another appealing aspect of second-generation products is that most require only once-daily dosing, whereas most first-generation antihistamines are dosed multiple times a day.

Sam’s medical history includes hypertension, and he has an extensive family history of cardiovascular disease. His blood pressure at the beginning of this visit was elevated, and he says he often forgets to take his blood pressure medication.

2. Which of the following products would be the least appropriate to recommend to Sam?
   a. Acrivastine
   b. Cetirizine
   c. Fexofenadine
   d. Loratadine

Answer A is correct. Acrivastine should be avoided in patients with severe hypertension or coronary artery disease. Cetirizine, fexofenadine, and loratadine do not have cardiovascular concerns and would be better recommendations for Sam to use.

Sam states that he frequently consumes alcoholic beverages and would like to avoid an allergy agent that is metabolized via the liver.

3. Which of the following medications requires dose adjustment or dose consideration with hepatic impairment?
   a. Cetirizine
   b. Desloratadine
   c. Levocetirizine
   d. Loratadine

Answer B is correct. Desloratadine requires dose adjustment for both hepatic and renal impairment (5 mg every other day). Cetirizine, levocetirizine, and loratadine require dose adjustment for renal impairment.

1.3 Other Antihistamines

H₂ antihistamines (cimetidine, famotidine, nizatidine, and ranitidine) are used to inhibit the secretion of gastric acid in patients with gastrointestinal (GI) disorders. Intranasal products should be used after a patient has tried an intranasal glucocorticoid. Intranasal antihistamines are most effective when used regularly and do not cause rebound effects as nasal decongestants do.

Bepotastine (See also the Antiallergic Agents section in the Eye, Ears, Nose, and Throat Preparations chapter)
Cimetidine (See also the Antiallergic Agents and Suppressants section in the Gastrointestinal Agents chapter)
Emedastine (See also the Antiallergic Agents section in the Eye, Ears, Nose, and Throat Preparations chapter)
Common Class Considerations

Anaphylaxis: A life-threatening allergic reaction. Signs and symptoms include an itchy rash, swelling of the tongue, bronchoconstriction, hypotension, and facial edema. Anaphylaxis presents suddenly, typically over a few minutes. Antihistamines alone are not a sufficient treatment, and patients should immediately receive epinephrine. Antihistamines and steroids are added as adjuvant treatments.

Excitation: In children, normal doses of first-generation antihistamines often result in an excitatory effect instead of a sedative effect. This phenomenon has also been infrequently reported in some adult cases at therapeutic doses, but is more common in overdose and toxic situations.

Sedation/somnolence: Increased sedation and somnolence are frequently reported with use of the first-generation antihistamines. When taken at bedtime, these drugs may also lead to a daytime “hangover” of drowsiness and somnolence. Second-generation antihistamines are referred to as “nonsedating” and have similar incidence of sedation as placebo in studies.

Toxicity: Toxicity of antihistamines has been reported in incidents of overdose or interactions with liver metabolism enzymes (CYP)-inhibiting medications (predominately macrolides andazole antifungal drugs), with patients experiencing higher than intended circulating antihistamine levels. Signs and symptoms of toxicity include hallucinations, incoordination, convulsions, cardiac arrhythmias, and fever.

Tips from the Field

1. Make sure your patients understand the difference between antihistamines and decongestants. Decongestants constrict nasal blood vessels, resulting in an improvement in nasal stuffiness but they do not affect histamine and won’t impact any of the other symptoms associated with hay fever, such as sneezing, runny nose, and itching. Caution patients that if they use nasal spray decongestants for more than a few days, these agents can produce a rebound swelling of the nasal tissues, resulting in even greater congestion.

2. Suggest use of OTC products, such as Claritin D, which contain both an antihistamine and a decongestant if symptoms warrant use. Make sure they understand the side effects associated with this combination.

3. Help patients determine the right antihistamine for them, for example, daytime use avoid sedating agents like diphenhydramine (Benadryl). Newer generation antihistamines, such as loratadine (Claritin), fexofenadine (Allegra), and cetirizine (Zyrtec), are generally a better choice since they are less sedating.

