# National PBM Drug Monograph
# Desloratadine (Clarinex®)
### VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel

## Methods

### Literature Search
MEDLINE [Pubmed 1966-2002] was searched using the terms desloratadine and Clarinex®.
Reference lists of review articles were searched for relevant clinical trials.
The manufacturers of desloratadine were contacted for relevant data on file and to ensure all clinical trials meeting criteria were included.

### Eligibility Criteria and Study Selection
Efficacy: All clinical trials, published in English and in peer-reviewed journals, comparing desloratadine to a first (sedating) or second-generation (low or nonsedating) antihistamine, were included. Because comparative trials were lacking, trials comparing desloratadine to placebo were included.
Safety: Published case reports, clinical trials, abstracts, and controlled clinical trials.

## Introduction

Allergic rhinitis (AR) is a condition that affects up to 40 million Americans and is the sixth most prevalent chronic disease in the Unites States[1-2]. In 1995, it was estimated that the direct and indirect costs for the management of allergic rhinitis was 2.7 billion dollars excluding costs for accompanying asthma or sinusitis [1]. In 1996, Ray et al, estimated the direct medical costs for AR, as a primary or secondary diagnosis, at 5.9 billion dollars accounting for related airway diseases [3].

There are two types of AR: seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR). Seasonal AR is seasonal and is usually caused by pollens or molds. Perennial AR tends to be present for more than 9 months of the year and can be attributed to dust mites, molds, animal dander, or pollen in areas where high pollen counts are present for much of the year[1].

Chronic idiopathic urticaria (CIU) is defined as the occurrence of wheals for a duration of at least 6 weeks and is estimated to occur in 0.1 to 3% of the population. Its primary manifestation is smooth, edematous wheals surrounded by a red flare. The presence of wheals is accompanied by intense itching and is associated with high morbidity. [4]

Histamine plays an important role in the pathophysiology of allergic rhinitis and chronic idiopathic urticaria. This mediator is found in its highest concentrations in the lungs, mast cells, and basophils. Exposure to a sensitizing allergen results in the attachment of IgE molecules to the cells causing release of histamine and other inflammatory mediators. The actions of histamine at the H-1 receptor produce the classic symptoms of an allergic response: pruritus, wheal and flare reactions of the skin; sneezing, nasal pruritis, rhinorrhea, palatal pruritis, itchy, red and watery eyes and congestion in the nose. In more severe circumstances, mucous membranes of the ears and paranasal sinuses can be involved producing symptoms of ear fullness and popping, itchy throat and pressure in the area above the cheeks and forehead. Fatigue, weakness and malaise can also be present. Patients with AR may be limited in their ability to perform daily activities and often note disturbances in sleep, work performance concentration, and quality of life. It is now considered crucial to optimally treat an individual with AR since chronic inflammation of the nasal mucosa and nasal obstruction, if left untreated, can lead to more serious conditions of the upper and lower airways including asthma, sinusitis, chronic otitis media with effusion and nasal or sinus polyps[1,5,6].

Desloratadine is a selective, $H_1$-receptor antihistamine. It is the major orally active metabolite of loratadine. The first dosage form approved by the FDA was the 5 mg tablet on December 21, 2001. Currently, there are 3 other available second-generation antihistamines (cetirizine, fexofenadine, and loratadine) approved for allergic rhinitis and/or chronic idiopathic urticaria.

## Pharmacology/Pharmacokinetics[7]

Desloratadine acts by selectively blocking histamine at the histamine $H_1$-receptor. In vitro, desloratadine inhibited histamine release from human mast cells.

**Table 1.**

| Pharmacokinetic Parameter | |
|---|---|
| **Absorption** | ▪ Mean peak plasma concentrations of desloratadine are reached within 3 hours.<br>▪ Neither food nor grapefruit juice had an effect on the bioavailability of desloratadine. |
| **Distribution** | ▪ Desloratadine and 3-hydroxydesloratadine are approximately 85% protein bound. |
| **Metabolism** | ▪ Desloratadine is metabolized to an active metabolite, 3-hydroxydesloratadine. This metabolite subsequently undergoes glucuronidation.<br>▪ Although the enzymes responsible for the formation of 3-hydroxydesloratadine have not been identified, it is known that some individuals (7%) are slow metabolizers of desloratadine and may be more susceptible to dose-related adverse events (somnolence). |
| **Excretion** | ▪ Half-life of desloratadine is 27 hours.<br>▪ In one study, recovery of approximately 87% of a $^{14}$C-desloratadine dose was found to be equally distributed in the urine and feces as metabolic products.<br>▪ 3-hydroxydesloratadine demonstrated a similar half-life to desloratadine. |

