

Drug Class Review on Newer Antihistamines

Update #2: Preliminary Scan Report #2

May 2008

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach. Oregon Health & Science University does not recommend or endorse any guideline or recommendation developed by users of these reports.

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OBJECTIVE

The purpose of this preliminary updated literature scan process is to provide the Participating Organizations with a preview of the volume and nature of new research that has emerged subsequent to the previous full review process. Provision of the new research presented in this report is meant only to assist with Participating Organizations' consideration of allocating resources toward a full update of this topic. Comprehensive review, quality assessment and synthesis of evidence from the full publications of the new research presented in this report would follow only under the condition that the Participating Organizations ruled in favor of a full update. The literature search for this report focuses only on new randomized controlled trials and actions taken by the FDA or Health Canada since the last report. Other important studies could exist.

Date of Last Update

April 2006 (searches through August 2005)

Date of Last Preliminary Update Scan

May 2007

Scope and Key Questions

The Oregon Evidence-based Practice Center wrote preliminary key questions, identifying the populations, interventions, and outcomes of interest, and based on these, the eligibility criteria for studies. These key questions were reviewed and revised by representatives of organizations participating in the Drug Effectiveness Review Project (DERP). The participating organizations of DERP are responsible for ensuring that the scope of the review reflects the populations, drugs, and outcome measures of interest to both clinicians and patients.

Key Questions

1. For outpatients with seasonal or perennial allergic rhinitis or urticaria, do newer antihistamines differ in effectiveness?
2. For outpatients with seasonal or perennial allergic rhinitis or urticaria, do newer antihistamines differ in safety or adverse events?
3. Are there subgroups of patients based on demographics (age, racial groups, gender), other medications (drug-drug interactions), comorbidities (drug-disease interactions), or pregnancy for which one newer antihistamine is more effective or associated with fewer adverse events?

Inclusion Criteria

Populations

Adult or pediatric outpatients with the following indications:

- Seasonal allergic rhinitis
- Perennial allergic rhinitis
- Urticaria

Interventions

Cetirizine hydrochloride (Zyrtec, Reactine)

Loratadine (Claritin)

Fexofenadine hydrochloride (Allegra)
Desloratadine (Clarinx)

Effectiveness outcomes

- Symptom alleviation (e.g., nasal congestion, rhinorrhoea, sneezing, itching and pain from skin irritations, etc.)
- Functional capacity (e.g., physical, social and occupational functioning, quality of life, etc.)
- Time to relief of symptoms (e.g., time to onset, duration of relief)
- Duration of effectiveness (e.g., switch rate)

Safety outcomes

- Overall adverse effects reported
- Withdrawals due to adverse effects
- Serious adverse events reported
- Specific adverse events or withdrawals due to specific adverse events (e.g., CNS effects, sedation, GI effects, dry mouth, urinary retention, etc.)

Study designs

1. For effectiveness, controlled clinical trials and systematic reviews
2. For safety, controlled clinical trials and observational studies

METHODS

Literature Search

To identify relevant citations, we searched Ovid MEDLINE from April 2007 to April 11, 2008 using terms for included drugs and indications, and limits for humans, English language, and randomized controlled trials or controlled clinical trials. We also searched FDA (<http://www.fda.gov/medwatch/safety.htm>) and Health Canada (http://www.hc-sc.gc.ca/dhp-mpps/medeff/advisories-avis/prof/2008/index_e.html) websites for identification of new drugs, indications, and safety alerts. All citations were imported into an electronic database (EndNote v 9.0[®]) and duplicate citations were removed.

Study Selection

One reviewer assessed abstracts of citations identified from literature searches for inclusion, using the criteria described above.

RESULTS

Overview

Searches resulted in 33 citations. Of those, there are 15 new, potentially relevant trials. Titles and abstracts (where available) appear in Appendix A. Trials included:

- One single-dose head-to head trial of desloratadine vs fexofenadine in which the outcome was suppression of histamine-induced wheal-and-flare.

