

Drug Class Review

Newer Antihistamines

Preliminary Scan Report #3

February 2015

Last Report: Update #2, May 2010

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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 to assist with Participating Organizations' consideration of allocating resources toward a full report update, a single drug addendum, or a summary review. 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 U.S. Food and Drug Administration (FDA) since the last report. Other important studies could exist.

Date of Last Update Report

Update #2, May 2010 (searches through December 2009)

Dates of Previous Scan Reports

Scan #1: November 2012

Scan #2: January 2014

Scope and Key Questions

The scope of the review and key questions were originally developed and refined by the Pacific Northwest Evidence-based Practice Center with input from a statewide panel of experts (pharmacists, primary care clinicians, pain care specialists, and representatives of the public). Subsequently, the key questions were reviewed and revised by representatives of organizations participating in the Drug Effectiveness Review Project. The Participating Organizations of Drug Effectiveness Review Project are responsible for ensuring that the scope of the review reflects the populations, drugs, and outcome measures of interest to both clinicians and patients. The Participating Organizations approved the following key questions to guide this review:

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 harms?
3. Are there subgroups of patients based on demographics (age, racial groups, gender), socioeconomic status, other medications (drug-drug interactions), co-morbidities (drug-disease interactions), or pregnancy for which one newer antihistamine is more effective or associated with fewer harms?

Inclusion Criteria

Populations

- Adult or pediatric outpatients with the following conditions:
 - Seasonal allergic rhinitis
 - Perennial allergic rhinitis
 - Urticaria (acute and chronic)
- Subgroups of interest included, but were not limited to, different races, ages (older adult compared with younger adult), concomitant use of other medications (in consideration of drug-drug interactions), persons with various comorbidities (pregnancy and consideration of drug-disease interactions), and sex.

Interventions

Table 1. Included drugs and their labeled indications

Drug	Trade name(s)	Labeled indications	Dosage form/Route
Cetirizine hydrochloride	Zyrtec®	SAR; PAR; Chronic Urticaria	Syrup/Oral
Loratadine	Claritin®	SAR; PAR; Chronic Urticaria	Tablet; ODT; Syrup; Capsule/Oral
Fexofenadine hydrochloride	Allegra®	SAR; PAR; Chronic Urticaria	Tablet; ODT; Suspension; Capsule/Oral
Desloratadine	Clarinex®	SAR; PAR; Chronic Urticaria	Tablet; ODT; Syrup/Oral
Levocetirizine	Xyzal®	SAR; PAR; Chronic Urticaria	Tablet; Solution/Oral
Azelastine	Astelin®	SAR	Spray; Metered/Nasal
	Astepro®	SAR; PAR	Spray; Metered/Nasal
Olopatadine	Patanase®	SAR	Spray; Metered/Nasal

Abbreviations: ODT, orally disintegrating tablet; PAR, perennial allergic rhinitis; SAR, seasonal allergic rhinitis.

Study designs (from previous update report)

1. Efficacy and effectiveness
 - a. Randomized controlled trials, controlled clinical trials, and systematic reviews of fair or better quality.
 - b. Direct comparisons (head-to-head studies) were preferred over indirect comparisons using active or placebo-controlled trials. Inclusion of indirect evidence will be considered where there is insufficient direct evidence.
 - c. Studies ≥ 1 week in duration were included.
 - d. Studies conducted in artificial study settings (for example, antigen exposure chambers) were not be included. Abstracts and conference proceedings are also excluded.
2. Harms
 - a. Randomized controlled trials, controlled clinical trials, pre-compared with post-design studies, and observational studies with comparative groups.

- b. To be included, reports about overall harms or adverse events had to report total withdrawals, withdrawals due to specific adverse events (for example, central nervous system effects, sedation, gastrointestinal effects, dry mouth, urinary retention, etc.), or the frequency and severity of these specific adverse events.