## FDA Approved Indications[7]

- Desloratadine is indicated for the relief of nasal and non-nasal symptoms of seasonal and perennial allergic rhinitis in individuals 12 years of age and older.
- Desloratadine is indicated for the relief of symptoms (pruritis and reduction in the size and number of hives) of chronic idiopathic urticaria in individuals 12 years of age and older.

## Current VA National Formulary Status

Desloratadine is nonformulary. Loratadine is the nonsedating antihistamine on the VA National Formulary.

## Dosage and Administration[7]

- The dose of desloratadine is 5 mg daily.
- In patients with liver or renal dysfunction, a starting dose of 5 mg every other day is recommended.

## Adverse Effects[7]

In multiple-dose, placebo-controlled clinical trials with desloratadine, adverse events were similar between desloratadine and placebo. Withdrawal for treatment related adverse events were also similar (2.4% desloratadine vs. 2.6% placebo). Laboratory and electrocardiographic (ECG) abnormalities did not differ in

the desloratadine and placebo groups. Adverse events reported in ≥2% of patients and more frequently in the desloratadine group vs. placebo are listed in table 2.

**Table 2.**

| Adverse Event | Desloratadine (n=1655) | Placebo (n=1652) |
|---|---|---|
| Pharyngitis | 4.1% | 2% |
| Dry Mouth | 3% | 1.9% |
| Myalgia | 2.1% | 1.8% |
| Fatigue | 2.1% | 1.2% |
| Somnolence | 2.1% | 1.8% |

Table adapted from Clarinex® product information

***Cardiac Safety:***

Two of the second-generation antihistamines (terfenadine and astemizole) were removed from the market because of their ability to block cardiac potassium channels resulting in prolongation of the $QT_c$ interval and development of torsades de pointes.[14] As a result of these events, manufacturers of second-generation antihistamines are required to evaluate the cardiac safety of their drug. Published clinical trials have not demonstrated evidence for concern of cardiac toxicity with desloratadine. [8-13]

To date, there are no published reports of QT prolongation or torsade de pointes associated with desloratadine. In one study, desloratadine 45 mg daily was given to volunteers for 10 days. In that study, mean heart rate increased 9.2 beats per minute in desloratadine treated patients compared to placebo. Additionally, there was a 0.4 msec mean increase in $QT_c$ in desloratadine vs. placebo recipients which was not considered to be significant.[7]

Cases of serious cardiotoxicity were reported in patients receiving terfenadine or astemizole, particularly in overdosage or when combined with drugs that may alter their metabolism. Table 3 includes three studies in which changes in ECG parameters (PR interval, QRS complex, QT and $QT_c$ interval and ventricular rate) were monitored as the primary safety endpoint. All patients included in these trials were considered healthy individuals. In all three trials, although there were some significant increases in either the mean maximum concentration ($C_{max}$) or the area under the concentration-time curve (AUC), no clinically relevant ECG changes were noted.

