OPTUMRx

Therapeutic Class Overview
Antihistamines, Second-generation

INTRODUCTION

- Oral antihistamines have been a mainstay in the treatment of allergic rhinitis and chronic idiopathic urticaria (CIU) since their development in the first half of the 20th century *(Janssen 1993)*.
- Although first-generation antihistamines are effective at ameliorating symptoms associated with allergic rhinitis, acute urticaria, and CIU, use in practice is limited by their lack of selectivity for the histamine 1 (H_1)-receptor and their ability to cross the blood-brain barrier, both resulting in adverse effects. Second-generation antihistamines were developed to maintain the efficacy of the first-generation agents, while reducing associated adverse effects. Due to a more complex chemical structure, the movement of second-generation antihistamines across the blood-brain barrier is reduced. In addition to a safer adverse event profile, second-generation agents have a longer duration of action, which allows for once- or twice-daily dosing for most products *(Lehman et al 2006)*.
- Despite the efficacy of second-generation antihistamines for the treatment of allergic rhinitis, they are not effective in the treatment of nasal congestion *(Lehman et al 2006, Seidman et al 2015)*. Because of this, they are often combined with a decongestant. Second-generation antihistamines combined with pseudoephedrine have been shown to improve symptoms and quality of life in patients with allergic rhinitis and nasal congestion compared to antihistamines alone *(Seidman et al 2015)*.
- This review focuses on the use of the second-generation antihistamines for the treatment of CIU, acute urticaria, perennial allergic rhinitis (PAR), and seasonal allergic rhinitis (SAR).
- Several products formerly available by prescription (Rx) are now available over-the-counter (OTC). This review includes Rx products and those that are sold both by Rx and OTC. Products sold solely OTC are identified as such but are not the focus of this review. The clinical efficacy section retains some information on OTC products that were formerly available by Rx for informational purposes.
- Medispan Class: Antihistamines – Non-Sedating and Cough/Cold/Allergy Combinations

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Cetirizine*	
cetirizine oral solution/syrup (Rx/OTC)	✓
Quzyttir (cetirizine) injection (Rx only)	-
OTC-only products include tablets, chewable tablets, liquid-filled capsules, and orally disintegrating tablets (ODT)	
Desloratadine	
Clarinex (desloratadine) tablet (Rx only)	✓
Clarinex (desloratadine) ODT (Rx only) ‡	✓
Fexofenadine*	
OTC-only products include tablets, oral suspension, and ODT	
Levocetirizine*	
levocetirizine tablet (Rx/OTC)	✓
levocetirizine oral solution (Rx/OTC)	✓
Loratadine*	
OTC-only products include tablets, capsules, chewable tablets, solution/syrup, and ODT	
Antihistamine – decongestant combinations*	
Clarinex-D 12 Hour (desloratadine/pseudoephedrine extended release tablet) (Rx only)	-
Clarinex-D 24 Hour (desloratadine/pseudoephedrine extended release tablet) (Rx only)‡	-†

Drug	Generic Availability
Semprex-D (acrivastine/pseudoephedrine capsule) (Rx only)	-
OTC-only combinations include fexofenadine/pseudoephedrine, loratadine/pseudoephedrine, and cetirizine/ pseudoephedrine extended release tablets	

*Medication or combination is available OTC in at least 1 dosage form or strength. OTC products are available in various brand and private label names.
‡Clarinex oral solution/syrup, Clarinex ODT, and Clarinex-D 24 Hour brands are no longer marketed. A generic Clarinex oral solution/syrup was approved by the FDA in 2015 but is not currently marketed.

