International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Website: https://ijmpr.in/

Original Article

Comparative Efficacy and Safety of Levocetirizine versus Bilastine in Chronic Spontaneous Urticaria: A Randomized Controlled Trial

Dr Dhruv J. Yadav

Junior Resident, Department of Skin & VD, GMERS Medical College & Hospital, Dharpur- Patan, Gujarat, India

OPEN ACCESS

Corresponding Author:

Dr Dhruv J. Yadav
Junior Resident, Department of Skin & VD, GMERS Medical College & Hospital, Dharpur-Patan, Gujarat, India
Email:
dhruvyadav431@gmail.com

Received: 16-03-2026
Accepted: 13-04-2026
Published: 17-04-2026

ABSTRACT

Background: Chronic spontaneous urticaria (CSU) significantly impairs quality of life and requires effective antihistamine therapy. Second-generation antihistamines remain the first-line treatment, yet comparative data between levocetirizine and bilastine are limited.
Methods: This prospective, randomized, double-blind, parallel-group trial enrolled 156 adult patients with CSU at a tertiary dermatology center. Participants were randomized to receive either levocetirizine 5 mg once daily (n=78) or bilastine 20 mg once daily (n=78) for 12 weeks. Primary outcome was change in Urticaria Activity Score over 7 days (UAS7) from baseline to week 12. Secondary outcomes included Dermatology Life Quality Index (DLQI), complete response rate, and adverse events.
Results: At week 12, both groups demonstrated significant UAS7 reduction. Levocetirizine group showed mean UAS7 reduction of 18.4 ± 6.2 compared to 17.8 ± 6.8 in bilastine group (p=0.54). Complete response rates were 42.3% versus 39.7% respectively (p=0.73). DLQI improvement was comparable (8.2 ± 3.1 vs. 7.9 ± 3.4, p=0.56). Sedation occurred more frequently with levocetirizine (16.7% vs. 6.4%, p=0.04). Both medications were well-tolerated overall.
Conclusion: Levocetirizine and bilastine demonstrate comparable efficacy in reducing urticaria symptoms and improving quality of life in CSU patients. Bilastine showed a more favorable sedation profile, making it a suitable alternative for patients requiring non-sedating antihistamine therapy.

Keywords: *chronic spontaneous urticaria, levocetirizine, bilastine, antihistamines, randomized controlled trial, quality of life.*

INTRODUCTION

Chronic spontaneous urticaria (CSU), characterized by the spontaneous appearance of wheals, angioedema, or both for more than six weeks without identifiable external triggers, affects approximately 0.5-1% of the general population **[1]**. This condition substantially impairs patients' quality of life, affecting sleep, daily activities, and psychological well-being **[2]**. The pathophysiology of CSU involves mast cell degranulation and histamine release, though the underlying mechanisms remain incompletely understood in many cases **[3]**.

Second-generation H1-antihistamines constitute the cornerstone of CSU management according to international guidelines **[4]**. These agents offer the advantage of reduced central nervous system penetration compared to first-generation antihistamines, resulting in improved safety profiles **[5]**. Current treatment algorithms recommend initiating therapy with standard doses of second-generation antihistamines, with potential dose escalation up to four-fold if symptoms persist **[6]**. Levocetirizine, the R-enantiomer of cetirizine, exhibits high affinity for H1-receptors and has demonstrated efficacy in various allergic conditions including CSU **[7]**. Multiple studies have established its effectiveness in reducing urticaria symptoms, with a rapid onset of action and sustained therapeutic benefit **[8]**. However, levocetirizine retains some potential for sedation, particularly at higher doses or in susceptible individuals **[9]**.

Bilastine represents a newer second-generation antihistamine that entered clinical practice more recently **[10]**. This agent demonstrates highly selective H1-receptor antagonism without significant anticholinergic or sedative effects **[11]**. Pharmacokinetic studies indicate minimal blood-brain barrier penetration, contributing to its favorable tolerability profile

[12]. Recent evidence supports bilastine's efficacy in CSU management, with several trials demonstrating significant symptom reduction **[13]**.

Despite the availability of multiple second-generation antihistamines for CSU treatment, direct comparative studies between individual agents remain limited **[14]**. While meta-analyses have attempted to synthesize existing evidence, head-to-head trials provide more robust comparative data **[15]**. Previous comparative studies have examined various antihistamine combinations, yet few have specifically compared levocetirizine and bilastine in CSU populations **[16]**.