**Table 3. Studies Assessing Cardiac Safety of Desloratadine**

| Study | Intervention | $C_{max}$ | $AUC_{0-24\ hrs}$ | ECG Changes |
|---|---|---|---|---|
| **Gupta S., etal** [15]<br>R, PC, TPB<br>N=90 volunteers (18/group)<br>7 days | 5 groups:<br>D 5mg/d + Az<br>D 5 mg/d + PL<br>Az + PL<br>F 60 mg bid + Az<br>F 60 mg bid + PL<br><br>Az started on day 3 of antihistamine as 500 mg load and 250 mgd for 4 days. | D + Az +15%<br>3-hydroxyD+Az +15%<br><br>F + Az +69%* | D + Az +5%<br>3-hydroxyD+Az +4%<br><br>F + Az +67%* | No change in any measured ECG variable (PR, QRS, QT, $QT_c$, ventricular rate) in D+Az group vs. D+PL or F + Az vs. F + PL. Subgroup analysis showed a difference in PR interval in men in F+Az vs. F+PL (p=0.04). |
| **Banfield C, etal.** [16]<br>R, PC, CO, TPB<br>N=24 volunteers<br>10 days on each treatment | D 7.5 mg/d + Erythro 500 mg q8h<br>Or<br>D 7.5 mg/d + PL<br>10 days on each treatment, 7- day washout and switch to alternate group for 10 days. | D + Erythro +23.9%*<br>3-hydroxyD +Erythro +44%* | D + Erythro +14%<br>3-hydroxyD + Erythro + 40%* | No changes in ECG parameters (PR, QRS, QT) between groups. Subgroup analysis did not reveal any differences between sexes. |
| **Banfield C, etal.** [17]<br>R, PC, CO, TPB<br>N=24 volunteers<br>10 days on each treatment | D 7.5 mg/d + Keto 200 mg bid<br>Or<br>D 7.5 mg/d + PL<br>10 days on each treatment, 7- day washout and switch to | D + Keto +27%*<br>3-hydroxyD + Keto +50%* | D + Keto +20.8%<br>3-hydroxyD + Keto +89.6%* | No changes in ECG parameters (PR, QRS, QT, $QT_c$) were noted between groups. Subgroup analysis did not reveal any differences between |

| | | | | |
|---|---|---|---|---|
| | alternate group for 10 days. | | | sexes. |

AUC=area under the concentration-time curve, A=azithromycin, Cmax=mean maximum concentration, CO=crossover, D=desloratadine, Erythro=erythromycin, F=fexofenadine, Keto=ketoconazole, PC=placebo-controlled, PL=placebo, R=randomized, TPB=third part blind (MD performing safety assessments), 3-hydroxyD=3-hydroxydesloratadine (metabolite).
*Statistically significant difference

***Cognitive Impairment:***

The primary reason for choosing a second-generation antihistamine is the apparent lack of a sedative effect or effect on performance of daily activities. In three published abstracts, the effect of desloratadine on driving, wakefulness and psychomotor performance and flying ability was assessed. In each of these studies, volunteers were randomized to receive a single dose of desloratadine 5 or 7.5 mg, diphenhydramine 50 mg or placebo in a 3-way crossover fashion, separated by a washout period, prior to performing specific tests measuring cognition and wakefulness. In each of those studies, desloratadine was not different than placebo indicating that it did not have an effect on cognition and/or wakefulness. [18-20]

**Monitoring**

The manufacturer does not recommend any specific monitoring other than symptomatic response.

**Contraindications**[7]

Desloratadine is contraindicated in patients who are hypersensitive to it, its ingredients, or to loratadine.

**Drug Interactions**[7] (Also see section on adverse effects: cardiac safety)

Desloratadine is primarily metabolized to 3-hydroxydesloratadine which undergoes glucuronidation. The enzymes responsible for the conversion of desloratadine to 3-hydroxydesloratadine are not known. There have been several studies to evaluate the effect of azole antifungals or macrolide antibiotics on the metabolic fate of desloratadine. In those controlled trials [15-17], the $C_{max}$ and/or the AUC were increased to some extent. However, the combination of azithromycin, erythromycin or ketoconazole with desloratadine did not change the safety profile of desloratadine as evidenced by no significant changes in ECG parameters, laboratory tests, vital signs or adverse effects.

**Efficacy Measures**

Table 4 describes the methods used to measure the effectiveness of desloratadine in the management of allergic rhinitis.

**Table 4. Scales and measures used to evaluate efficacy**

| | |
|---|---|
| Nasal symptom scores | Mean of 4 individual scores (congestion, rhinorrhea, nasal pruritus, sneezing). Each sx scored 0-3 with 0=none, 1= mild (sx noticeable but not bothersome), 2=moderate (sx noticeable and bothersome but tolerable), 3= severe (signs and symptoms hard to tolerate, interfered with activities) |
| Nonnasal symptoms scores | Mean of 4 individual scores (eye pruritis, eye tearing, eye redness, itching of ears-palate). Each sx scored 0-3 with 0=none, 1= mild (sx noticeable but not bothersome), 2=moderate (sx noticeable and bothersome but tolerable), 3= severe (signs and symptoms hard to tolerate, interfered with activities) |
| Total nasal symptom score (TNSS) | Sum of all 4 nasal symptom scores |
| Total nonnasal symptom score (TNNSS) | Sum of all 4 nonnasal symptoms scores |
| Total symptom score (TSS) | Sum of TNSS and TNNSS |
| Patient and physician global score | Compared to when entering the study, nose and nonose symptoms were rated on 7 point scale from 0 (very much better) – 3 (unchanged) - 6 (very much worse) |
| Rhinoconjunctivitis quality of life (RQLQ) | Made up of 28 items and 7 domains: activity, sleep, nasal symptoms, ocular symptoms, non-nose/non-eye symptoms, practical problems, and emotions. Each item is rated from 0 (not troubled) – 6 (extremely troubled) |
| Nasal peak inspiratory flow rate | Has been used to objectively measure nasal airflow obstruction and has shown good correlation with patients' rhinitis symptoms and treatment response (r= -0.51) |