(*Clinical Pharmacology 2020, Drugs@FDA 2020, Facts and Comparisons 2020, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2020*)

INDICATIONS

Table 2a. FDA-Approved Indications – Single Entity and Combination Prescription Agents

Indication	Cetirizine	Desloratadine*	Levocetirizine	Acrivastine/ Pseudoephedrine	Desloratadine/ Pseudoephedrine
CIU	✓† (age 6 months to 5 years)	✓ (age 6 months and older)	✓ (age 6 months and older)		
Acute urticaria	✓‡§ (age 6 months and older)				
PAR	✓† (age 6 to 23 months)	✓ (age 6 months and older)	✓ (age 6 months to 2 years)		
SAR		✓ (age 2 years and older)			
Relief of symptoms of SAR, including nasal congestion				✓ (12 years and older)	✓ (12 years and older)

*The ODT formulation is not recommended for use in patients ≤ 6 years of age because the oral solution (which is not currently marketed) is better suited for these patients.
†Oral solution indications
‡Intravenous solution indications
§Limitations of use: Not recommended in pediatric patients less than 6 years of age with impaired renal or hepatic function

(*Clinical Pharmacology 2020, Facts and Comparisons 2020, Prescribing information: Cetirizine 2020, Clarinex 2020, Clarinex-D [12 hour] 2019, Quzyttir 2020, Semprex-D 2019, Xyzal 2019*)

Table 2b. OTC Indications – Single Entity OTC Agents

Indication	Cetirizine	Fexofenadine	Levocetirizine	Loratadine
Temporary relief of runny nose; sneezing; itchy, watery eyes; or itching of the nose and throat due to hay fever or other upper respiratory allergies	✓ (age 2 to 64 years)	✓ (age 2 to 64 years)	✓ (age 2 to 64 years)	✓ (age 2 years and older)

(*OTC label: Allegra Allergy 2020, Children's Allegra Allergy 2019, Claritin 2020, Children Claritin Allergy 2020, Xyzal 2017, Children's Xyzal Allergy 2019, Zyrtec 2020, Children's Zyrtec Allergy 2018*)

Table 2c. OTC Indications – Combination OTC Agents*

Indication	Cetirizine/ Pseudoephedrine	Fexofenadine/ Pseudoephedrine	Loratadine/ Pseudoephedrine
Temporary relief of runny nose; sneezing; itchy, watery eyes; or itching of the nose and throat due to hay fever or other upper respiratory allergies	✓ (age 12 to 64 years)	✓ (age 12 to 64 years)	✓ (age 12 years and older)
Temporary relief of nasal congestion due to the common cold, hay fever or other upper respiratory allergies		✓ (age 12 to 64 years)	✓ (age 12 years and older)
Reduction of swelling of nasal passages	✓ (age 12 to 64 years)	✓ (age 12 to 64 years)	✓ (age 12 years and older)
Temporary relief of sinus congestion and pressure	✓ (age 12 to 64 years)	✓ (age 12 to 64 years)	✓ (age 12 years and older)
Temporary restoration of freer breathing through the nose	✓ (age 12 to 64 years)	✓ (age 12 to 64 years)	✓ (age 12 years and older)

*Although these agents do not require a prescription, they are available behind the pharmacy counter and do have some restriction (based on federal and/or state law) on total quantity purchased per month

(*OTC label: Allegra-D 2020, Claritin-D 12 hour 2019, Claritin-D 24 hour 2019, Zyrtec-D 2017*)