- 2 new reports from the Early Prevention of Asthma in Atopic Children Study (levocetirizine vs placebo)
- 2 placebo-controlled trials of fexofenadine in children aged 18 months to 2 years, and aged 2 years to 5 years
- 10 new placebo-controlled trials in adults:
 - 4 trials of cetirizine for allergic rhinitis
 - 3 trials of desloratadine (1 allergic rhinitis, 2 urticaria)
 - 2 trials of loratadine with wheal and flare outcomes in skin prick tests
 - 1 trial of fexofenadine for urticaria

New Drugs/Indications

- Over-the-counter cetirizine was FDA-approved in January 2008.
- The loratadine OTC label was revised to allow the phrase “indoor & outdoor allergies” on the principal display panel (PDP) and/or Drug Facts.

New Safety Alerts

No new safety alerts were identified.

Appendix A. Abstracts of potentially relevant trials of Newer Antihistamines (N=15)

Enomoto, T., T. Ide, et al. (2007). "Construction of an environmental exposure unit and investigation of the effects of cetirizine hydrochloride on symptoms of cedar pollinosis in Japan." Journal of Investigational Allergology & Clinical Immunology **17**(3): 173-81.

BACKGROUND: Cedar pollinosis is a widespread seasonal allergy that is unique to Japan. Environmental exposure units (EEU) assist in the development of effective therapeutic and preventive measures because outdoor studies are limited by seasonal variation in pollen exposure. **OBJECTIVES:** We constructed an EEU to conduct a randomized cross-over double-blind placebo-controlled study of the efficacy of cetirizine (Zyrtec), a second-generation antihistamine. **METHODS:** The spatial and temporal homogeneity of pollen distribution in the EEU was evaluated by counting the number of pollen grains on petroleum-jelly-smear glass slides and by real-time pollen monitors. In the clinical study, 20 volunteers with known cedar pollinosis were exposed to pollen for 5 hours, randomly allocated to receive either cetirizine hydrochloride or placebo 30 minutes after exposure. Symptoms and the degree of somnolence were recorded every 30 minutes for 5.5 hours. As a measure of psychomotor performance, the Uchida-Kraepelin test was used to determine work quantity and error rate. **Results:** The cedar pollen grains were scattered evenly in the exposure room. In the clinical study, symptom scores were elevated in both groups, showing significant symptom induction 30 minutes after exposure. Test drugs were administered 30 minutes after exposure, and 1 hour later patients in the cetirizine hydrochloride group experienced a significant decrease in sneezing, nose-blowing frequency, and nasal congestion compared with the placebo group. There were no significant differences between the 2 groups in terms of subjective somnolence or objective psychomotor performance. **CONCLUSION:** The first EEU in Japan was used successfully to evaluate cetirizine as a treatment for cedar pollinosis. The results confirmed those from studies in other countries, except for the degree of somnolence, which increased in both groups and may have been related to postprandial sleepiness.

Grob, J. J., P. Auquier, et al. (2008). "Quality of life in adults with chronic idiopathic urticaria receiving desloratadine: a randomized, double-blind, multicentre, placebo-controlled study." Journal of the European Academy of Dermatology & Venereology **22**(1): 87-93.

OBJECTIVE: To assess the effect of desloratadine on quality of life (QoL) in chronic idiopathic urticaria (CIU). **STUDY POPULATION:** Patients with a history of CIU (pruritus and weals lasting = 6 weeks) were included in this multicentre, randomized, double-blind placebo-controlled study that took place in dermatology centres throughout France. During the study, patients were randomized to receive desloratadine 5 mg daily or placebo for 42 days. **MAIN OUTCOME MEASURES:** Variation of the scores of two QoL dermatology-specific tools between baseline and day 42, the French translation version of the Dermatology Life Quality Index (DLQI) and the VQ-Dermato (a French-language scoring instrument). **RESULTS:** The intent-to-treat population comprised 137 patients [desloratadine (n = 65) or placebo (n = 72)]. Desloratadine treatment was associated with significantly greater improvements from baseline to day 42 compared with placebo in DLQI overall score (-6 vs. -2.2 points; P < 0.002) and VQ-Dermato score (18.5 vs. 29.1 points; P = 0.009). Mean scores for sleep disruption and disruption of daily

activities were significantly lower in the desloratadine group than in the placebo group from day 1 to the end of the study. **CONCLUSIONS:** Desloratadine 5 mg/day was associated with significant improvements in two separate dermatology-specific measures of QoL in patients with CIU. QoL proved to be a relevant primary outcome measure for therapeutic trials in CIU.