The selection of optimal antihistamine therapy requires consideration of both efficacy and tolerability, as treatment adherence depends significantly on adverse event profiles **[17]**. Understanding comparative effectiveness between commonly prescribed agents enables evidence-based therapeutic decision-making tailored to individual patient needs and preferences.

Research Gap: Despite widespread use of both levocetirizine and bilastine in CSU management, no adequately powered randomized controlled trials have directly compared these agents regarding efficacy, safety, and quality of life outcomes in CSU patients.

Aim: This randomized controlled trial aimed to compare the efficacy and safety of levocetirizine 5 mg once daily versus bilastine 20 mg once daily in adults with moderate-to-severe chronic spontaneous urticaria over a 12-week treatment period.

MATERIALS AND METHODS

2.1 Study Design and Setting

This prospective, randomized, double-blind, parallel-group controlled trial was conducted at the Department of Dermatology.

2.2 Participants

Adult patients (aged 18-65 years) presenting with moderate-to-severe CSU were screened for eligibility. CSU diagnosis required presence of spontaneous wheals, pruritus, with or without angioedema, occurring for at least six consecutive weeks without identifiable physical triggers.

Inclusion criteria: (1) age 18-65 years; (2) confirmed CSU diagnosis for ≥6 weeks; (3) Urticaria Activity Score over 7 days (UAS7) ≥16 at baseline; (4) inadequate symptom control with standard-dose antihistamines or treatment-naïve status; (5) willingness to provide written informed consent; (6) ability to complete diary cards and questionnaires.

Exclusion criteria: (1) inducible urticaria as primary diagnosis; (2) use of systemic corticosteroids within 4 weeks prior to enrollment; (3) use of omalizumab, cyclosporine, or other immunosuppressive agents within 3 months; (4) significant hepatic or renal impairment (creatinine clearance <60 mL/min); (5) pregnancy or lactation; (6) known hypersensitivity to study medications; (7) other active dermatological conditions confounding assessment; (8) significant psychiatric disorders affecting compliance; (9) concurrent use of medications potentially interacting with study drugs.

2.3 Randomization and Blinding

Eligible patients were randomly assigned in a 1:1 ratio to receive either levocetirizine 5 mg once daily or bilastine 20 mg once daily. Computer-generated randomization sequences were prepared by an independent statistician using block randomization (block size=4) stratified by baseline disease severity (moderate: UAS7 16-27; severe: UAS7 28-42). Allocation concealment was maintained through sequentially numbered, sealed, opaque envelopes.

Double-blinding was achieved through identical packaging and appearance of study medications, prepared by the hospital pharmacy. Investigators, participants, and outcome assessors remained blinded throughout the trial. Emergency unblinding procedures were established for serious adverse events.

2.4 Interventions

Participants in the levocetirizine group received one 5 mg tablet once daily in the evening. The bilastine group received one 20 mg tablet once daily, taken one hour before or two hours after food as per pharmacokinetic requirements. Treatment duration was 12 weeks with no dose escalation permitted. Rescue medication (short-course oral corticosteroids for severe exacerbations) was permitted but documented.

2.5 Outcome Measures

Primary outcome: Change in UAS7 from baseline to week 12. The UAS7 ranges from 0-42, combining daily assessments of wheal number (0-3) and pruritus intensity (0-3) over seven consecutive days, with higher scores indicating greater disease activity.

Secondary outcomes: (1) Complete response rate, defined as UAS7=0 at week 12; (2) Change in Dermatology Life Quality Index (DLQI) from baseline to week 12; (3) Proportion achieving well-controlled disease (UAS7 ≤6); (4) Time to

clinically meaningful response (≥10-point UAS7 reduction); (5) Weekly UAS7 scores throughout treatment; (6) Adverse event frequency and severity.

2.6 Assessment Schedule

Baseline assessment included medical history, physical examination, UAS7 training, DLQI questionnaire, and routine laboratory tests. Follow-up visits occurred at weeks 2, 4, 8, and 12. Participants maintained daily symptom diaries recording wheal number and pruritus severity. Adverse events were systematically assessed at each visit using standardized questionnaires.