| | |
|---|---|
| Active anterior rhinomanometry | After clearing nasal secretions, an airtight facemask is placed on the subject. Subjects keep their mouths closed and breath through one nostril to measure the airflow while a sensor in the other nostril measures the difference in prenasal and postnasal pressures. Nasal airflow is the sum of recorded airflow through the right and left nostrils at a pressure difference of 150 Pa across the nasal passages. |
| Asthma symptoms | Mean of 3 individual scores (cough, wheezing, difficulty breathing) ). Each sx scored 0-3 with 0=none, 1= mild (sx noticeable but not bothersome), 2=moderate (sx noticeable and bothersome but tolerable), 3= severe (signs and symptoms hard to tolerate, interfered with activities) |
| Reflective assessment of symptoms | Patient assessment of symptom severity over the previous 12 hours |

***Desloratadine versus Placebo in SAR:*** (study details in table 5)

Since there is only one published trial comparing desloratadine to another second-generation antihistamine, all four published trials comparing desloratadine to placebo were included. Three of these trials focused on desloratadine's ability to reduce nasal congestion which is of interest since most of the available second-generation antihistamines are not effective for this symptom.

In the first trial by Horek, etal [8], 47 patients with seasonal allergic rhinitis were screened in an allergen exposure unit to determine their response to grass pollen. During the 2 hour screening in the unit, nasal airflow, measured by active anterior rhinomanometry, had to be reduced by 30% to be eligible. Eligible patients were randomized to receive desloratadine 5 mg daily or placebo for 7 days. On day 7, patients were placed in the allergen exposure unit with a controlled concentration of grass pollen for 6 hours. After a 10-day washout phase, patients were crossed over to the alternative treatment for another 7 days after which they spent another 6 hours in the allergen exposure unit. Efficacy measures included nasal airflow, nasal secretions, individual nasal and nonnasal allergy symptom scores, and composite symptoms scores (TNSS, TNNSS, TSS). Nasal airflow was reduced from baseline for both desloratadine and placebo. However, the reduction in nasal airflow was significantly greater in the placebo versus desloratadine group throughout the allergen exposure ($p=0.002$). Nasal secretions were also less in the desloratadine group. As for nasal and nonnasal symptoms, individual and composite scores were lower in the desloratadine group.

In the second study by Berger, etal [9], 331 patients with asthma, nasal congestion and SAR were randomized to desloratadine 5 mg or placebo daily. In this study, subjects in the desloratadine group had a statistically significant reduction in both individual and composite nasal and nonnasal symptoms scores compared to placebo. As for nasal congestion, the mean reduction in symptom score from baseline was 0.56 for desloratadine and 0.38 for placebo ($p<0.006$). The use of beta-agonist inhalers was significantly reduced for the first 2 weeks of the study in the desloratadine group but the reduction did not persist throughout the study.

In the third study, Nayak, etal [10] randomized 346 patients with moderate symptoms of SAR, including nasal congestion, to desloratadine 5 mg daily or placebo for 2 weeks. The primary efficacy variable was mean change from baseline in nasal congestion. In the desloratadine group, the mean reduction in nasal congestion score was 0.5 versus 0.4 for placebo ($p<0.05$). Although this difference was found to be statistically significant, the clinical significance is questionable. Total symptom score was found to be reduced significantly more in the desloratadine versus placebo group (-4.3 vs. -2.5, respectively; $p<0.01$).