Hampel, F. C., B. Kittner, et al. (2007). "Safety and tolerability of fexofenadine hydrochloride, 15 and 30 mg, twice daily in children aged 6 months to 2 years with allergic rhinitis." Annals of Allergy, Asthma, & Immunology **99**(6): 549-54.

BACKGROUND: Antihistamines are an established first-line treatment for allergic rhinitis and are widely prescribed in infants for allergic symptoms. **OBJECTIVE:** To establish the safety and tolerability of fexofenadine hydrochloride in children aged 6 months to 2 years in 2 studies (T/3001 and T/3002). **METHODS:** Both studies had a multicenter, randomized, placebo-controlled design. Mean treatment duration was 8 days. Subjects were randomized (T/3001, n = 174; and T/3002, n = 219) to twice-daily fexofenadine hydrochloride, 15 or 30 mg, or placebo mixed with a standard vehicle. **RESULTS:** In the combined population, the incidence of treatment-emergent adverse events (TEAEs) was comparable between groups (placebo, 48.2% [96/199]; fexofenadine hydrochloride, 15 mg, 40.0% [34/85]; and fexofenadine hydrochloride, 30 mg, 35.2% [38/108]). Vomiting was the most common TEAE (placebo, 13.6%; fexofenadine hydrochloride, 15 mg, 14.1%; and fexofenadine hydrochloride, 30 mg, 5.6%). Most TEAEs were unrelated to study medication, as evaluated by investigators; those possibly related to study medication were mild or moderate in intensity. No clinical differences were seen between fexofenadine and placebo for vital signs, electrocardiographic results, or physical examination results. **CONCLUSION:** Fexofenadine hydrochloride, 15 or 30 mg, given for a mean duration of 8 days is well tolerated, with a good safety profile, in children aged 6 months to 2 years.

Ho, C.-Y. and C.-T. Tan (2007). "Comparison of antileukotrienes and antihistamines in the treatment of allergic rhinitis." American Journal of Rhinology **21**(4): 439-43.

BACKGROUND: The aim of this study was to compare the effect of antileukotriene (anti-LT), antihistamine, and a combination of anti-LT and antihistamine on the symptoms and nasal resistance in allergic rhinitis patients. **METHODS:** We performed a placebo-controlled study, with 120 persistent, moderate to severe allergic rhinitis patients randomly selected to receive the different treatments for 4 weeks: no treatment, 10 mg of cetirizine once per day, 20 mg of zafirlukast once per day, 20 mg of cafirlukast twice per day, a combination of 20 mg of zafirlukast and 10 mg of cetirizine once per day, or a combination of 20 mg of zafirlukast twice per day and 10 mg cetirizine once per day. The nasal secretion nitric oxide (NO) concentration, nasal symptom score, and nasal resistance were measured before and after treatment. **RESULTS:** Total symptom scores improved in each treated group compared with the control group ($p < 0.05$). Nasal obstruction significantly improved in the anti-LT-treated groups ($p < 0.05$). High-dose anti-LT or the combination of low-dose anti-LT and antihistamine significantly improved allergy symptoms compared with no treatment, low-dose anti-LT, or antihistamine alone ($p < 0.05$). Furthermore, anti-LT decreased NO concentration in nasal secretions ($p < 0.05$), regardless of the dose administered. **CONCLUSION:** These results suggest that

high-dose anti-LT alone or the combination of low-dose anti-LY and antihistamine can effectively treat allergic rhinitis.