Outcomes

- Efficacy and effectiveness
 - Symptoms (nasal congestion, rhinorrhea, sneezing, itching and pain from skin irritations)
 - Functional capacity (physical, social and occupational functioning, quality of life)
 - Time to relief of symptoms (time to onset, duration of relief)
 - Duration of effectiveness (switch rate)
- Harms
 - Total withdrawals
 - Withdrawals due to adverse events
 - Serious adverse events or withdrawals due to specific adverse events (central nervous system effects, sedation, gastrointestinal effects, dry mouth, urinary retention)

METHODS FOR SCAN

Literature Search

To identify relevant citations, we searched Ovid MEDLINE® and Ovid MEDLINE® In-Process & Other Non-Indexed Citations from January 2014 through January 2015 using terms for included drugs. We limited results to randomized controlled trials and controlled clinical trials conducted in humans and published in English. We also searched the FDA website (<http://www.fda.gov/medwatch/safety.htm> and <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>) for identification of new drugs, new populations, and new serious harms. To identify new drugs, we also searched CenterWatch (<http://www.centerwatch.com>), a privately-owned database of clinical trials information, and conducted a limited internet search. To identify comparative effectiveness reviews, we searched the websites of the Agency for Healthcare Research and Quality (<http://www.ahrq.gov/>) (<http://www.effectivehealthcare.ahrq.gov/>), the Canadian Agency for Drugs and Technology in Health (<http://www.cadth.ca/>), the VA Evidence-based Synthesis Program (<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>), and University of York Centre for Reviews and Dissemination (<http://www.york.ac.uk/inst/crd/crdreports.htm>) - “Our Publications” and “Our Databases”). All citations were imported into an electronic database (EndNote X7) and duplicate citations were removed.

Study Selection

We included only potentially relevant randomized controlled trials, controlled clinical trials, and comparative effectiveness reviews. One reviewer assessed abstracts of citations identified from literature searches for inclusion, using the criteria described above.

RESULTS

New Drugs

Identified in this Preliminary Update Scan

None.

Identified in previous Preliminary Update Scan(s)

Dymista™ (azelastine hydrochloride and fluticasone propionate) was approved in May 2012 for the relief of symptoms of seasonal allergic rhinitis in patients 12 years of age and older who require treatment with both azelastine hydrochloride and fluticasone propionate for symptomatic relief.

New Serious Harms

Identified in this Preliminary Update Scan

None.

Identified in previous Preliminary Update Scan(s)

None.

Comparative Effectiveness Reviews

Identified in this Preliminary Update Scan

The Agency for Healthcare Research and Quality comparative effectiveness review identified in the previous scan was published on July 16, 2013. The review, entitled “Treatments for Seasonal Allergic Rhinitis” is potentially relevant, but would not stand in place of a DERP review because it does not include perennial allergic rhinitis or urticaria. The executive summary for this review can be found at the following link:

<http://www.effectivehealthcare.ahrq.gov/ehc/products/376/1587/allergy-seasonal-executive-130711.pdf>

No other new comparative effectiveness reviews were identified that would stand in place of a DERP review.

Identified in previous Preliminary Update Scan(s)

We identified a protocol of a potentially relevant comparative effectiveness review produced by the Agency for Healthcare Research and Quality Effective Health Care Program. See Appendix A for the key questions that describe the scope of the project.

Treatments for Seasonal Allergic Rhinitis, published online March 8, 2012

http://effectivehealthcare.ahrq.gov/ehc/products/376/1000/SAR_Protocol_20120308.pdf

Randomized Controlled Trials

Trials identified since the most recent Full Report

Medline searches for this scan resulted in 21 citations. Of these, 1 is a potentially relevant new head-to-head trial. This trial compared the effectiveness and safety of olopatadine, a newer

antihistamine, in treating chronic urticaria in comparison to the established second generation antihistamine levocetirizine.

Together with trials found in previous scans, we have identified a total of 26 potentially relevant new trials since the last update report (8 head-to-head and 18 placebo-controlled trials). Table 1 summarizes the populations and comparisons included in these studies. The majority of the head-to-head evidence pertains to levocetirizine in populations with allergic rhinitis or urticaria. The majority of the placebo-controlled trial evidence pertains to azelastine in populations with seasonal allergic rhinitis. Abstracts for head-to-head trials are provided in Appendix B. Abstracts for placebo-controlled trials are available upon request.