In the fourth study, Meltzer, etal [11] randomized 346 patients with moderate symptoms of SAR during the spring allergy season to desloratadine 5 mg or placebo once daily for 2 weeks. The primary endpoint was the mean change from baseline in the average reflective am/pm total symptom score (TSS) reflecting the patients' perception of their allergy symptoms in the previous 12 hours. Another 328 patients with moderate symptoms of SAR in the fall season were randomized to desloratadine 5 mg or placebo daily for 2 weeks and efficacy was based upon the same primary endpoint. In both studies, desloratadine was associated with a statistically significant greater mean reduction from baseline in average am/pm reflective TSS compared to placebo.

***Desloratadine vs. Fexofenadine in SAR:*** (study details in table 5)

Only one published trial was identified that compared desloratadine to another second-generation antihistamine for SAR. This trial was a double-blind, crossover study in which 49 patients with SAR were randomized to receive desloratadine 5 mg or fexofenadine 180 mg daily for 2 weeks. Prior to randomization, patients underwent a 7-10 day placebo run-in phase. Patients were switched over to the alternate therapy for 2 weeks after a 7-10 day placebo washout period. The primary endpoint was the mean change in peak nasal inspiratory flow measured using a nasal inspiratory flow meter intended to assess nasal function. Subjects were also instructed to rate their nasal and nonnasal allergy symptoms twice daily. Authors observed a significantly greater nasal inspiratory flow after desloratadine and fexofenadine compared to placebo but there was no difference between active groups. There was also a statistically greater reduction in nasal, but not nonnasal, allergy symptoms in both the desloratadine and fexofenadine groups compared to placebo. Again, there was no difference in allergic symptoms found between the desloratadine and fexofenadine recipients.

***Desloratadine in PAR:***

To date, there are no trials that have been published in full form evaluating desloratadine's safety and efficacy in perennial allergic rhinitis.

***Desloratadine vs. placebo in Chronic Idiopathic Urticaria (CIU):*** (study details in table 5)

In the study by Ring, etal.[13], investigators randomized 190 patients with at least a 6-week history of chronic idiopathic urticaria to desloratadine 5 mg or placebo once daily for 6 weeks. The primary endpoint in this study was reduction in mean am/pm reflective (subjective symptom severity in previous 12 hours) pruritis score. Other efficacy measures included number and size of hives, effect of desloratadine vs. placebo on sleep and daily activities and provider and patient assessment of severity of CIU and response to therapy. Desloratadine was associated with a significantly greater reduction in mean am/pm reflective pruritis severity scores compared to placebo ($p<0.001$). Authors reported that all measures significantly favored desloratadine over placebo. Nearly 15% of patients were not included in the efficacy analysis for various reasons.