4. Note that even the newer nonsedating generation antihistamines can cause drowsiness and other symptoms in some people, especially older adults, particularly if they take them at higher doses. Make sure they understand importance of starting the drug at the lowest dose and evaluate its effectiveness.

5. Most of these agents can be purchased OTC and there is no difference between the generic brand versus the name brand.
6. Explain to your elderly patients that antihistamines can cause other central nervous system effects, including coordination problems, fatigue, and temporary cognitive impairment. Research has shown an increased risk of long-term cognitive decline in older people who take the drugs regularly.

7. First-generation antihistamines are also more likely than the newer products to cause serious side effects, such as a rapid heart rate or urinary retention (which can be especially problematic in men who have BPH).

8. Several first-generation antihistamines can reduce motion sickness such as diphenhydramine, doxylamine, dimenhydrinate (as found in Dramamine), and meclizine (the active ingredient in Bonine). These are all OTC and are the most commonly used motion sickness medications. Make sure they understand that it can take at least 30 minutes for them to take effect.

9. People suffering closed or narrow-angle glaucoma, COPD (chronic obstructive pulmonary disease), kidney disease, prostate problems, hypertension, heart disease, and thyroid problems should not take any OTC antihistamines without first consulting with their provider.

10. The FDA Nonprescription Drug Advisory Committee and the Pediatric Advisory Committee has recommended that nonprescription cough and cold products should not be used in children less than 2 years of age and an official ruling regarding the use of these products in children older than 2 has not yet been announced. Refer to pediatric drug references for additional information (FDA, 2008).

References


Renal impairment: Dose adjustment is recommended.

Hepatic impairment: Dose adjustment is recommended.

Black box warning exists for this drug.

QTc prolongation effects have been reported.

Symbols

- Beers list criteria (avoid in elderly).
- FDA-approved pediatric doses are available.
- FDA-approved geriatric doses are available.
- See primary body system.

Antihistamines

Universal prescribing alerts:

- Known serious hypersensitivity to the specific drug or any other component of the product/formulation selected warrants a contraindication for use.
- Adverse reactions associated with the use of some antihistamine agents include dizziness, drowsiness, vertigo, or fatigue; these drugs may also impair the ability to perform tasks requiring mental alertness. Caution should always be recommended when using any new drug for the first time, when there is a dose change, and with continued use of known offending agents.
- Doses expressed are for the usual adult dosage ranges only. “Geriatric doses” are assumed to be the same as the adult doses unless otherwise noted with a symbol. Where FDA-approved geriatric or pediatric dosing is available, a symbol will guide the reader to additional prescribing references. Refer to real-time prescribing references for these age-specific doses. Please also refer to the narrative chapter overview to learn more about the FDA Nonprescription Drug Advisory Committee and the Pediatric Advisory Committee recommendations for cough and cold products in pediatric patients.
- Use of antihistamines in pregnancy is based on clinical risk versus benefit; safety concerns are not represented in this grid. Refer to the package insert (PI) for more information. Clinicians should continue to provide education about the reproductive risks of any medication use and offer risk-reduction strategies (which may include contraceptive use) to women of childbearing age and understand that these reproductive risks may also extend to males.
- Brand names are provided for those agents still available on the market. Due to the ever-changing product availability, refer to Food and Drug Administration (FDA) resources to confirm the actual brands available. This drug summary is for educational purposes only. Prescribing decisions should be based on real-time comprehensive drug databases that are updated on a regular basis.

First-Generation Antihistamines

Universal prescribing alerts:

- Central nervous depression can be additive if first-generation antihistamines are combined with other medications with sedative properties or alcohol; patients should be cautioned about driving and operating machinery while using these medications.
- First-generation antihistamines are largely anticholinergic agents and can cause dry mouth, dry eyes, urinary retention, constipation, and cognitive disturbances; their use should be avoided in patients with underlying closed-angle glaucoma, urinary retention, peptic ulcer disease, and uncontrolled asthma. Anticholinergic side effects can be further exacerbated by other anticholinergic medications, such as tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs).
- First-generation antihistamines should not be used within 2 weeks of MAOIs.
- There is a potential for sedative properties to still be present the following morning if these agents are used for sleep.
- First-generation antihistamines are on the Beers list and are considered potentially harmful in elderly patients; other medication options should be explored if possible.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>FDA-Approved Indications</th>
<th>Dosage Range</th>
<th>Precautions and Clinical Pearls</th>
</tr>
</thead>
</table>
| Generic Name    | Brompheniramine maleate          | Allergic rhinitis, Common cold                                                | • Take with food, water, or milk to minimize gastric irritation  
• Dexbrompheniramine maleate is a chemically related ingredient  
• Use is generally *as needed*  
• Some brompheniramine containing products are OTC and others require a prescription  
• Different salt forms are available (maleate and tannate) requiring different dose schedules. Available in multiple combination products. Please see individual product for indications, dosing, and name brand. |
| Brand Name      |                                  |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | J-Tan PD                         |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Respa-BR                         |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Bromax LoHist                    |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
| Generic Name    | Carbinoxamine maleate            | Allergies and related symptoms such as rhinitis, pruritus, rhinorrhea and urticaria | • Take on an empty stomach with water  
• Available by prescription only  
• Extended release and immediate release product dosing schedules are different, review directions prior to use                                                                                                                                                                                                                                                                 |
| Brand Name      |                                  |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Arbinoxo                         |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Karbinal ER                      |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
| Generic Name    | Chlorpheniramine maleate         | Allergic rhinitis, pruritus, rhinorrhea, and urticaria                        | • Dexchlorpheniramine maleate is a chemically related ingredient  
• OTC and prescription (higher doses) are available  
• Extended release and immediate release product dosing schedules are different, review directions prior to use Available in multiple combination products. Please see individual product for indications, dosing, and name brand. |
<p>| Brand Name      |                                  |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Aller-Chlor                      |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Chlor-Trimeton Allergy           |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Chlor-Trimeton                   |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Chlorphen                        |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Ed-ChlorPed                      |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Ed-Chlortan                      |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |
|                 | Pharbechlor                      |                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                     |</p>
<table>
<thead>
<tr>
<th><strong>Generic Name</strong></th>
<th><strong>Brand Name</strong></th>
<th><strong>Allergic rhinitis, pruritus, urticaria, symptoms of the common cold and angioedema</strong></th>
<th><strong>Dose varies depending on product selected</strong></th>
<th><strong>• Take with food or milk if patient experiences stomach upset</strong>&lt;br&gt;<strong>• Prescription products available for use at higher doses</strong>&lt;br&gt;<strong>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clemastine fumarate</td>
<td>Dayhist Allergy 12 Hour Relief</td>
<td><strong>Illustrative OTC oral dose:</strong> 1.34 mg twice daily (MDD 8.04 mg including prescription dosing)</td>
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<tr>
<td>Cyproheptadine hydrochloride</td>
<td>Benadryl and various others</td>
<td><strong>Illustrative indications for use:</strong>&lt;br&gt;Allergic rhinitis, pruritus, urticaria, and angioedema</td>
<td><strong>Usual oral dose:</strong>&lt;br&gt;4 to 20 mg daily in divided doses (MDD 0.5 mg/kg per day or 32 mg whichever is less)</td>
<td><strong>• Hepatic impairment dose adjustment recommended, however, no specific dose suggestion provided by manufacturer</strong>&lt;br&gt;<strong>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</strong></td>
</tr>
<tr>
<td>Diphenhydramine hydrochloride</td>
<td></td>
<td><strong>Illustrative indications for use:</strong>&lt;br&gt;Allergic rhinitis, contact dermatitis, antitussive, drug-induced EPS, Parkinsonian syndromes, insomnia, motion sickness, adjunct treatment of anaphylaxis</td>
<td><strong>Dose varies depending on combination product selected</strong>&lt;br&gt;<strong>Illustrative oral dose:</strong>&lt;br&gt;25 to 50 mg every 4 to 8 hours (max 300 mg per 24 hours)&lt;br&gt;<strong>Usual parenteral dose:</strong>&lt;br&gt;IM/IV: 10 to 50 mg per dose (max 100 mg per dose; max 400 mg per day)</td>
<td><strong>• Topical application can cause an allergic-type contact dermatitis</strong>&lt;br&gt;<strong>• Drug interactions may require dose adjustments</strong>&lt;br&gt;<strong>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</strong></td>
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<tr>
<td>Doxylamine succinate</td>
<td>Doxytex Nitetime Sleep-Aid Sleep Aid Unisom</td>
<td><strong>Allergic rhinitis, insomnia</strong></td>
<td><strong>Dose varies depending on product selected</strong>&lt;br&gt;<strong>Illustrative oral dose:</strong>&lt;br&gt;25 mg daily or at bedtime</td>
<td><strong>• Optimal dose schedule for insomnia is take dose 30 minutes prior to planned 8-hour sleep (bedtime)</strong>&lt;br&gt;<strong>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</strong></td>
</tr>
<tr>
<td><strong>Generic Name</strong></td>
<td><strong>Brand Name</strong></td>
<td><strong>Allergic conditions, motion sickness, antiemetic, sedative</strong></td>
<td><strong>Dose varies depending on product selected</strong></td>
<td><strong>Mild to moderate akathisia and extrapyramidal symptoms possible after injection or long-term use</strong></td>
</tr>
<tr>
<td>------------------</td>
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<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Promethazine</td>
<td>Phenadøz, Phenergan, Promethegan</td>
<td></td>
<td>Illustrative oral dose for nausea/vomiting: 12.5 mg before meals and HS</td>
<td>Use is associated with QT prolongation</td>
</tr>
<tr>
<td>Hydrochloride</td>
<td></td>
<td></td>
<td>Illustrative rectal dose for nausea/vomiting: 12.5 to 25 mg every 4 to 6 hours as needed</td>
<td>Drug interactions may require dose adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Illustrative IM dose for nausea/vomiting: 12.5 to 25 mg every 4 to 6 hours as needed</td>
<td>When treating nausea/vomiting; administer before meals or snack</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Deep IM injection preferred route of parenteral administration</td>
</tr>
</tbody>
</table>