Table 2. Characteristics of potentially relevant head-to-head trials* (N=8)

Author, Year	N, Duration	Population	Comparison	Focus
Allergic Rhinitis				
Tzanetos, 2011	30, 1 week	Patients with perennial allergic rhinitis	Cetirizine vs. Levocetirizine	Sedation
Ciebiada, 2011	40, 32 weeks	Adults with allergic rhinitis	Desloratadine vs. Levocetirizine	Symptom relief and score
LaForce, 2010	NR, 14 days	Patients ≥12 years of age with seasonal allergic rhinitis	Olopatadine vs. Azelastine	Symptom relief and scores, harms
Urticaria				
Hong, 2010 (no abstract)	NR	Chronic idiopathic urticaria	Desloratadine vs. Levocetirizine	NR
Staevska, 2010	80, NR	Adults with urticaria	Desloratadine vs. Levocetirizine	Symptom relief and scores, harms
Okubo, 2013	51, 13 days	Patients with urticaria	Olopatadine vs. Cetirizine	Wheal, itching, quality of life
Sil, 2013	120, 9 weeks	Adults with chronic urticaria	Olopatadine 5 mg vs. Levocetirizine 5 mg	Urticaria activity and severity scores and adverse events
Other				
Wang, 2013	174, 2 weeks	Chinese patients with cutaneous pruritus	Cetirizine vs. Olopatadine	Symptom score, harms

*Shading indicates studies found in the current scan.

Placebo-controlled trials (N=18)

Azelastine

- Hampel, 2010 (seasonal allergic rhinitis)
- Howland, 2011 (seasonal allergic rhinitis)
- Meltzer, 2012 (seasonal allergic rhinitis)
- Meltzer, 2013 (*post-hoc*; seasonal allergic rhinitis)
- Shah, 2009 (seasonal allergic rhinitis)
- Van Bavel, 2009 (seasonal allergic rhinitis)

Desloratadine

- Bousquet, 2009 (intermittent allergic rhinitis)

- Bousquet, 2010 (persistent allergic rhinitis)
- Bousquet, 2013 (persistent allergic rhinitis)
- Weller, 2013 (chronic urticaria)

Fexofenadine

- Mosges, 2009 (seasonal allergic rhinitis)

Levocetirizine

- Hampel, 2009 (**2 studies**; chronic urticaria)
- Mansfield, 2010 (seasonal allergic rhinitis)
- Segall, 2010 (seasonal allergic rhinitis)

Olopatadine

- Berger, 2009 (children with allergic rhinitis)
- Okubo, 2010 (children with perennial allergic rhinitis)
- Yamamoto, 2010 (seasonal allergic rhinitis)

SUMMARY

No new drugs were identified in the present scan. One new drug, the azelastine hydrochloride and fluticasone propionate combination product Dymista™, has been identified since the most recent update report. No new serious harms have been identified since the last update report. One new comparative effectiveness review for which the protocol was identified in the previous scan has since been published. However, it would not stand in place of a DERP review on newer antihistamines because it pertains only to seasonal allergic rhinitis (not perennial allergic rhinitis or urticaria). No other potentially relevant new comparative effectiveness reviews have been identified since the last update report.

We have identified 26 new trials of newer antihistamines since the last update report (8 head-to-head trials and 18 placebo-controlled trials). One new head-to-head trial studying the effects of olopatadine versus levocetirizine on activity and severity scores and adverse events in adults with chronic urticaria was identified in the present scan.

APPENDIX A. SYSTEMATIC REVIEW PRODUCED BY THE EFFECTIVE HEALTH CARE PROGRAM

Treatments for Seasonal Allergic Rhinitis

The Key Questions

Question 1

What is the comparative effectiveness of pharmacologic treatments, alone or in combination with each other, for adults and adolescents (≥ 12 years of age) with mild or with moderate/severe seasonal allergic rhinitis (SAR)?

1. How does effectiveness vary with long-term (months) or short-term (weeks) use?
2. How does effectiveness vary with intermittent or continuous use?
3. For those with symptoms of allergic conjunctivitis, does pharmacologic treatment of SAR provide relief of eye symptoms (itching, tearing)?
4. For those codiagnosed with asthma, does pharmacologic treatment of SAR provide asthma symptom relief?

Question 2

What are the comparative adverse effects of pharmacologic treatments for SAR for adults and adolescents (≥ 12 years of age)?

1. How do adverse effects vary with long-term (months) and short-term (weeks) use?
2. How do adverse effects vary with intermittent or continuous use?

Question 3

For the subpopulation of pregnant women, what are the comparative effectiveness and comparative adverse effects of pharmacologic treatments, alone or in combination with each other, for mild and for moderate/severe seasonal allergic rhinitis (SAR)?

1. How do effectiveness and adverse effects vary with long-term (months) or short-term (weeks) use?
2. How do effectiveness and adverse effects vary with intermittent or continuous use?

Question 4

For the subpopulation of children (< 12 years of age), what are the comparative effectiveness and comparative adverse effects of pharmacologic treatments, alone or in combination with each other, for mild and for moderate/severe seasonal allergic rhinitis (SAR)?