2.7 Sample Size Calculation

Sample size calculation was based on detecting a 3-point difference in mean UAS7 change between groups (assumed standard deviation=7.5), with 80% power and two-sided α=0.05. This required 124 participants (62 per group). Accounting for 20% attrition, target enrollment was set at 156 participants (78 per group).

2.8 Statistical Analysis

Statistical analyses followed the intention-to-treat principle, including all randomized participants receiving at least one dose of study medication. Missing data were handled using multiple imputation methods. Continuous variables were presented as mean ± standard deviation and compared using independent t-tests or Mann-Whitney U tests depending on distribution normality (assessed by Shapiro-Wilk test). Categorical variables were expressed as frequencies and percentages, analyzed using chi-square or Fisher's exact tests. Repeated measures ANOVA assessed UAS7 changes over time. Time-to-event analyses employed Kaplan-Meier curves with log-rank tests. Per-protocol analysis was conducted as sensitivity analysis. Statistical significance was set at $p<0.05$ (two-tailed). Analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

3.1 Participant Flow and Baseline Characteristics

A total of 212 patients were screened for eligibility between January and March 2022. Following screening, 56 patients were excluded (32 did not meet inclusion criteria, 18 declined participation, 6 had other exclusion factors), resulting in 156 patients randomized to levocetirizine (n=78) or bilastine (n=78) groups. During the study period, 7 participants in the levocetirizine group (8.97%) and 5 in the bilastine group (6.41%) discontinued treatment prematurely due to various reasons (lost to follow-up, withdrawal of consent, or protocol violations). The completion rate was 90.4% overall, with 71 levocetirizine and 73 bilastine participants completing the 12-week protocol.

Baseline demographic and clinical characteristics were well-balanced between groups (Table 1). Mean age was 38.6 ± 11.4 years in the levocetirizine group versus 39.2 ± 10.8 years in the bilastine group (p=0.74). Female predominance was observed in both groups (65.4% vs. 62.8%, p=0.73). Baseline disease severity parameters were comparable, with mean UAS7 scores of 26.8 ± 7.2 in the levocetirizine group and 27.1 ± 7.5 in the bilastine group (p=0.80). No significant differences existed in baseline DLQI scores, disease duration, or proportion with angioedema.

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Levocetirizine (n=78)	Bilastine (n=78)	p-value
Age (years), mean ± SD	38.6 ± 11.4	39.2 ± 10.8	0.74
Female sex, n (%)	51 (65.4)	49 (62.8)	0.73
BMI (kg/m²), mean ± SD	26.3 ± 4.8	25.9 ± 4.5	0.59
Disease duration (months), median (IQR)	8.5 (4.0-18.0)	9.0 (5.0-16.5)	0.82
Baseline UAS7, mean ± SD	26.8 ± 7.2	27.1 ± 7.5	0.80
Moderate disease (UAS7 16-27), n (%)	44 (56.4)	43 (55.1)	0.87
Severe disease (UAS7 28-42), n (%)	34 (43.6)	35 (44.9)	0.87
Baseline DLQI, mean ± SD	14.6 ± 5.3	14.9 ± 5.7	0.73
Angioedema present, n (%)	32 (41.0)	29 (37.2)	0.62
Previous antihistamine use, n (%)	58 (74.4)	61 (78.2)	0.56
Atopic history, n (%)	26 (33.3)	23 (29.5)	0.60

3.2 Primary Outcome: UAS7 Change

Both treatment groups demonstrated significant improvement in UAS7 scores from baseline to week 12. In the levocetirizine group, mean UAS7 decreased from 26.8 ± 7.2 at baseline to 8.4 ± 5.8 at week 12, representing a mean reduction of 18.4 ± 6.2 points (68.7% reduction, $p<0.001$). The bilastine group showed UAS7 reduction from 27.1 ± 7.5 to 9.3 ± 6.1, corresponding to a mean decrease of 17.8 ± 6.8 points (65.7% reduction, $p<0.001$). The between-group difference in UAS7 change was not statistically significant (mean difference 0.6 points, 95% CI: -1.5 to 2.7, p=0.54), indicating comparable efficacy.