- **Mild to moderate akathisia and extrapyramidal symptoms possible after injection or long-term use**
- **Use is associated with QT prolongation**
- **Drug interactions may require dose adjustment**
- **When treating nausea/vomiting; administer before meals or snack**
- **Deep IM injection preferred route of parenteral administration**

**Associated with:**
- Injection can cause severe tissue injury
- Subcutaneous and intra-arterial administration
- Use in patients in a coma
- Use in patients with asthma

Available in multiple combination products. Please see individual product for indications, dosing, and name brand.

**Generic Name**
Triprolidine hydrochloride

**Brand Name**
Histex PD, Histex

<table>
<thead>
<tr>
<th><strong>Allergies, rhinitis, urticaria</strong></th>
<th><strong>Dose varies depending on product selected</strong></th>
<th><strong>May be administered without regard to meals, however may take with food or milk to minimize stomach upset</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Illustrative oral dose: 2.5 mg every 4 to 6 hours (max 10 mg per 24 hours)</td>
<td>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</td>
<td></td>
</tr>
</tbody>
</table>

- **May be administered without regard to meals, however may take with food or milk to minimize stomach upset**
- Available in multiple combination products. Please see individual product for indications, dosing, and name brand.

**Available in multiple combination products. Please see individual product for indications, dosing, and name brand.**

- **Refer to the Gastrointestinal Agents chapter.**
  | **Dimenhydrinate** | **Refer to the Gastrointestinal Agents chapter.** |

- **Refer to the Central Nervous System chapter.**
  | **Hydroxyzine** | **Refer to the Central Nervous System chapter.** |

- **Refer to the Gastrointestinal Agents chapter.**
  | **Meclizine** | **Refer to the Gastrointestinal Agents chapter.** |
### Second-Generation Antihistamines