1. How do effectiveness and adverse effects vary with long-term (months) or short-term (weeks) use?
2. How do effectiveness and adverse effects vary with intermittent or continuous use?

APPENDIX B. ABSTRACTS OF POTENTIALLY RELEVANT NEW HEAD-TO-HEAD TRIALS OF NEWER ANTIHISTAMINES (N=8)

*Shading indicates trials identified in the current scan

Ciebiada, M., M. Gorska-Ciebiada, et al. (2011). "Use of montelukast alone or in combination with desloratadine or levocetirizine in patients with persistent allergic rhinitis." American Journal of Rhinology & Allergy **25**(1): e1-6.

BACKGROUND: We assessed the course of treatment in patients with persistent allergic rhinitis (AR) treated with montelukast, levocetirizine, or desloratadine alone or combinations of antihistamine and montelukast.

METHODS: A 32-week randomized, double-blind, placebo-controlled, crossover, double-armed study in 40 adult patients with history of persistent AR, clinical allergy to house-dust mites, and a total nasal symptom score of at least 5 (congestion of at least 2) has been performed. Patients with asthma, chronic obstructive pulmonary disease, nonallergic rhinitis with clinical allergy associated with seasonal allergens, and other serious diseases were excluded. There were four 6-week treatment periods separated by 2-week washout periods. Twenty patients received either montelukast or antihistamine, a combination of montelukast and antihistamine, or placebo. The sequence of treatment was randomly assigned. Nasal symptoms were assessed using a 4-point scale at baseline, daily during the 1st week and on days 14, 21, 28, 35, and 42 of treatment.

RESULTS: Montelukast alone, levocetirizine alone, desloratadine alone, and the montelukast/antihistamine combinations significantly improved nasal symptoms during the first 24 hours. Improvement gradually increased during the 6 weeks of treatment, especially in patients receiving montelukast alone or in combination therapy with the antihistamine in both arms. Improvement at 42 days of treatment was significantly greater than that achieved on the 1st day of therapy in patients treated with the combination of montelukast and levocetirizine.

CONCLUSION: Montelukast alone or in combination with antihistamines gave a gradual increase in nasal symptom improvement within 6 weeks of treatment in patients with persistent AR.

Hong, J.-B., H.-C. Lee, et al. (2010). "A randomized, double-blind, active-controlled, parallel-group pilot study to compare the efficacy and sedative effects of desloratadine 5 mg with levocetirizine 5 mg in the treatment of chronic idiopathic urticaria." Journal of the American Academy of Dermatology **63**(5): e100-102.

LaForce, C. F., W. Carr, et al. (2010). "Evaluation of olopatadine hydrochloride nasal spray, 0.6%, used in combination with an intranasal corticosteroid in seasonal allergic rhinitis." Allergy & Asthma Proceedings **31**(2): 132-140.

The combination of intranasal antihistamines and intranasal corticosteroids results in superior relief of seasonal allergic rhinitis (SAR) symptoms compared with monotherapy. This study was designed to evaluate the safety and efficacy of olopatadine hydrochloride nasal spray, 0.6% (OLO), administered in combination with fluticasone nasal spray, 50 micrograms (FNS), relative to azelastine nasal spray, 0.1% (AZE), administered in combination with FNS in the treatment of SAR. This was a multicenter, double-blind,

randomized, parallel-group comparison of OLO + FNS versus AZE + FNS administered for 14 days to patients ≥ 12 years of age with histories of SAR. Efficacy assessments recorded by patients in a daily diary included nasal symptom scores. Safety was evaluated based on adverse events (AEs). Pretreatment values for reflective total nasal symptoms scores (rTNSS) were similar for both treatment groups. The mean (SD) 2-week average rTNSS was 4.28 (2.63) for OLO + FNS and 4.15 (2.63) for AZE + FNS; these scores were not statistically different between treatment groups. No significant differences ($p > 0.05$) between OLO + FNS and AZE + FNS were observed for the average 2-week percent changes from baseline in rTNSS or in the individual nasal symptoms (nasal congestion, rhinorrhea, itchy nose, and sneezing). Compared with baseline, both groups had statistically significant improvement in rTNSS ($p < 0.05$). No serious AEs were reported in either group during the study period. Overall, 19 AEs were reported in the OLO + FNS group and 29 AEs were reported in the AZE + FNS group. OLO, when administered adjunctively with FNS, is effective, safe, and well-tolerated in patients with SAR.