Korsgren, M., M. Andersson, et al. (2007). "Clinical efficacy and pharmacokinetic profiles of intranasal and oral cetirizine in a repeated allergen challenge model of allergic rhinitis." Annals of Allergy, Asthma, & Immunology **98**(4): 316-21.

BACKGROUND: Intranasal and oral antihistamines are effective in treating allergic rhinitis. Studies comparing these routes of administration of an antihistamine regarding efficacy and pharmacokinetic profile are lacking. **OBJECTIVE:** To compare topical and oral routes of administration of cetirizine regarding efficacy, plasma exudation, and systemic drug levels in a repeated allergen challenge model of allergic rhinitis. **METHODS:** Oral cetirizine dihydrochloride, 10 mg once daily, and topical cetirizine dinitrate in a dose corresponding to 4.4 mg of the dihydrochloride salt twice daily were given to grass pollen-sensitive individuals for 12 days in a double-blind, placebo-controlled, crossover design. Timothy grass pollen allergen challenges were given once daily for 7 days using a nasal spray device. Nasal symptoms and peak inspiratory flow were recorded in the morning, 10 minutes after allergen challenge, and in the evening. The pharmacokinetics of the treatments was monitored in 8 patients. The remaining 28 patients were challenged topically with histamine 12 and 24 hours after the final topical and oral cetirizine doses, respectively. Nasal lavage levels of alpha2-macroglobulin were determined to evaluate histamine-induced mucosal plasma exudation. **RESULTS:** During the last 3 days of the repeated allergen challenge model, chronic symptoms were established. Both treatments reduced symptoms 10 minutes after allergen challenge ($P < .001$ vs placebo). Neither treatment reduced morning and evening symptoms or nasal peak inspiratory flow. Topical, but not oral, cetirizine reduced histamine-induced plasma exudation ($P < .01$ vs placebo) when systemic drug levels were similar in the 2 treatment regimens. **CONCLUSIONS:** Topical and oral cetirizine reduced acute nasal symptoms produced by allergen challenges in patients with established chronic symptoms. There were also antihistaminic effects of topical cetirizine not related to systemic drug levels.

Kupczyk, M., I. Kuprys, et al. (2007). "Ranitidine (150 mg daily) inhibits wheal, flare, and itching reactions in skin-prick tests." Allergy & Asthma Proceedings **28**(6): 711-5.

H(1)-receptor antagonists are known to suppress reactions in skin-prick tests (SPTs); however, the effect of H(2)-receptor antagonists, which are widely used in our everyday practice, remains unclear. The aim of this study was to determine the influence of ranitidine on wheal, flare, and itching sensation in SPTs. Twenty-one atopic patients (5 women and 16 men) with an average age of 28.04 years (SD, +/-8.24) were tested with histamine, codeine, negative control solution, and standard allergen extracts. Ranitidine (150 mg daily), loratadine (10 mg daily), or placebo were given to the volunteers for 5 days in a double-blind manner with 14 days of washout period. SPTs were applied to the volar surface of a forearm. There was no difference in wheal, flare, and itching between SPTs performed after placebo and washout period. The analysis revealed a statistically significant suppression of wheal and flare by ranitidine and loratadine ($p = 0.013$ and <0.00001 , respectively, for wheals after allergens solutions tests, Wilcoxon rank-sum test). We found a significant suppression of itching induced by ranitidine (reduction of 26.85%; $p = 0.005$) and loratadine (29.6%; $p = 0.005$) as compared with placebo ($p = 0.068$ versus washout). Our data show a suppressive effect of ranitidine on the wheal,

flare, and itching sensation in SPT. Because the sensitivity and specificity of skin testing requires withholding medication that could change the skin reactivity, it seems important to take into account the possible influence of H₂-receptor antagonists on allergy diagnosis and therapy.

Kupczyk, M., I. Kuprys, et al. (2007). "The effect of montelukast (10mg daily) and loratadine (10mg daily) on wheal, flare and itching reactions in skin prick tests." Pulmonary Pharmacology & Therapeutics **20**(1): 85-9.

