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## A Clinical Review of 24-Hour OTC Antihistamines for Allergy Symptom Relief

**AS MANY AS 60 MILLION** Americans are affected each year by allergic rhinitis (AR), or hay fever. This common condition is characterized by 1 or more allergy symptoms, including runny nose, sneezing, itchy and watery eyes, itching around the nose, nasal congestion, sinus pressure, and rhinorrhea (excessive mucous secretion in the back of the nasal cavity or throat, which can cause sore throat and coughing).<sup>1</sup>

AR can be classified by the pattern and time of allergy symptom presentation and the type of triggering allergen. From spring through early fall, exposure to increased outdoor allergens in the air (eg, tree, weed, and grass pollens) can trigger a range of seasonal AR (SAR) allergy symptoms that can occur at the same time every year or persist throughout the season. Perennial AR (PAR) is caused by year-round exposures to indoor allergens (eg, house dust mites, pet dander, mold, mildew). Some patients may have both SAR and PAR.<sup>1</sup>

The burden of AR symptoms can substantially affect quality of life, including impaired work performance, productivity, social activities, interpersonal relationships, and overall psychological well-being.<sup>1,2</sup>

### OTC ALLERGY PRODUCTS

Updated recommendations for class agents for relief from ocular and nasal PAR and SAR symptoms were jointly published in 2020 by the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology (AAAI/ACAAI). Many of these agents are available over the counter (OTC).<sup>1</sup> The AAAI/ACAAI noted that onset of action and effectiveness for fast and consistent symptom relief are important considerations when choosing an OTC allergy medication.<sup>1</sup>

The **TABLE** provides information about the leading allergy products to help pharmacists prepare to address questions or provide a recommendation, if asked.<sup>3-9</sup>

#### **Intranasal corticosteroids**

OTC and prescription intranasal corticosteroid sprays (eg, fluticasone propionate [Flonase®]) are available to temporarily relieve nasal congestion, runny nose, sneezing, and itchy nose. However, the onset of action may take up to 12 hours, with maximum therapeutic effect within 2 to 4 weeks when used consistently for several days.<sup>1</sup>

#### **Nasal decongestants**

Nasal decongestants (eg, pseudoephedrine) reduce swelling of nasal passages and temporarily restore nasal airflow. They are

effective for relief of nasal congestion but don't provide relief from the full spectrum of SAR and PAR nasal and ocular symptoms. Products that combine antihistamines and nasal decongestants are also available—eg, cetirizine and pseudoephedrine (ZYRTEC-D®).<sup>1,10</sup>

#### **Antihistamines**

Because first-generation OTC antihistamines are associated with potential adverse effects such as sedation and anticholinergic-mediated symptoms (eg, dry eyes, dry mouth, constipation, urinary hesitancy and retention), second-generation antihistamines are preferred for AR.<sup>1</sup>

Second-generation 24-hour OTC oral antihistamine products have different active ingredients, including cetirizine (ZYRTEC®), loratadine (Claritin®), fexofenadine (Allegra®), and levocetirizine (Xyzal®). They provide temporary relief from sneezing; runny nose; itchy, watery eyes; and itching of the nose or throat due to hay fever or other upper respiratory allergies.<sup>1,6-9</sup> These products all provide 24-hour relief from allergy symptoms; however, there are differences in the onset of action.<sup>1</sup>

#### **ZYRTEC®**

Among OTC oral antihistamines, ZYRTEC® (cetirizine) is the number-1 allergist-recommended brand. ZYRTEC® allergy products are available in several formulations (tablets, liquid gels, dissolvable tablets, syrup) for different ages and allergy stages. For children, Children's ZYRTEC® is available in dissolvable tablet and syrup forms.

Once-daily ZYRTEC® tablets temporarily relieve sneezing; runny nose; itchy, watery eyes; and itching of the nose or throat due to hay fever or other upper respiratory allergies in adults and children 6 years of age and older.<sup>8</sup>

ZYRTEC® was evaluated in clinical studies for its relief from SAR and PAR symptoms compared with 2 other 24-hour OTC oral antihistamine products, Claritin® (loratadine) and Allegra® (fexofenadine).<sup>4,5,11</sup>

#### **Faster onset of allergy symptom relief: ZYRTEC® vs Claritin®**

In 2 studies, the comparative efficacy of ZYRTEC® and Claritin® in SAR symptom relief was investigated using an environmental exposure unit (EEU), a standard validated method of determining onset of action and duration of antiallergic treatments.<sup>4,5</sup>

An EEU is an indoor chamber used to expose large groups of study populations to controlled levels of pollen comparable