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

- Clinical trials have demonstrated that second-generation antihistamines are more effective in treating and providing symptomatic relief of CIU, PAR, and SAR compared to placebo *(Kaplan et al 2005, Kapp et al 2006, Kim et al 2006, Monroe et al 2003, Nathan et al 2006, Nayak et al 2017, Nettis et al 2006, Potter et al 2003, Potter et al 2005, Okubo et al 2005, Ring et al 2001, Simons et al 2003)*.
- Within-class comparisons have not consistently demonstrated superior efficacy with any one agent over another *(Anuradha et al 2010, Boyle et al 2005, Ciprandi et al 2005, Day et al 1998, Day et al 2001, Day et al 2004, Garg et al 2007, Handa et al 2004, Lee et al 2009, Meltzer et al 1996, Nayak et al 2017, Potter et al 2009, Prenner et al 2000, Purohit et al 2004, Van Cauwenberge et al 2000)*.
- The efficacy of intravenous cetirizine was demonstrated in a randomized, controlled, single-dose study of adults with acute urticaria randomized to intravenous cetirizine 10 mg or diphenhydramine 50 mg. The primary efficacy endpoint, change from baseline in patient-rated pruritis score at 2 hours, demonstrated noninferiority of intravenous cetirizine (adjusted mean difference, 0.06; 95% confidence interval [CI], -0.28 to 0.4). Intravenous cetirizine was also associated with a lower rate of return to the emergency department (6% vs 14%) and time between treatment and discharge (1.7 vs 2.1 hours). The efficacy of intravenous cetirizine in pediatric patients 6 months and older is based on extrapolation of data in adults *(Berger et al 2019, Ernst 2019)*.
- In a systematic review by Benninger et al, second-generation antihistamines were associated with a 23.5% reduction from baseline in total nasal symptom scores for SAR, and a 51.4% reduction in symptoms of PAR. Although intranasal corticosteroids were more effective for SAR (40.7% reduction), they were not as effective as long-term oral antihistamines in patients with PAR (37.3% reduction) (*Benninger et al 2010*).
- In a comparative effectiveness review by the Agency for Healthcare Research and Quality (AHRQ), oral selective antihistamines were equivalent to montelukast for nasal and eye symptoms in patients with SAR. Based on evidence of safety, in order to avoid insomnia, an oral selective antihistamine was preferred over the combination of an oral selective antihistamine with a decongestant or monotherapy with a decongestant *(Glacy et al 2013)*.

- In a systematic review of 73 randomized controlled trials in CIU, at standard treatment doses, the second-generation antihistamines were effective when compared with placebo. Cetirizine 10 mg once daily in the short term and in the intermediate term was effective in completely suppressing urticaria. Evidence was limited for desloratadine given at 5 mg once daily in the intermediate term and at 20 mg in the short term. Levocetirizine at 5 mg was effective for complete suppression in the intermediate term but not in the short term. No single agent was demonstrated to be more effective than another, and there is a lack of available head-to-head trials *(Sharma et al 2014)*.

CLINICAL GUIDELINES

- According to current clinical guidelines for the management of allergic rhinitis, intranasal corticosteroids should be considered first-line therapy in the majority of patients with moderate to severe allergic rhinitis and may also be effective in some forms of nonallergic rhinitis. Although intranasal corticosteroids are the most effective drugs for treating allergic rhinitis, second-generation antihistamines may be used in patients with mild-to-moderate disease, especially those with a preference for oral therapy and with complaints of sneezing and itching. Considering their safety profile, second-generation antihistamines should be considered as first-line symptomatic treatment for acute and chronic urticaria *(Bernstein et al 2014, Brozek et al 2017, Dykewicz et al 2017, Grattan et al 2007, Seidman et al 2015, Wallace et al 2008, Zuberbier et al 2018)*.

SAFETY SUMMARY

- Levocetirizine is contraindicated in patients with severe renal impairment and in pediatric patients 6 months to 11 years of age with impaired renal function.
- Due to the pseudoephedrine component, the combination agents are contraindicated in patients with narrow angle glaucoma, severe hypertension or coronary artery disease, or urinary retention. The combination agents should not be used when there has been treatment with a monoamine oxidase inhibitor within the last 14 days.
- The most common adverse effects are associated with sedation and fatigue or dry mouth. The most common adverse effect with cetirizine oral solution was headache.

DOSING AND ADMINISTRATION

- For the combination agents, at least 14 days must elapse after discontinuation of a monoamine oxidase inhibitor before starting treatment.
- Extended-release products should be swallowed whole; tablets should not be broken, chewed, or crushed.