Antileukotriene agents are widely used for the treatment of allergic conditions including bronchial asthma and allergic rhinitis. The influence of montelukast on skin reactivity has not been clearly evaluated. The aim of this study was to determine the effect of montelukast on wheal, flare and itching in skin prick tests (SPTs). **METHODS:** Fifteen atopic patients (5 women and 10 men) with average age 28.04 (SD±8.24) were tested with histamine, codeine, negative control solution and allergen extract (grasses). Montelukast (10mg), loratadine (10mg) or placebo were given to the volunteers for 5 days in a double-blind manner, followed by SPT, with 14 days of wash-out period. **RESULTS:** There was no differences in wheal, flare and itching ($p=0.205$; 0.086 and 0.069 , respectively, Wilcoxon rank-sum test) between SPT performed after placebo and wash-out period. The analysis revealed a statistically significant suppression of wheal and flare by loratadine ($p<0.05$ for all tested solutions). Pre-treatment with montelukast did not influence wheal size ($p=0.099$, 0.21 , 0.066 for histamine, codeine and allergens, respectively), but significantly reduced flare ($p=0.005$; 0.003 ; 0.02 for histamine, codeine and allergens, respectively). We found a significant suppression of itching produced by montelukast ($p=0.02$) and loratadine ($p=0.03$) as compared to placebo ($p=0.068$ vs. wash out). **CONCLUSIONS:** Our data show a tendency to suppressive effect of montelukast on flare and itching but not on wheal which is basic for SPT interpretation. We conclude that found suppression have little impact on clinical effectiveness of SPT as a diagnostic tool.

Meltzer, E. O. and S. A. Gillman (2007). "Efficacy of fexofenadine versus desloratadine in suppressing histamine-induced wheal and flare." Allergy & Asthma Proceedings **28**(1): 67-73.

To date, no published articles exist comparing the H₁-receptor antagonist activities of fexofenadine and desloratadine using the histamine-induced skin wheal-and-flare model. The aim of this study was to compare the efficacy of fexofenadine versus desloratadine in suppressing histamine-induced skin flares and wheals in adults and adolescents. This was a two-center, randomized, placebo-controlled, complete-crossover study. Subjects were administered either single-dose fexofenadine HCl, 180 mg; desloratadine, 5 mg; or placebo and their response to skin-prick testing with histamine and diluent was recorded at predetermined time intervals. The primary end point was change in size of histamine-induced summation skin flares. Secondary end points included change in skin wheal summation measurements, onset, duration, maximum percent suppression, and time to maximum suppression of flares and wheals. Fexofenadine suppressed skin flares significantly more than desloratadine from 2 to 6 hours, and wheals from 2 to 4 hours, 6 to 9 hours, and 12 hours posttreatment. In addition, fexofenadine suppressed flares more than placebo at all time points from 2 to 24 hours and wheals more than placebo at all time points from 2 to 12 hours posttreatment. Desloratadine suppressed flares significantly more than placebo from 6 to 10 hours and at 12 and 24 hours but suppressed wheals significantly versus placebo only at 10 hours. Fexofenadine had a faster onset of

flare suppression than desloratadine (1 hour versus 5 hours) and an equally rapid onset of wheal suppression. Fexofenadine HCl, 180 mg, was superior to desloratadine, 5 mg, in histamine-induced wheal-and-flare suppression, suggesting increased in vivo H1-receptor antagonist potency of fexofenadine versus desloratadine.

Milgrom, H., B. Kittner, et al. (2007). "Safety and tolerability of fexofenadine for the treatment of allergic rhinitis in children 2 to 5 years old." Annals of Allergy, Asthma, & Immunology **99**(4): 358-63.