**TABLE. KEY FEATURES OF OTC ALLERGY MEDICATIONS<sup>3-9,a</sup>**

|  | 24-hour OTC Antihistamines |                       |                      |                    | INS spray              |
|--|----------------------------|-----------------------|----------------------|--------------------|------------------------|
|  | ZYRTEC <sup>®</sup>        | Claritin <sup>®</sup> | Allegra <sup>®</sup> | Xyzal <sup>®</sup> | Flonase <sup>®</sup>   |
| Active ingredient  | Cetirizine                 | Loratadine            | Fexofenadine         | Levocetirizine     | Fluticasone propionate |
| Number-1 allergist-recommended brand among OTC oral antihistamines | ✓                          |                       |                      |                    |                        |
| Starts working at hour 1 <sup>b</sup>                              | ✓                          |                       | ✓                    | ✓                  |                        |
| Proven effective in SAR/PAR  | ✓                          | ✓                     | ✓                    | ✓                  | ✓                      |
| 24-hour relief   | ✓                          | ✓                     | ✓                    | ✓                  | ✓                      |
| No juice warnings on label   | ✓                          | ✓                     |                      | ✓                  | ✓                      |
| Membership program for HCPs  | ✓                          | ✓                     |                      |                    |                        |

HCP, health care provider; INS, intranasal corticosteroid; OTC, over the counter; PAR, perennial allergic rhinitis; SAR, seasonal allergic rhinitis.

<sup>a</sup>The third-party trademarks used herein are registered trademarks of their respective owners.

<sup>b</sup>ZYRTEC<sup>®</sup> 10 mg starts working at hour 1, based on first dose on the first day of a 2-day study in 2 pollen chamber studies. Primary end point measured mean improvement from baseline in major symptom complex severity score (included runny nose, sniffles, itchy nose, nose blows, sneezes, and watery eyes).<sup>4</sup>

with those experienced outdoors during peak allergy season, and it can be replicated regardless of time of year.<sup>4,5</sup>

Patients 16 years and older with a diagnosis of SAR were treated with either ZYRTEC<sup>®</sup> 10 mg or Claritin<sup>®</sup> 10 mg daily.<sup>4,5</sup> The mean improvement from baseline in major symptom severity complex (MSC) score was measured, which assessed symptoms including runny nose, sniffles, itchy nose, nose blows, sneezes, and watery eyes.<sup>4,5</sup>

In both of these EEU studies, the results demonstrated that ZYRTEC<sup>®</sup> 10 mg starts working at hour 1 and Claritin starts working at hour 3, based on the first dose on the first day of each 2-day study.<sup>4,5</sup> Across the 2 studies, ZYRTEC<sup>®</sup> 10 mg provided a significantly greater reduction in MSC scores overall from baseline compared with Claritin<sup>®</sup> ( $P < .05$ ).<sup>4,5</sup>

### Greater 24-hour allergy symptom relief:

#### ZYRTEC<sup>®</sup> vs Allegra<sup>®</sup>

In a separate EEU study, patients with SAR were randomized to receive either ZYRTEC<sup>®</sup> 10 mg (n=240), Allegra<sup>®</sup> 180 mg (n=239), or placebo (n=96). The primary efficacy end point of the change in total symptom severity complex (TSSC) score from baseline at hours 21 to 24 was defined as the sum of self-assessed severity scores of 4 symptoms: runny nose; sneezing; itchy nose, palate, and throat; and itchy, watery eyes.<sup>11</sup>

ZYRTEC<sup>®</sup> provided 33% greater relief than Allegra<sup>®</sup> at 21 to 24 hours (as measured by reduction in TSSC score) based on the first dose on the first day of the 2-day EEU study.<sup>11</sup>

#### Overall SAR and PAR symptom relief with ZYRTEC<sup>®</sup>

Across several multicenter, randomized, placebo-controlled, double-blind studies, which included a minimum of 100 participants with a previous diagnosis of PAR or SAR, ZYRTEC<sup>®</sup>

was shown to provide long-term, consistent relief from PAR and SAR symptoms. ZYRTEC<sup>®</sup> provided consistent relief from PAR symptoms over a 4- to 8-week treatment period and SAR symptoms over a 2- to 4-week treatment period.<sup>3</sup>

In 2 separate studies of adults with SAR, ZYRTEC<sup>®</sup> provided relief from bothersome ocular symptoms (itchy and watery eyes) and nasal symptoms (sneezing, runny nose, and itchy nose) with improvements within the first week of treatment that continued over the 2-week treatment period of each study.<sup>3,12,13</sup>

Treatment with ZYRTEC<sup>®</sup> 10 mg also improved measures of overall quality-of-life performance across several additional randomized, placebo-controlled studies of adults with SAR or PAR.<sup>2,14-16</sup>

## ROLE OF THE PHARMACIST

With many OTC allergy products available, with different active ingredients in numerous formulations, pharmacists can familiarize themselves with the options. If asked for a recommendation, they can prepare to provide information on the options that provide clinically proven, consistent relief from SAR/PAR symptoms.

Pharmacists can educate those with SAR and PAR symptoms about the clinical data for ZYRTEC<sup>®</sup> and other 24-hour OTC oral antihistamines. In comparative studies, ZYRTEC<sup>®</sup> starts working at hour 1 (compared with Claritin<sup>®</sup> at hour 3) on the first day it is taken, and ZYRTEC<sup>®</sup> provided greater symptom relief (compared with Allegra<sup>®</sup>) at 21 to 24 hours.<sup>4,5,11</sup> ■

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