Table 3. Dosing and Administration of the Single Entity and Combination Prescription Agents

Drug	Dosage Form(s)	Usual Recommended Frequency	Comments
Single Entity Agents			
Cetirizine	Oral solution	Once or twice daily	Dosage adjustment in renal and hepatic impairment is required.
Cetirizine	Solution for intravenous injection	Once daily as needed	Dosage adjustments in children 6 months to 11 years of age are required. Not recommended in patients < 6 years of age with impaired renal or hepatic function.
Desloratadine	Tablet, ODT	Once daily	Dosage adjustment in renal and hepatic impairment is required.
Levocetirizine	Tablet, oral solution	Once daily in the evening	Dosage adjustment in renal impairment is required.
Combination Agents			
Acrivastine/ pseudoephedrine	Capsule	Four times per day	Avoid use in patients with creatinine clearance ≤ 48 mL/minute.

Drug	Dosage Form(s)	Usual Recommended Frequency	Comments
Desloratadine/ pseudoephedrine	Extended-release tablet	Once or twice daily (the once-daily product is not currently marketed)	Avoid use in patients with renal and hepatic impairment (combination product was not studied in these populations).

See the current prescribing information for full details.

CONCLUSION

- Second-generation antihistamines have been shown to significantly improve the symptoms of allergic rhinitis and CIU, without the unwanted adverse effects associated with the first-generation agents *(Sur et al 2010)*.
- Currently, all of the single entity second-generation antihistamines are available as generics and/or OTC in at least 1 dosage form. Cetirizine, fexofenadine, levocetirizine, and loratadine can be purchased OTC, and several different dosage forms are available for the OTC products. Cetirizine is also available as an intravenous formulation approved for acute urticaria. *(Clinical Pharmacology 2020, Facts and Comparisons 2020, Micromedex 2020)*.
- Current evidence supports the use of second-generation antihistamines in the treatment of seasonal and perennial allergic rhinitis as well as CIU. In a systematic review by Benninger et al, second-generation antihistamines were associated with a 23.5% reduction from baseline in total nasal symptom scores for SAR, and a 51.4% reduction in symptoms of PAR *(Benninger et al 2010)*.
- Overall, clinical trials have not consistently demonstrated one single-entity second-generation antihistamine agent to be more efficacious or safe than the others. Furthermore, there is a lack of head-to-head trials comparing the combination second-generation antihistamine products, rendering a comparison of the agents difficult.
- Current consensus guidelines are consistent among organizations that antihistamines are somewhat less effective than intranasal corticosteroids, but may be used on a daily or as-needed basis. Second-generation antihistamines are recommended as they are less sedating and cause less central nervous system impairment compared to first-generation agents. Oral decongestants can be a useful addition to antihistamines in the treatment of nasal congestion *(Brozek et al 2017, Dykewicz et al 2017, Seidman et al 2015)*.
- Considering their efficacy and safety profile, second-generation antihistamines should be considered as first-line symptomatic treatment of urticaria. Additionally, patients should be offered the choice of at least 2 nonsedating antihistamines as response varies among individuals *(Bernstein et al 2014, Grattan et al 2007, Zuberbier et al 2018)*.