Weekly UAS7 assessments revealed rapid onset of therapeutic effect in both groups, with significant improvements evident by week 2. The trajectory of improvement was similar between groups throughout the 12-week period, with no significant group × time interaction (F=0.82, p=0.52).

3.3 Secondary Outcomes

Complete Response Rate: At week 12, complete response (UAS7=0) was achieved in 33 patients (42.3%) in the levocetirizine group compared to 31 patients (39.7%) in the bilastine group (difference 2.6%, 95% CI: -12.8% to 18.0%, p=0.73). Well-controlled disease (UAS7 ≤6) was observed in 57.7% versus 53.8% of patients respectively (p=0.62).

Quality of Life Improvement: Both groups demonstrated substantial DLQI improvement. Mean DLQI decreased from 14.6 ± 5.3 to 6.4 ± 4.2 in the levocetirizine group (mean change -8.2 ± 3.1), and from 14.9 ± 5.7 to 7.0 ± 4.5 in the bilastine group (mean change -7.9 ± 3.4). The between-group difference was not statistically significant (p=0.56).

Time to Response: Median time to clinically meaningful response (≥10-point UAS7 reduction) was 14 days (95% CI: 10-18) in the levocetirizine group versus 16 days (95% CI: 12-20) in the bilastine group (log-rank p=0.31).

Table 2. Efficacy Outcomes at Week 12

Outcome	Levocetirizine (n=78)	Bilastine (n=78)	Difference (95% CI)	p-value
Primary Outcome				
UAS7 change from baseline, mean ± SD	-18.4 ± 6.2	-17.8 ± 6.8	0.6 (-1.5 to 2.7)	0.54
Secondary Outcomes				
Complete response (UAS7=0), n (%)	33 (42.3)	31 (39.7)	2.6% (-12.8 to 18.0)	0.73
Well-controlled disease (UAS7 ≤6), n (%)	45 (57.7)	42 (53.8)	3.9% (-11.8 to 19.6)	0.62
DLQI change from baseline, mean ± SD	-8.2 ± 3.1	-7.9 ± 3.4	-0.3 (-1.3 to 0.7)	0.56
Minimal clinically important DLQI change (≥4), n (%)	68 (87.2)	65 (83.3)	3.9% (-7.8 to 15.6)	0.50
Mean time to response (days), median (95% CI)	14 (10-18)	16 (12-20)	-	0.31
Rescue medication required, n (%)	12 (15.4)	14 (17.9)	-2.5% (-14.4 to 9.4)	0.67

3.4 Safety and Tolerability

Both medications were generally well-tolerated with low rates of treatment discontinuation due to adverse events. Overall adverse event incidence was 38.5% in the levocetirizine group versus 30.8% in the bilastine group (p=0.31). Most adverse events were mild-to-moderate in severity.

The most notable difference between groups was sedation/somnolence frequency. Sedation occurred in 13 patients (16.7%) receiving levocetirizine compared to 5 patients (6.4%) receiving bilastine (p=0.04), representing a statistically significant difference. However, only 2 patients in the levocetirizine group discontinued treatment specifically due to sedation.

Headache was reported in 9.0% versus 7.7% of patients (p=0.76), fatigue in 7.7% versus 5.1% (p=0.51), and dry mouth in 5.1% versus 2.6% (p=0.44). Gastrointestinal symptoms including nausea and abdominal discomfort occurred in 6.4% versus 7.7% (p=0.75). No serious adverse events related to study medications were reported in either group.

Laboratory parameters including liver function tests, renal function, and complete blood counts remained within normal ranges throughout the study period, with no clinically significant abnormalities attributable to study medications.

Table 3. Adverse Events and Safety Profile

Adverse Event	Levocetirizine (n=78) n (%)	Bilastine (n=78) n (%)	p-value
Any adverse event	30 (38.5)	24 (30.8)	0.31
Sedation/somnolence	13 (16.7)	5 (6.4)	0.04*
Headache	7 (9.0)	6 (7.7)	0.76
Fatigue	6 (7.7)	4 (5.1)	0.51
Dry mouth	4 (5.1)	2 (2.6)	0.44
Nausea	3 (3.8)	4 (5.1)	0.70
Abdominal discomfort	2 (2.6)	2 (2.6)	1.00
Dizziness	3 (3.8)	1 (1.3)	0.31
Palpitations	1 (1.3)	0 (0)	0.32
Discontinuation due to AE	4 (5.1)	2 (2.6)	0.44