Okubo, Y., Y. Shigoka, et al. (2013). "Double dose of cetirizine hydrochloride is effective for patients with urticaria resistant: a prospective, randomized, non-blinded, comparative clinical study and assessment of quality of life." Journal of Dermatological Treatment **24**(2): 153-160.

OBJECTIVE: An increased dose of the prescribed drug or a change of the drug is recommended in the treatment for the patients with urticaria refractory to the standard dose of antihistamines. Efficacy and safety of doubling the dose of cetirizine were compared with olopatadine in the patients with symptoms like wheal or itching, despite the treatment with the standard dose of cetirizine.

METHODS: Cetirizine was administered at 10 mg once daily to 51 patients with urticaria for a mean of 10.1 ± 7.3 days (period A). Patients with inadequate responses were randomized to either cetirizine 20 mg once daily (dose-increase group) or olopatadine 5 mg twice daily (drug-change group) for a mean of 13.3 ± 8.3 days (Period B). The severity of wheal and itching, and the quality of life (QOL) measured by Skindex-16 were evaluated.

RESULTS: In period A, an adequate response was obtained in 64.7% (33/51). Nine patients each with inadequate response were randomized to either the drug-change or dose-increase groups. A significant improvement was observed in the severity of wheal and itching in the dose-increase group in period B. The QOL was significantly improved in all sub-scales of Skindex-16.

CONCLUSION: Doubling the dose of cetirizine may be efficacious to the patients with urticaria refractory to the regular dose of cetirizine.

Sil, A., et al. (2013). "Olopatadine versus levocetirizine in chronic urticaria: an observer-blind, randomized, controlled trial of effectiveness and safety." Journal of Dermatological Treatment **24**(6): 466-472.

OBJECTIVES: Chronic urticaria (CU) is characterized by frequent appearance of wheals for > 6 weeks. This study was undertaken to compare effectiveness and safety of olopatadine, a newer antihistamine with additional anti-inflammatory properties, in treating CU in comparison to the established second-generation antihistamine levocetirizine.

METHODS: A single center, assessor-blind, randomized (1:1), active-controlled, parallel group, Phase IV trial (CTRI/2011/08/001965) was conducted with 120 adult CU patients of

either sex. Subjects received either olopatadine (5 mg b.i.d.) or levocetirizine (5 mg/day) for 9 weeks, continuously for first 4 weeks and then on demand basis for last 5 weeks. Primary outcome measures were urticaria activity score (UAS) and urticaria total severity score (TSS). Routine hematological and biochemical tests and treatment-emergent adverse events were monitored for safety.

RESULTS: Data from 54 subjects on olopatadine and 51 on levocetirizine were analyzed for effectiveness. UAS and TSS values declined significantly with both drugs over the treatment period but the reduction was greater with olopatadine. Adverse event profiles were comparable with sedation being the commonest complaint.

CONCLUSIONS: Olopatadine is a safe and more effective alternative to levocetirizine in the treatment of CU.

Staevska, M., T. A. Popov, et al. (2010). "The effectiveness of levocetirizine and desloratadine in up to 4 times conventional doses in difficult-to-treat urticaria." Journal of Allergy & Clinical Immunology **125**(3): 676-682.

BACKGROUND: H(1)-antihistamines are first line treatment of chronic urticaria, but many patients do not get satisfactory relief with recommended doses. European guidelines recommend increased antihistamine doses of up to 4-fold.

OBJECTIVE: To provide supportive evidence for the European guidelines.

METHODS: Eighty tertiary referral patients with chronic urticaria (age range, 19-67 years) were randomized for double-blind treatment with levocetirizine or desloratadine (40/40).

Treatment started at the conventional daily dose of 5 mg and then increased weekly to 10 mg, 20 mg, or 20 mg of the opposite drug if relief of symptoms was incomplete. Wheal and pruritus scores, quality of life, patient discomfort, somnolence, and safety were assessed.

RESULTS: Thirteen patients became symptom-free at 5 mg (9 levocetirizine vs 4 desloratadine), compared with 28 subjects on the higher doses of 10 mg (8/7) and 20 mg (5/1). Of the 28 patients nonresponsive to 20 mg desloratadine, 7 became symptom-free with 20 mg levocetirizine. None of the 18 levocetirizine nonresponders benefited with 20 mg desloratadine. Increasing antihistamine doses improved quality of life but did not increase somnolence. Analysis of the effect of treatment on discomfort caused by urticaria showed great individual heterogeneity of antihistamine responsiveness: approximately 15% of patients were good responders, approximately 10% were nonresponders, and approximately 75% were responders to higher than conventional antihistamine doses. No serious or severe adverse effects warranting discontinuation of treatment occurred with either drug.