BACKGROUND: The safety of fexofenadine has been examined extensively in adults and school-age children. However, the safety of fexofenadine in children younger than 6 years has not been reported to date. **OBJECTIVE:** To compare the safety and tolerability of twice-daily fexofenadine hydrochloride, 30 mg, and placebo in preschool children aged 2 to 5 years with allergic rhinitis. **METHODS:** This was a multicenter, double-blind, randomized, placebo-controlled, parallel-group study, conducted between February 29, 2000, and June 14, 2001. Participants were randomized to either fexofenadine hydrochloride, 30 mg, or placebo twice daily for a 2-week period. To facilitate dosing, capsule content was mixed with applesauce (approximately 10 mL). Safety assessments depended on date of entry into the study because of an amendment to the protocol. Before the amendment, assessments included physical examination, vital signs reporting (oral temperature, heart rate, and respiratory rate), and adverse event (AE) reporting. After the amendment, safety assessments included laboratory testing (blood chemistry and hematology profiles), physical examination, 12-lead electrocardiography, and vital signs (oral temperature, blood pressure, heart rate, and respiratory rate) and AE reporting. **RESULTS:** Treatment-emergent AEs were observed in 116 of 231 participants receiving placebo and 111 of 222 receiving fexofenadine. These AEs were possibly related to study medication in 19 (8.2%) and 21 (9.5%) of the participants receiving placebo and fexofenadine, respectively, and most frequently involved the digestive system. No clinically relevant differences in laboratory measures, vital signs, and physical examinations were observed. **CONCLUSIONS:** The findings show that fexofenadine hydrochloride, 30 mg, is well tolerated and has a good safety profile in children aged 2 to 5 years with allergic rhinitis.

Ortonne, J.-P., J.-J. Grob, et al. (2007). "Efficacy and safety of desloratadine in adults with chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled, multicenter trial." American Journal of Clinical Dermatology **8**(1): 37-42.

BACKGROUND AND OBJECTIVE: Chronic idiopathic urticaria (CIU), a condition characterized by pruritus and wheals, can cause patients physical and psychological distress. Desloratadine, a second-generation histamine H(1) receptor antagonist (antihistamine), is a first-line treatment option for CIU. The objective of this study was to evaluate the efficacy and safety of once-daily desloratadine 5mg versus placebo for the treatment of CIU symptoms and disease severity in adults. **METHODS:** This was a randomized, placebo-controlled, multicenter trial of 137 adult patients with active CIU who received oral once-daily desloratadine 5mg or placebo for 6 weeks. Outcome measures included pruritus severity, number of wheals, and the size of the largest wheal. Patients assessed signs and symptoms on a four-point scale twice daily. The overall therapeutic response at the end of the 6-week treatment period was also rated. **RESULTS:** Desloratadine treatment was associated with significant improvements compared with

placebo in pruritus scores and in the size of the largest wheals as early as day 1. These improvements continued through to the end of the trial. The mean score for the number of wheals was significantly lower in the desloratadine group than in the placebo group on days 14 and 42 ($p < \text{or} = 0.016$). Overall improvement in CIU (complete, marked, or moderate therapeutic response) was also greater at the end of the study in the desloratadine group compared with placebo ($p < 0.001$). Adverse events occurred with similar frequency among desloratadine- and placebo-treated patients. **CONCLUSION:** Once-daily desloratadine 5mg is well tolerated and superior to placebo in reducing pruritus and wheals associated with CIU. Desloratadine provided rapid and sustained relief of CIU symptoms as early as after the first dose and maintained this effect until the end of the 6-week treatment period.

Philip, G., D. Williams-Herman, et al. (2007). "Efficacy of montelukast for treating perennial allergic rhinitis." *Allergy & Asthma Proceedings* **28**(3): 296-304.