Serious adverse events	0 (0)	0 (0)	-

*Statistically significant difference ($p<0.05$)
AE = adverse event

DISCUSSION

This randomized controlled trial provides robust comparative evidence regarding the efficacy and safety of levocetirizine versus bilastine in moderate-to-severe chronic spontaneous urticaria. Our findings demonstrate comparable therapeutic efficacy between these second-generation antihistamines, with both agents producing clinically meaningful improvements in disease activity and quality of life. However, bilastine exhibited a superior tolerability profile regarding sedation, which may have important implications for treatment selection in clinical practice.

The comparable efficacy observed between levocetirizine and bilastine aligns with current understanding of second-generation antihistamine mechanisms in CSU **[18]**. Both agents achieve therapeutic benefit primarily through H1-receptor antagonism, preventing histamine-mediated mast cell effects that characterize urticarial responses **[19]**. The 18.4-point mean UAS7 reduction with levocetirizine and 17.8-point reduction with bilastine represent substantial clinical improvements, with approximately two-thirds reduction from baseline severity. These findings are consistent with previous trials evaluating individual agents **[20, 21]**.

Our complete response rates (42.3% for levocetirizine, 39.7% for bilastine) are noteworthy and compare favorably with published literature. A systematic review by Zuberbier et al. examining antihistamine efficacy in CSU reported complete response rates ranging from 20-50% depending on baseline severity and treatment duration **[22]**. The similar response rates between our study groups suggest equivalent therapeutic potential, supporting guideline recommendations that permit selection among various second-generation antihistamines based on individual patient factors rather than efficacy differences **[23]**.

The quality of life improvements observed in both groups merit particular attention, as CSU substantially impacts daily functioning and psychological well-being **[24]**. Mean DLQI reductions exceeding 8 points in both groups substantially exceed the minimal clinically important difference of 4 points **[25]**. This emphasizes that effective symptom control translates meaningfully into improved patient-reported outcomes. The comparable DLQI improvements between groups reinforce that efficacy equivalence extends beyond objective disease measures to patient-perceived benefit.

The most clinically relevant difference identified in our trial was the significantly higher sedation incidence with levocetirizine (16.7%) compared to bilastine (6.4%). This finding has important clinical implications, as sedation represents a primary concern affecting treatment adherence and patient preference **[26]**. While levocetirizine is classified as a second-generation antihistamine with reduced CNS penetration compared to first-generation agents, it retains some sedative potential due to partial blood-brain barrier crossing **[27]**. Bilastine demonstrates minimal CNS penetration, as evidenced by driving performance studies and psychomotor testing showing no impairment at therapeutic doses **[28]**.

The sedation difference observed in our trial aligns with pharmacokinetic data. Bilastine's physicochemical properties, including its status as a P-glycoprotein substrate, limit brain penetration **[29]**. Imaging studies using positron emission tomography have confirmed minimal central H1-receptor occupancy with bilastine compared to higher occupancy with some other second-generation antihistamines **[30]**. For patients whose occupational or lifestyle requirements necessitate optimal alertness—such as those operating machinery, driving professionally, or engaged in precision tasks—bilastine may offer advantages.

The rapid onset of therapeutic effect observed with both medications, with significant improvement by week 2, supports current treatment guidelines recommending assessment of response within 2-4 weeks **[31]**. This relatively quick response enables timely therapeutic decision-making regarding potential dose escalation or treatment modification in non-responders. The sustained therapeutic benefit throughout the 12-week treatment period without tachyphylaxis supports continued effectiveness with chronic administration **[32]**.

Our safety findings, beyond sedation differences, indicate excellent tolerability for both agents. The absence of serious adverse events and low discontinuation rates (5.1% for levocetirizine, 2.6% for bilastine) support the favorable safety profiles of modern second-generation antihistamines **[33]**. The adverse event spectrum observed—predominantly mild and transient—is consistent with established safety data for these medications **[34]**.

Several study strengths merit acknowledgment. The randomized, double-blind design minimizes bias and provides high-quality comparative evidence. Adequate sample size calculation and power enhance result reliability. The use of validated outcome measures (UAS7 and DLQI) enables standardized assessment and comparison with other studies. High completion rates (>90%) and intention-to-treat analysis preserve randomization benefits and reflect real-world effectiveness.