<table>
<tr><th>Study</th><th>Entry Criteria</th><th>Intervention</th><th>Measured Outcomes</th><th>Results</th><th>Safety/Comments</th></tr>
<tr>
<td>Horek F., etal.[8]<br>R, DB, PC, CO<br><br>*Allergen exposure unit<br>*Desloratadine vs. placebo<br>*47 patients<br>*7 days on each treatment<br>*Not ITT (1 patient not included in efficacy analysis).</td>
<td>*19-45 years of age) with SAR for ≥ 2 years demonstrating a sensitivity to grass pollen through a positive skin prick test and positive RAST result of class 2 or greater at screening or within 1 year.<br>*They were required to have no or mild nasal congestion.<br>*After a 2 hour screening in an allergen exposure unit, their nasal congestion had to have increased to moderate or greater and nasal airflow reduced by 30%</td>
<td>Desloratadine 5 mg daily or placebo once daily for 7 days Then subjects were crossed over to the alternate treatment for another 7 days after a 10 day washout.<br><br>On the seventh day of treatment, patients spent 6 hours in an allergen exposure unit with a uniform concentration of grass pollen.</td>
<td>1) Nasal airflow<br>2) Nasal secretion weights (preweighed tissue, reweighed after clearing nasal secretions)<br>3) Individual nasal and nonnasal symptom scores.<br>4) Composite scores:<br>TNSS, TNNSS, TSS</td>
<td>1) Nasal airflow decreased more in the placebo vs. desloratadine group (p=0.002) as measured via anterior rhinomanometry. Observed nasal airflow was better in the desloratadine group (p=0.004)<br>2) Nasal secretion weights were higher in the placebo group (p<0.001)<br>3) and 4)<br><br>Individual and Composite Scores:
<table>
<tr><th>Measure</th><th>D</th><th>PL</th><th>p</th></tr>
<tr><td>NC</td><td>1.6</td><td>2</td><td><.001</td></tr>
<tr><td>Sneeze</td><td>0.8</td><td>1.7</td><td><.001</td></tr>
<tr><td>Rhinorr</td><td>1.1</td><td>1.8</td><td><.001</td></tr>
<tr><td>TNSS</td><td>4.4</td><td>7.3</td><td><.001</td></tr>
<tr><td>TNNSS</td><td>1.7</td><td>3</td><td><.001</td></tr>
<tr><td>TSS</td><td>6.1</td><td>10.4</td><td><.001</td></tr>
</table>
</td>
<td>No differences in reported AEs. One patient dropped out of the desloratadine group due to somnolence.</td>
</tr>
<tr>
<td>Berger WE., etal [9]<br>MC, DB, PC<br><br>*Fall/winter allergy season<br>*Desloratadine vs. placebo<br>*331 patients with asthma<br>*4 weeks<br>*Not ITT (5 patients not included in efficacy analysis).</td>
<td>*15 years of age or ><br>*2 year hx of SAR<br>*Increased asthma signs or symptoms with SAR with demonstrated reversibility in last 2 years.<br>*TNSS=6, TNNSS=5, and moderate nasal rhinorrhea</td>
<td>Desloratadine 5 mg or placebo daily for 4 weeks.<br><br>Patients maintained a diary of their allergy symptoms recording both am and pm scores daily.</td>
<td>1) Mean change from baseline of reflective (prior 12 hours) am/pm TSS for averages of days 1-15.<br>2) Mean change from baseline in am/pm reflective nasal congestion, am/pm TNSS and TNNSS and am instantaneous TSS.<br>3) am/pm asthma symptom score, individual asthma symptom scores, number of times using beta-agonist rescue medication.</td>
<td>Mean change from baseline (Days1-15)
<table>
<tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr>
<tr><td>R-TSS</td><td>-4.9</td><td>-2.98</td><td><.001</td></tr>
<tr><td>NC</td><td>-.56</td><td>-.38</td><td><.006</td></tr>
<tr><td>R-TNSS</td><td>-2.31</td><td>-1.44</td><td>=.001</td></tr>
<tr><td>R-TNNSS</td><td>-2.57</td><td>-1.55</td><td>=.001</td></tr>
<tr><td>I-TSS</td><td>-2.57</td><td>-.85</td><td><.001</td></tr>
<tr><td>B-agonist</td><td colspan="3">No actual numbers provided.</td></tr>
</table>
I-instantaneous, R-reflective</td>
<td>There were no differences in AEs. Fatigue occurred in 2.4% of desloratadine vs. <1% of placebo recipients. EKGs were monitored in this study. No cardiovascular AEs EKG changes, including $QT_c$ interval changes were noted.<br>47 patients dropped out of study. Reasons for d/c were not different except for failures occurring more in the placebo group.</td>
</tr>
</table>