REFERENCES

- Allegra Allergy [OTC label]. Cedar Rapids, IA: Lil' Drug Store Products, Inc.; January 2020.
- Allegra-D [OTC label]. Libertyville, IL; A-S Medication Solutions; January 2020.
- Anuradha P, Maiti R, Jyothirmai J, et al. Loratadine vs levocetirizine in chronic idiopathic urticaria: A comparative study of efficacy and safety. *Indian J Pharmacol*. 2010;42(1):12-6.
- Benninger M, Farrar JR, Blaiss M, et al. Evaluating approved medications to treat allergic rhinitis in the United States: an evidence-based review of efficacy for nasal symptoms by class. *Ann Allergy Asthma Immunol*. 2010;104(1):13-29.
- Berger W, Blaiss M, Stiell I, et al. Intravenous (IV) cetirizine shows greater overall benefit to IV diphenhydramine for acute urticaria. *Ann Allergy Asthma Immunol*. 2018;121(5):S34. doi: 10.1016/j.anai.2018.09.109.
- Bernstein JA, Lang DM, Khan DA et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol*. 2014;133:1270-7.
- Boyle J, Ridout F, Meadows R, et al. Suppression of the histamine-induced wheal and flare response by fexofenadine HCl 60 mg twice daily, loratadine 10 mg once daily and placebo in healthy Japanese volunteers. *Curr Med Res Opin*. 2005;21(9):1495-503.
- Brozek JL, Bousquet J, Agache I, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2016 revision. *J Allergy Clin Immunol*. 2017 Oct;140(4):950-8.
- Cetirizine oral solution [package insert], Bridgewater, NJ: Amneal Pharmaceuticals LLC; February 2020.
- Children Claritin Allergy [OTC label]. Boca Raton, FL: Bayer HealthCare LLC; January 2020.
- Children's Allegra Allergy [OTC label]. Chattanooga, TN: Chattem, Inc.; February 2019.
- Children's Xyzal Allergy [OTC label]. Chattanooga, TN: Chattem, Inc.; April 2019.
- Children's Zyrtec Allergy [OTC label]. Fort Washington, PA: McNeil Consumer Healthcare; December 2018.
- Ciprandi G, Cirillo I, Vizzaccaro A, et al. Desloratadine and levocetirizine improve nasal symptoms, airflow, and allergic inflammation in patients with perennial allergic rhinitis: a pilot study. *Int Immunopharmacol*. 2005;5(13-14):1800-8.
- Clarinex tablets and oral solution [package insert], Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; May 2020.
- Clarinex-D 12 Hour [package insert], Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; March 2019.