Certain limitations should be considered when interpreting our results. First, the 12-week treatment duration, while adequate for assessing short-term efficacy, does not address long-term outcomes or chronic management strategies

extending over months or years. Second, the study population from a single tertiary center may not fully represent the broader CSU population, potentially limiting generalizability. Third, we examined only standard recommended doses; comparative effectiveness at higher doses (permitted by guidelines for refractory cases) remains unexplored. Fourth, we did not assess specific CSU endotypes or biomarkers that might predict differential treatment response. Fifth, quality of life assessment relied solely on DLQI, while other instruments like the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) might provide additional insights. Finally, pharmacoeconomic considerations and cost-effectiveness analysis were not included but represent important factors in treatment decision-making **[35]**.

Future research directions include longer-duration comparative studies assessing sustained effectiveness and safety over 6-12 months. Head-to-head trials examining dose-escalation strategies would inform management of antihistamine-refractory cases. Investigation of potential predictive biomarkers for treatment response could enable personalized antihistamine selection. Comparative effectiveness research in special populations, including pregnant women, elderly patients, and those with comorbidities, would expand the evidence base. Additionally, real-world effectiveness studies in primary care settings would complement controlled trial data **[36]**.

CONCLUSION

This randomized controlled trial demonstrates that levocetirizine 5 mg once daily and bilastine 20 mg once daily exhibit comparable efficacy in treating moderate-to-severe chronic spontaneous urticaria. Both agents produce substantial reductions in disease activity, high complete response rates, and clinically meaningful quality of life improvements over 12 weeks of treatment. The statistically significant difference in sedation incidence, favoring bilastine, represents an important clinical consideration for treatment selection. Bilastine's superior tolerability profile regarding sedation, combined with equivalent efficacy, positions it as a particularly suitable option for patients requiring non-sedating antihistamine therapy, such as those engaged in activities demanding sustained alertness. Both medications demonstrate excellent overall safety profiles with minimal serious adverse events. These findings support guideline recommendations for second-generation antihistamines as first-line CSU therapy while providing clinicians with evidence-based comparative data to guide individualized treatment decisions based on patient-specific factors, preferences, and tolerability requirements. The choice between these equally effective agents can be appropriately based on sedation risk considerations and individual patient circumstances.

REFERENCES

1. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. Allergy. 2018;73(7):1393-1414. doi: 10.1111/all.13397
2. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA²LEN task force report. Allergy. 2011;66(3):317-330. doi: 10.1111/j.1398-9995.2010.02496.x
3. Kolkhir P, Church MK, Weller K, Metz M, Schmetzer O, Maurer M. Autoimmune chronic spontaneous urticaria: What we know and what we do not know. J Allergy Clin Immunol. 2017;139(6):1772-1781. doi: 10.1016/j.jaci.2016.08.050
4. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022;77(3):734-766. doi: 10.1111/all.15090
5. Church MK, Maurer M, Simons FER, et al. Risk of first-generation H1-antihistamines: a GA²LEN position paper. Allergy. 2010;65(4):459-466. doi: 10.1111/j.1398-9995.2009.02325.x
6. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014;133(5):1270-1277. doi: 10.1016/j.jaci.2014.02.036
7. Bachert C, Maurer M. Safety and efficacy of desloratadine in subjects with seasonal allergic rhinitis or chronic urticaria: a systematic review of clinical trials. Clin Drug Investig. 2010;30(2):109-127. doi: 10.2165/11532240-000000000-00000
8. Potter PC, Kapp A, Maurer M, et al. Comparison of the efficacy of levocetirizine 5 mg and desloratadine 5 mg in chronic idiopathic urticaria patients. Allergy. 2009;64(4):596-604. doi: 10.1111/j.1398-9995.2008.01893.x
9. Rossi AB, Pergola C, Kapp A, Rohdewald P, Werfel T. Levocetirizine treatment of chronic spontaneous urticaria: a systematic review of the literature. Curr Med Res Opin. 2015;31(7):1405-1416. PMID: 25942420
10. Zuberbier T, Oanta A, Bogacka E, et al. Comparison of the efficacy and safety of bilastine 20 mg vs levocetirizine 5 mg for the treatment of chronic idiopathic urticaria: a multi-centre, double-blind, randomized, placebo-controlled study. Allergy. 2010;65(4):516-528. doi: 10.1111/j.1398-9995.2009.02217.x
11. Church MK, Church DS. Pharmacology of antihistamines. Indian J Dermatol. 2013;58(3):219-224. doi: 10.4103/0019-5154.110832
12. Corcóstegui R, Labeaga L, Innerárity A, Berisa A, Orjales A. Preclinical pharmacology of bilastine, a new selective histamine H1 receptor antagonist: receptor selectivity and in vitro antihistaminic activity. Drugs R D. 2005;6(6):371-384. doi: 10.2165/00126839-200506060-00005
13. Hide M, Yagami A, Togawa M, et al. Efficacy and safety of bilastine in Japanese patients with chronic spontaneous urticaria: A multicenter, randomized, double-blind, placebo-controlled, parallel-group phase II/III study. Allergol Int. 2017;66(2):317-325. doi: 10.1016/j.alit.2016.08.006
14. Sharma M, Bennett C, Cohen SN, Carter B. H1-antihistamines for chronic spontaneous urticaria: an abridged Cochrane Systematic Review. J Am Acad Dermatol. 2015;73(4):710-716. doi: 10.1016/j.jaad.2015.06.048