Perennial allergic rhinitis (PAR) is a chronic inflammatory nasal condition in individuals exposed year-round to allergens. This was a double-blind study of 15- to 85-year-old patients randomly allocated to montelukast, 10 mg (n=630), placebo (n=613), or the positive control cetirizine, 10 mg (n=122) for 6 weeks. The primary efficacy end point was change from baseline in Daytime Nasal Symptoms Score (DNSS; mean of congestion, rhinorrhea, sneezing, and itching scores, rated daily by patients [scale: 0=none to 3=severe]) averaged during the initial 4 weeks (primary analysis) or entire 6 weeks of treatment. Also assessed were combined post hoc results of primary end point data from this study and another similarly designed study (Patel P, et al. Randomized, double-blind, placebo-controlled study of montelukast for treating perennial allergic rhinitis, *Ann Allergy Asthma Immunol* 95:551, 2005). Over 4 weeks, montelukast showed numerical improvement over placebo in DNSS (least-squares mean difference of -0.04 [95% confidence interval (CI), -0.09, 0.01]); the difference between cetirizine and placebo was significant: -0.10 (95% CI, -0.19, -0.01). However, when averaged over 6 weeks, neither active treatment was significantly different from placebo. The Rhinoconjunctivitis Quality-of-Life score was significantly improved by montelukast ($p < 0.05$), but not by cetirizine, during 4 and 6 weeks. The treatment effect of montelukast, but not cetirizine, generally remained consistent through the 6 weeks of treatment. In pooled data, montelukast consistently improved DNSS versus placebo during all 6 weeks of treatment (-0.07 [95% CI, -0.10, -0.04]). In conclusion, montelukast produced numerical improvement in daytime nasal symptoms and significant improvement in quality of life. In a pooled post hoc analysis, montelukast provided consistent improvement in daytime nasal symptoms over 6 weeks, supportive of an overall benefit in PAR.

Pradalier, A., C. Neukirch, et al. (2007). "Desloratadine improves quality of life and symptom severity in patients with allergic rhinitis." *Allergy* **62**(11): 1331-4.

BACKGROUND: Desloratadine is associated with decreased signs and symptoms and improved nasal airflow in multiple clinical trials in patients with allergic rhinitis (AR). The effect of desloratadine on quality of life (QOL) in AR has not been widely reported to date. We compared the effects of desloratadine and placebo on QOL in seasonal AR using validated, disease-specific measures. **METHODS:** This was a multicenter, double-blind, randomized, parallel-group study of desloratadine 5 mg or placebo daily for 2

weeks in patients with symptomatic seasonal AR. QOL was assessed at baseline and at day 14 using the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). AR signs/symptoms and the global response to therapy were measured at baseline and at day 14; signs/symptoms were also rated AM/PM in patient diaries. Adverse events (AE) were recorded. RESULTS: Overall 234 patients received desloratadine and 249 received placebo. At day 14 desloratadine was associated with a significantly larger improvement from baseline in the mean total RQLQ score vs placebo ($P = 0.0003$). Desloratadine also led to significant improvements from baseline in all RQLQ sub-domains ($P < \text{or} = 0.043$). At day 14 significant decreases from baseline were noted in the desloratadine group for total nasal ($P = 0.0003$), total non-nasal ($P = 0.001$) and total symptoms scores ($P = 0.0001$). Morning AR symptoms were significantly decreased in the desloratadine group after 1 day of treatment. Desloratadine was well tolerated, with an AE rate similar to placebo. CONCLUSION: Significant reductions in signs and symptoms of AR with desloratadine treatment were accompanied by improved disease-specific QOL measures.

Simons, F. E. R. and G. Early Prevention of Asthma in Atopic Children Study (2007). "H1-antihistamine treatment in young atopic children: effect on urticaria." Annals of Allergy, Asthma, & Immunology **99**(3): 261-6.