<table>
<tr>
<td>Nayak AS, etal [10]<br>R, DB, PC<br><br>*Desloratadine vs. placebo<br>*346 patients<br>*2 weeks<br>*(?) ITT</td>
<td>*12 years of age or ><br>*2 year hx of SAR<br>*At least moderate nasal and nonnasal allergy symptoms.<br>*Allergic condition documented by skin test within last year</td>
<td>Desloratadine 5 mg or placebo daily for 2 weeks.<br><br>Patients recorded their nasal allergy symptom scores in a diary bid.</td>
<td>1) Mean change from baseline in nasal congestion.<br>2) Mean change from baseline in other individual allergy symptom and composite scores</td>
<td>Mean change from baseline (Days2-15)<br><table><tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr><tr><td>NC</td><td>0.5</td><td>0.4</td><td>P<.05</td></tr><tr><td>TSS</td><td>4.3</td><td>2.5</td><td>P<.01</td></tr></table>No actual numbers provided for improvement in other individual nasal and nonnasal symptom score. Authors commented that these were improved significantly more in the D than the PL group.</td>
<td>No mention of study withdrawal. No difference in reported AEs.<br>The focus of this investigation was Ds ability to reduce NC compared to PL since the 2nd generation antihistamines typically do not work for NC. The difference, although statistically significant, may not be clinically significant.</td>
</tr>
<tr>
<td>Meltzer EO, etal [11]<br>R, DB, PC, MC<br><br>*Desloratadine vs. placebo in Spring and Fall allergy seasons (2 separate studies)<br>*346 patients (spring)<br>*328 patients (fall)<br>*2 weeks each<br>*(?) ITT</td>
<td>*12 years of age or ><br>*2 year hx of SAR<br>*At least moderate nasal and nonnasal allergy symptoms.<br>*Allergic condition documented by skin test within 12 months.</td>
<td>Desloratadine 5 mg or placebo daily for 2 weeks.<br><br>Patients recorded their nasal and nonnasal allergy symptoms based on how they felt in previous 12 hours (reflective) and how they felt at the time of assessment in a diary bid.</td>
<td>1) Mean change from baseline in average reflective am/pm TSS (averaged over 2 week period).<br>2) AM instantaneous TSS (reflects 24 duration of effect for D)<br>3) TNSS, TNNSS</td>
<td>Mean change from baseline (Days2-15)<br>Spring:<br><table><tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr><tr><td>R-TSS</td><td>4.3</td><td>2.5</td><td>P<.01</td></tr><tr><td>I-TSS</td><td>2.9</td><td>1.5</td><td>P<.01</td></tr><tr><td>TNSS</td><td>1.9</td><td>0.9</td><td>P<.01</td></tr><tr><td>TNNSS</td><td>1.7</td><td>0.7</td><td>P<.01</td></tr></table>I-instantaneous, R-reflective<br>Fall:<br><table><tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr><tr><td>R-TSS</td><td>5.1</td><td>3.8</td><td>P=.02</td></tr><tr><td>I-TSS</td><td colspan="3">Not reported</td></tr><tr><td>TNSS</td><td>2.6</td><td>2</td><td>P<.05</td></tr><tr><td>TNNSS</td><td>2.5</td><td>1.9</td><td>P<.05</td></tr></table>I-instantaneous, R-reflective</td>
<td>Fifteen subjects withdrew from the spring study due to AEs (5-D, 10-PL) and approximately 10 in the Fall study (5-D, 5-PL). It was not clear from the study if these patients were included in the efficacy analysis.<br><br>No serious AEs were reported.<br>Somnolence was similar in both groups.</td>
</tr>
<tr>
<td>Wilson AM, etal [12]<br>R, DB, PC, CO<br><br>*Desloratadine vs. Fexofenadine in SAR<br>*49 patients<br>*2 weeks<br>*Not ITT (9 not included in final analysis)</td>
<td>*Skin prick positive for grass pollen<br>*Present and past hx of SAR requiring treatment.</td>
<td>Desloratadine 5 mg/d<br>Fexofenadine 180 mg/d<br>Patients received PL for 7-10 days (run-in) prior to active treatment and between active treatments (wash-out).<br><br>After blowing their nose, patients inspired forcefully through their nose with their mouths closed bid. Patients also recorded their allergic symptoms bid.</td>
<td>1) Peak nasal inspiratory flow (sensitive method for assessing nasal function).<br>2) TNSS, TNNSS</td>
<td>PL reflects baseline values:<br><table><tr><th>Measure</th><th>PL</th><th>D</th><th>P</th></tr><tr><td>PNIF (L/min)</td><td>122</td><td>133</td><td>P<.05</td></tr><tr><td>TNSS</td><td>3.4</td><td>2.6</td><td>P<.05</td></tr><tr><td>TNNSS</td><td>1.4</td><td>1</td><td>NS</td></tr></table><br><table><tr><th>Measure</th><th>PL</th><th>Fex</th><th>P</th></tr><tr><td>PNIF (L/min)</td><td>126</td><td>136</td><td>P<.05</td></tr><tr><td>TNSS</td><td>3.2</td><td>2.5</td><td>P<.05</td></tr><tr><td>TNNSS</td><td>1.2</td><td>0.9</td><td>NS</td></tr></table>There were no differences in PNIF or other allergy symptoms between D and Fex.</td>
<td>No differences in reported AEs between active groups or PL. There were no reports of increased drowsiness.<br><br>Nine patients withdrew from study. Five before first active treatment phase. One patient in the D group withdrew due to exacerbation of the SAR.</td>
</tr>
</table>