- **Universal prescribing alerts:**
  Many of these second-generation agents cause CNS depression (albeit not to the same extent as the first-generation antihistamines). Patients should use caution when performing tasks that require mental alertness.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>FDA-Approved Indications</th>
<th>Dosage Range</th>
<th>Precautions and Clinical Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td><strong>Br</strong>iard Name</td>
<td><strong>Dosage Range</strong></td>
<td><strong>Precautions and Clinical Pearls</strong></td>
</tr>
<tr>
<td>Acrivastine</td>
<td>Semprex-D</td>
<td><strong>Usual oral dose:</strong></td>
<td>• Avoid use in patients with CrCl less than 48 mL/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 mg every 4 to 6 hours (32 mg maximum per day)</td>
<td>• Use in caution in patients with diabetes or thyroid dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Available in combination with pseudoephedrine only</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 8 mg acrivastine tablets also contain 60 mg pseudoephedrine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Recommended for use as needed up to 14 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Contraindications:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Coronary artery disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Uncontrolled hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Drug interactions may preclude use (i.e., MAOIs)</td>
</tr>
<tr>
<td>Cetirizine hydrochloride</td>
<td>All Day Allergy Zyrtec</td>
<td>Dose varies depending on product selected</td>
<td>• Cetirizine is not removed with hemodialysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Illustrative oral dose:</strong></td>
<td>• ISMP safety alert (may sound like or look like other medications, thus mistakes may be more common with this drug)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 to 10 mg daily</td>
<td>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</td>
</tr>
<tr>
<td>Desloratadine</td>
<td>Clarinex</td>
<td>Dose varies depending on product selected</td>
<td>• Desloratadine is not removed by hemodialysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Illustrative oral dose:</strong></td>
<td>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 mg daily</td>
<td></td>
</tr>
<tr>
<td>Generic Name</td>
<td>Allergic rhinitis</td>
<td>Dose varies depending on product selected</td>
<td>Available in multiple combination products. Please see individual product for indications, dosing, and name brand.</td>
</tr>
<tr>
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<td>--------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Fexofenadine hydrochloride</td>
<td>Allergic rhinitis, Chronic idiopathic urticaria</td>
<td>Illustrative oral dose: 60 mg twice daily or 180 mg once daily</td>
<td></td>
</tr>
<tr>
<td>Brand Name Allegra</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Generic Name</td>
<td>Allergic rhinitis</td>
<td>Usual oral dose: 5 mg once daily</td>
<td>• Diarrhea and constipation common adverse effects</td>
</tr>
<tr>
<td>Levocetirizine dihydrochloride</td>
<td>Chronic idiopathic urticaria</td>
<td></td>
<td>Contraindications:  • End-stage renal disease  • Use of levocetirizine in patients undergoing dialysis</td>
</tr>
<tr>
<td>Brand Name Xyzal</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Generic Name</td>
<td>Allergic rhinitis, urticaria, pruritus</td>
<td>Dose varies depending on product selected</td>
<td>• Headache is the most common side effect  • Orally dissolvable tablets are available (tablet disintegrates with or without water)  • Loratadine is not removed by hemodialysis  • Brand name Claritin oral products do not contain the same ingredient as Claritin eye products (ketotifen fumarate)—use care when prescribingAvailable in multiple combination products. Please see individual product for indications, dosing, and name brand.</td>
</tr>
<tr>
<td>Loratadine</td>
<td></td>
<td>Illustrative oral dose: 10 mg once daily or 5 mg twice daily</td>
<td></td>
</tr>
<tr>
<td>Brand Name Alavert, Allergy, Claritin, Loradamed</td>
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<td></td>
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</tr>
<tr>
<td>Generic Name</td>
<td>Refer to the Eye, Ears, Nose, and Throat Preparations chapter.</td>
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<td></td>
</tr>
<tr>
<td>Azelastine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brand Name Various based on product selected and area of application</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other Antihistamines

Universal prescribing alerts:
- Intranasal antihistamines are most effective when used regularly and do not cause rebound effects as nasal decongestants do.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>FDA-Approved Indications</th>
<th>Dosage Range</th>
<th>Precautions and Clinical Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bepotastine</td>
<td>Refer to the Eye, Ears, Nose, and Throat Preparations chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Refer to the Gastrointestinal Agents chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emedastine</td>
<td>Refer to the Eye, Ears, Nose, and Throat Preparations chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Famotidine</td>
<td>Refer to the Gastrointestinal Agents chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketotifen</td>
<td>Refer to the Eye, Ears, Nose, and Throat Preparations chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nizatidine</td>
<td>Refer to the Gastrointestinal Agents chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olopatadine</td>
<td>Refer to the Eye, Ears, Nose, and Throat Preparations chapter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Refer to the Gastrointestinal Agents chapter.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>