BACKGROUND: There are few published, randomized, double-masked, placebo-controlled, clinical trials of interventions for urticaria in the pediatric population. OBJECTIVE: To study the effect of long-term treatment with the H1-antihistamine levocetirizine on urticaria in young atopic children. METHODS: In the randomized, double-masked, parallel-group Early Prevention of Asthma in Atopic Children Study, children with atopic dermatitis aged 12 to 24 months at enrollment received levocetirizine, 0.125 mg/kg, or matching placebo twice daily for 18 months. On a diary card, the child's caregiver recorded the days on which urticaria was observed. This was validated by the study investigator and entered into the electronic case report form, along with any additional relevant information. RESULTS: A total of 510 atopic children (mean +/- SEM age, 19.4 +/- 0.2 months) composed the intention-to-treat population. During the subsequent 18 months, 27.5% (70/255) of the children taking levocetirizine and 41.6% (106/255) of the children taking placebo experienced urticaria ($P < .001$). The mean +/- SEM number of urticaria episodes was 0.71 +/- 0.11 in those receiving levocetirizine and 1.71 +/- 0.25 in those receiving placebo ($P < .001$). The mean +/- SEM duration of urticaria episodes was 4.43 +/- 1.57 days in those receiving levocetirizine and 5.36 +/- 1.27 days in those receiving placebo ($P < .001$). CONCLUSIONS: Urticaria is common in atopic toddlers and deserves recognition as an important disorder that occurs early in the atopic march. Regular long-term treatment with levocetirizine effectively prevents and treats urticaria in young children. The results of this study strengthen the evidence base for the use of relatively nonsedating, second-generation H1-antihistamines in the pediatric population.

Simons, F. E. R. and G. Early Prevention of Asthma in Atopic Children Study (2007). "Safety of levocetirizine treatment in young atopic children: An 18-month study." Pediatric Allergy & Immunology **18**(6): 535-42.

There are more than 40 H(1)-antihistamines available worldwide. Most of these medications have never been optimally studied in prospective, randomized, double-masked, placebo-controlled trials in children. The aim was to perform a long-term study

of levocetirizine safety in young atopic children. In the randomized, double-masked Early Prevention of Asthma in Atopic Children Study, 510 atopic children who were age 12-24 months at entry received either levocetirizine 0.125 mg/kg or placebo twice daily for 18 months. Safety was assessed by: reporting of adverse events, numbers of children discontinuing the study because of adverse events, height and body mass measurements, assessment of developmental milestones, and hematology and biochemistry tests. The population evaluated for safety consisted of 255 children given levocetirizine and 255 children given placebo. The treatment groups were similar demographically, and with regard to number of children with: one or more adverse events (levocetirizine, 96.9%; placebo, 95.7%); serious adverse events (levocetirizine, 12.2%; placebo, 14.5%); medication-attributed adverse events (levocetirizine, 5.1%; placebo, 6.3%); and adverse events that led to permanent discontinuation of study medication (levocetirizine, 2.0%; placebo, 1.2%). The most frequent adverse events related to: upper respiratory tract infections, transient gastroenteritis symptoms, or exacerbations of allergic diseases. There were no significant differences between the treatment groups in height, mass, attainment of developmental milestones, and hematology and biochemistry tests. The long-term safety of levocetirizine has been confirmed in young atopic children.

Spector, S. L., R. Shikiar, et al. (2007). "The effect of fexofenadine hydrochloride on productivity and quality of life in patients with chronic idiopathic urticaria." *Cutis* **79**(2): 157-62. The present study examined the impact of once-daily fexofenadine hydrochloride (HCl) 180 mg on health-related quality of life (HRQL) in subjects with chronic idiopathic urticaria (CIU). This was a multicenter, randomized, double-blind, parallel-group, placebo-controlled study. Subjects completed the Dermatology Life Quality Index (DLQI) and the Work Productivity and Activity Impairment (WPAI) questionnaire at baseline and at weeks 2 and 4. The primary HRQL end point was mean change from baseline to week 4 in total DLQI score. Subjects in the fexofenadine HCl treatment group (n = 163) experienced significantly greater improvements in mean total DLQI score (P = .0219) and in the individual domains of symptoms and feelings (P = .0119) and personal relationships (P = .0091) compared with those in the placebo group (n = 91). Subjects who received fexofenadine HCl experienced less work productivity impairment, overall work impairment, and activity impairment than those who received placebo. The results indicated that once-daily fexofenadine HCl 180 mg improved the HRQL of subjects with CIU, as assessed by change in total DLQI score.