- Claritin [OTC label]. Boca Raton, FL: Bayer HealthCare LLC; February 2020.
- Claritin-D 12 hour [OTC label]. Boca Raton, FL: Bayer HealthCare LLC; November 2019.
- Claritin-D 24 hour [OTC label]. Boca Raton, FL: Bayer HealthCare LLC; November 2019.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. https://www.clinicalkey.com/pharmacology/. Accessed May 15, 2020.
- Day JH, Briscoe M, Rafeiro E, et al. Comparative onset of action and symptom relief with cetirizine, loratadine, or placebo in an environmental exposure unit in subjects with seasonal allergic rhinitis: confirmation of a test system. *Ann Allergy Asthma Immunol*. 2001;87(6):474-81.
- Day JH, Briscoe M, Widlitz MD. Cetirizine, loratadine, or placebo in subjects with seasonal allergic rhinitis: effects after controlled ragweed pollen challenge in an environmental exposure unit. *J Allergy Clin Immunol*. 1998;101(5):638-45.
- Day JH, Briscoe MP, Rafeiro E, et al. Comparative clinical efficacy, onset and duration of action of levocetirizine and desloratadine for symptoms of seasonal allergic rhinitis in subjects evaluated in the Environmental Exposure Unit (EEU). *Int J Clin Pract*. 2004;58(2):109-18.
- Drugs@FDA [database on the Internet]. Rockville (MD): Food and Drug Administration (US), Center for Drug Evaluation and Research; 2020. https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed May 15, 2020.
- Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: An evidence-based focused 2017 guideline update. *Ann Allergy Asthma Immunol*. 2017;119(6):489-511.
- Ernst D. Quzyttir approved for the treatment of acute urticaria. MPR website. https://www.empr.com/home/news/quzyttir-approved-for-the-treatment-of-acute-urticaria/. Published October 11, 2019. Accessed May 15, 2020.
- Facts & Comparisons [database on the Internet]. St. Louis, MO: Wolters Kluwer Health; 2020. Available from: https://fco.factsandcomparisons.com/lco/action/home. Accessed May 15, 2020.
- Garg G, Thami GP. Comparative efficacy of cetirizine and levocetirizine in chronic idiopathic urticaria. *J Dermatolog Treat*. 2007;18(1):23-4.
- Glacy J, Putnam K, Godfrey S, et al. Treatments for Seasonal Allergic Rhinitis. Comparative Effectiveness Review No. 120. AHRQ Publication No. 13-EHC098-EF. Rockville, MD: Agency for Healthcare Research and Quality; July 2013. https://www.ncbi.nlm.nih.gov/books/NBK153714/. Accessed May 15, 2020.
- Grattan CE, Humphreys, FY, British Association of Dermatologists Therapy Guidelines and Audit Subcommittee. Guidelines for evaluation and management of urticaria in adults and children. *Br J Dermatol. 2007*;157:1-68.
- Handa S, Dogra S, Kumar B. Comparative efficacy of cetirizine and fexofenadine in the treatment of chronic idiopathic urticaria. *J Dermatolg Treat*. 2004;15(1):55-7.
- Janssen ML. Second-generation antihistamines. *Clin Rev Allergy*. 1993;11(3):1-3.
- Kaplan AP, Spector SL, Meeves S, et al. Once-daily fexofenadine treatment for chronic idiopathic urticaria: a multicenter, randomized, double-blind, placebo-controlled study. *Ann Allergy Asthma Immunol*. 2005;94(6):622-9.
- Kapp A, Pichler WJ. Levocetirizine is an effective treatment in patients suffering from chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled, parallel, multicenter study. *Int J Dermatol*. 2006;45(4):469-74.
- Kim K, Sussman G, Hébert J, et al. Desloratadine therapy for symptoms associated with perennial allergic rhinitis. *Ann Allergy Asthma Immunol*. 2006;96(3):460-5.
- Lee CF, Sun HL, Lu KH, et al. The comparison of cetirizine, levocetirizine and placebo for the treatment of childhood perennial allergic rhinitis. *Pediatr Allergy Immunol*. 2009;20(5):493-9.
- Lehman JM, Blaiss MS. Selecting the optimal oral antihistamine for patients with allergic rhinitis. *Drugs*. 2006;66(18):2309-19.
- Meltzer EO, Weiler JM, Widlitz MD. Comparative outdoor study of the efficacy, onset and duration of action, and safety of cetirizine, loratadine, and placebo for seasonal allergic rhinitis. *J Allergy Clin Immunol*. 1996;97(2):617-26.
- Micromedex Solutions® [database on the Internet]. Truven Health Analytics; 2020. http://www.micromedexsolutions.com/home/dispatch. Accessed May 15, 2020.
- Monroe E, Finn A, Patel P, et al. Efficacy and safety of desloratadine 5 mg once daily in the treatment of chronic idiopathic urticaria: A double-blind, randomized, placebo-controlled trial. *J Am Acad Dermatol*. 2003;48(4):535-41.
- Nathan RA, Finn AF Jr, LaForce C, et al. Comparison of cetirizine-pseudoephedrine and placebo in patients with seasonal allergic rhinitis and concomitant mild-to-moderate asthma: randomized, double-blind study. *Ann Allergy Asthma Immunol*. 2006;97(3):389-96.
- Nayak AS, Berger WE, LaForce CF. Randomized, placebo-controlled study of cetirizine and loratadine in children with seasonal allergic rhinitis. *Allergy Asthma Proc*. 2017;38(3):222-30.
- Nettis E, Colanardi MC, Barra L, et al. Levocetirizine in the treatment of chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled study. *Br J Dermatol*. 2006;154(3):533-8.
- Okubo K, Gotoh M, Shimada K, et al. Fexofenadine improves the quality of life and work productivity in Japanese patients with seasonal allergic rhinitis during the peak cedar pollinosis season. *Int Arch Allergy Immunol*. 2005;136(2):148-54.
- Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations [database on the internet]. Silver Spring, MD: Food and Drug Administration (US), Center for Drug Evaluation and Research; 2020. https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. Accessed May 15, 2020.
- Potter PC, Bailey MJ, Bateman M, et al [Levocetirizine Study Group]. Efficacy and safety of levocetirizine on symptoms and health-related quality of life of children with perennial allergic rhinitis: a double-blind, placebo-controlled randomized clinical trial. *Ann Allergy Asthma Immunol*. 2005;95(2):175-80.
- Potter PC, Bailey RM, Davis G, et al [Levocetirizine Study Group]. Levocetirizine is effective for symptom relief including nasal congestion in adolescent and adult (PAR) sensitized to house dust mites. *Allergy*. 2003;58(9):893-9.
- Potter PC, Kapp A, Maurer M, et al. Comparison of the efficacy of levocetirizine 5 mg and desloratadine 5 mg in chronic idiopathic urticaria patients. *Allergy*. 2009;64(4):596-604.
- Prenner BM, Capano D, Harris AG. Efficacy and tolerability of loratadine vs fexofenadine in the treatment of seasonal allergic rhinitis: a double-blind comparison with crossover treatment of nonresponders. *Clin Ther*. 2000;22(6):760-9.
- Purohit A, N'Gom AS, Deslandes B, et al. Similar rapid onset of action and magnitude of effect of fexofenadine and cetirizine as assessed by inhibition of histamine-induced wheal-and-flare reaction. *Ann Allergy Asthma Immunol*. 2004;93(6):562-7.
- Quzyttir [package insert], Lake Forest, IL: TerSera Therapeutics LLC; March 2020.