CONCLUSION: Increasing the dosage of levocetirizine and desloratadine up to 4-fold improves chronic urticaria symptoms without compromising safety in approximately three quarters of patients with difficult-to-treat chronic urticaria.

Tzanetos, D. B., J. M. Fahrenholz, et al. (2011). "Comparison of the sedating effects of levocetirizine and cetirizine: a randomized, double-blind, placebo-controlled trial." Annals of Allergy, Asthma, & Immunology **107**(6): 517-522.

BACKGROUND: Compared with placebo, levocetirizine has been found to be less sedating than cetirizine in separate trials. However, whether levocetirizine is less sedating than its parent drug cetirizine has not yet been studied in a randomized trial.

OBJECTIVE: To determine whether levocetirizine is less sedating than cetirizine.

METHODS: We conducted a randomized, double-blind, crossover, placebo-controlled trial examining sedation and allergy symptoms in patients with perennial allergic rhinitis who had previously reported significant sedation with cetirizine. Enrollment ran from January 28, 2009, to February 25, 2009. All patients completed the study by April 17, 2009. Thirty patients enrolled, and 29 patients completed the study (1 patient did not return her questionnaire). In a double-blind fashion, the 29 study participants received levocetirizine, 5 mg daily for 1 week, cetirizine, 10 mg daily for 1 week, and an equivalent placebo pill for 1 week in randomized order with washout periods before each treatment arm. At the end of each washout period and each treatment period, participants completed a 1-page questionnaire. This questionnaire included questions about sedation or sleepiness in the form of a modified Epworth Sleepiness Scale, a Likert scale measuring general or global sedation, and allergy symptoms as measured by the total rhinitis symptom score.

RESULTS: Sedation as measured by both the modified Epworth Sleepiness Scale and the Likert scale was not significantly different between the levocetirizine and cetirizine treatments.

CONCLUSIONS: In patients with a perceived history of sedation with cetirizine, most were able to tolerate levocetirizine. However, this controlled trial also suggests that many of these patients would tolerate cetirizine if given in a masked manner. Therefore, patients with a history of mild to moderate sedation with cetirizine are unlikely to experience a different sedation profile with levocetirizine. Copyright Copyright 2011 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Wang, T., Y. Liu, et al. (2013). "A multicenter, double-blind, randomized, noninferiority comparison of 14 days' treatment with oral olopatadine 10 mg or cetirizine 10 mg in Chinese adults with cutaneous pruritus." *Pharmacology* **91**(1-2): 117-122.

OBJECTIVES: To assess whether olopatadine hydrochloride (OH) was noninferior to cetirizine in the treatment of cutaneous pruritus (CP).

PATIENTS AND METHODS: Patients with CP presenting at seven centers in China were randomly allocated to double-blind treatment with 5 mg of OH orally twice a day or cetirizine 10 mg orally once a day for 2 weeks. Patients were followed up on days 7 and 14. Noninferiority was predefined as a 20% maximum difference in the reduction of symptom score reducing indices (SSRI). Both intention-to-treat (ITT) and per-protocol populations were analyzed.

RESULTS: 174 patients (86 receiving OH and 88 cetirizine) were included in the ITT population. In the ITT population, the mean reduction in SSRI was 0.640 ± 0.274 in the OH group and 0.603 ± 0.289 in the cetirizine group. The one-sided 97.5% CI (-0.047) met the criteria for noninferiority. Noninferiority was also demonstrated for SSRI in the per-protocol population, with reductions of 0.640 ± 0.271 with OH and 0.596 ± 0.287 with cetirizine (97.5% CI -0.043). The total effectiveness rate (TER) was similar in the OH (90.0%) and cetirizine (80.0%) groups. The corresponding one-sided 97.5% CI (-1.0%) also demonstrated noninferiority. The incidence of adverse events was 47.1% in the OH group and 41.4% in the cetirizine group ($p = 0.453$).

CONCLUSION: The efficacy of OH was noninferior to that of cetirizine in controlling itching indicating that it can be considered as a clinically relevant alternative therapy to cetirizine

for the management of CP in adult Chinese patients. Copyright 2013 S. Karger AG, Basel.