<table>
<tr>
<td>Ring J, etal. [13]<br>R, DB, PC, MC<br><br>*Desloratadine vs. placebo in CIU<br>*190 patients<br>*6 weeks<br>*Not ITT (28 patients excluded from efficacy analysis)</td>
<td>*12 years or ><br>* 6-week hx of CIU with active flare 3 weeks prior to screening.<br>* Moderate disease severity with pruritis and wheals present ≥3 days/week</td>
<td>Desloratadine 5 mg/d or placebo qd for 6 weeks.<br><br>Patients scored the severity of their symptoms for the preceding 12 hr (reflective) and at the time of assessment (instantaneous) bid.</td>
<td>1) Symptoms were evaluated on a 4-point scale bid: (0=none, 3=severe) pruritis (primary endpoint), number of hives, size of largest hives. The sum of these scores was the total symptom score (TSS).<br>2) Reflective scores were used to evaluate interference with sleep (am) and daily activities (pm).<br>3) CIU severity was assessed jointly by patient and investigator after the diaries were reviewed using the same 4-point scale.<br>4) Therapeutic response was assessed jointly by patient and investigator using a 5-point scale: (1=complete relief, 5=treatment failure).</td>
<td>1) Mean reduction in am/pm reflective pruritis score from baseline in the first 7 days:
<table>
<tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr>
<tr><td>Pruritis</td><td>1.22</td><td>0.49</td><td>P<.001</td></tr>
</table>
Mean % reduction in am/pm reflective pruritis score from baseline at 6 weeks: (Mean scores not provided)
<table>
<tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr>
<tr><td>Pruritis</td><td>74</td><td>48.7</td><td>P<.001</td></tr>
</table>
Mean % reduction in am instantaneous pruritis score from baseline at 6 weeks:
<table>
<tr><th>Measure</th><th>D</th><th>PL</th><th>P</th></tr>
<tr><td>Pruritis</td><td>68.9</td><td>46</td><td>P=.033</td></tr>
</table>
2) Although no actual values or percentages provided, authors commented that desloratadine improved sleep and daily activities statistically more than placebo at 6 weeks but no p value provided. Number and size of hives was also significantly reduced in the desloratadine vs. placebo group.<br>3) Authors reported significant improvement in CIU with desloratadine vs. placebo (p=0.002).<br>4) Assessment of response was also reported to be significantly in favor of desloratadine vs. placebo (no statistical values provided).</td>
<td>No patient withdrew due to treatment related AEs.<br><br>15% of randomized patients not included in the efficacy analysis for various reasons.</td>
</tr>
</table>

AEs=adverse events, CO=crossover, D=desloratadine, DB=double-blind, Fex=fexofenadine, hx=history, ITT=intent to treat, MC=multicenter, NC=nasal congestion, p=p-value, PC=placebo-controlled, PL=placebo, PNIF=peak nasal inspiratory flow, R=randomized, RAST=radioallergosorbent test, SAR=seasonal allergic rhinitis, TNNSS=total nonnasal symptom score, TNSS=total nasal symptom score, TSS=total symptom score

## Acquisition Cost

**Table 6.**

| Drug | Cost/Dose($) | Cost/Month($) |
|---|---|---|
| Desloratadine 5 mg | 1.36 | 40.80 |
| Fexofenadine 60 mg bid | 0.59 | 35.40 |
| Fexofenadine 180 mg SR qd | 1.29 | 38.70 |
| Loratadine 10 mg qd | 0.38 | 11.40 |

## Conclusion

Desloratadine is the major orally active metabolite of loratadine. It is FDA approved for the management of signs and symptoms of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria. There is only one published comparative trial of desloratadine to another second-generation antihistamine and only one published trial of desloratadine versus placebo in the management of chronic idiopathic urticaria. There are currently no published trials assessing the safety and effectiveness of desloratadine in perennial allergic rhinitis. Although the evidence is relatively limited, desloratadine does not appear to possess cardiac toxicity, has no published reports of QT prolongation or torsade de pointes and was well tolerated in controlled clinical trials.

There is no obvious advantage of using desloratadine over other available second-generation antihistamines on the VA National Formulary (loratadine). As a result, desloratadine should not be added to the VA National Formulary or VISN formularies.

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