- Ring J, Hein R, Gauger A, et al. Once-daily desloratadine improves the signs and symptoms of chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled study. *Int J Dermatol*. 2001;40(1):72-6.
- Seidman MD, Gurgel RK, Lin ST, et al. Clinical practice guideline: allergic rhinitis. *Otolaryngol Head Neck Surg*. 2015;152(1 Suppl):SI-S43.
- Semprex-D [package insert], Malvern, PA: Endo Pharmaceuticals; January 2019.
- Sharma M, Bennett C, Cohen SN, et al. H1-antihistamines for chronic spontaneous urticaria. *Cochrane Database of Systematic Reviews*. 2014, Issue 11. Art. No.: CD006137.
- Simons FE, Prenner BM, Finn A Jr. Efficacy and safety of desloratadine in the treatment of perennial allergic rhinitis. *J Allergy Clin Immunol*. 2003;111(3):617-22.
- Sur DK, Scandale S. Treatment of allergic rhinitis. *Am Fam Physician*. 2010;81(12):1440-6.
- Van Cauwenberge P, Juniper EF. Comparison of the efficacy, safety and quality of life provided by fexofenadine hydrochloride 120 mg, loratadine 10 mg and placebo administered once daily for the treatment of seasonal allergic rhinitis. *Clin Exp Allergy*. 2000;30(6):891-9.
- Wallace DV, Dykewicz MS, Bernstein DI, et al. The diagnosis and management of rhinitis: an updated practice parameter. *J Allergy Clin Immunol*. 2008;122:S1-S84.
- Xyzal [OTC label]. Chattanooga, TN: Chattem, Inc.; March 2017.
- Xyzal tablets and oral solution [package insert], Bridgewater, NJ: Sanofi-Aventis, U.S. LLC; April 2019.
- Zuberbier T, Aberer W, Asero R, et al. EAACI/GA(2)LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2018;73(7):1393-1414.
- Zyrtec [OTC label]. Fort Washington, PA: McNeil Consumer Healthcare; March 2020.
- Zyrtec-D [OTC label]. Fort Washington, PA: McNeil Consumer Healthcare; September 2017.

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