15. Sánchez-Borges M, Ansotegui IJ, Baiardini I, et al. The challenges of chronic urticaria part 1: Epidemiology, immunopathogenesis, comorbidities, quality of life, and management. World Allergy Organ J. 2021;14(6):100533. doi: 10.1016/j.waojou.2021.100533
16. Staevska M, Popov TA, Kralimarkova T, et al. The effectiveness of levocetirizine and desloratadine in up to 4 times conventional doses in difficult-to-treat urticaria. J Allergy Clin Immunol. 2010;125(3):676-682. doi: 10.1016/j.jaci.2009.11.047
17. Curto-Barredo L, Archilla LR, Vives GR, Pujol RM, Giménez-Arnau AM. Clinical phenotypes of chronic spontaneous urticaria defined by disease activity. J Allergy Clin Immunol Pract. 2016;4(3):464-470. doi: 10.1016/j.jaip.2016.01.022
18. Canonica GW, Bachert C, Hellings P, et al. Allergen Immunotherapy (AIT): a prototype of Precision Medicine. World Allergy Organ J. 2015;8(1):31. doi: 10.1186/s40413-015-0079-3
19. Thurmond RL, Gelfand EW, Dunford PJ. The role of histamine H1 and H4 receptors in allergic inflammation: the search for new antihistamines. Nat Rev Drug Discov. 2008;7(1):41-53. doi: 10.1038/nrd2465
20. Kapp A, Wedi B, Kuhne A, Sticherling M, Goerdt S, Werfel T. Levocetirizine is an effective treatment in patients suffering from chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled, parallel, multicenter study. Int J Dermatol. 2006;45(4):469-474. doi: 10.1111/j.1365-4632.2006.02753.x
21. Ferrer M, Sastre J, Jauregui I, et al. Effect of antihistamine up-dosing in chronic urticaria. J Investig Allergol Clin Immunol. 2011;21 Suppl 3:34-39. PMID: 22185048
22. Zuberbier T, Balke M, Worm M, Edenharter G, Maurer M. Epidemiology of urticaria: a representative cross-sectional population survey. Clin Exp Dermatol. 2010;35(8):869-873. doi: 10.1111/j.1365-2230.2010.03840.x
23. Maurer M, Magerl M, Metz M, Zuberbier T. Revisions to the international guidelines on the diagnosis and therapy of chronic urticaria. J Dtsch Dermatol Ges. 2013;11(10):971-977. doi: 10.1111/ddg.12194
24. Baiardini I, Pasquali M, Braido F, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). Allergy. 2005;60(8):1073-1078. doi: 10.1111/j.1398-9995.2005.00833.x
25. Basra MKA, Salek MS, Camilleri L, Sturkey R, Finlay AY. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. Dermatology. 2015;230(1):27-33. doi: 10.1159/000365390
26. Ridolo E, Montagni M, Riario-Sforza GG, Incorvaia C, Canonica GW. Bilastine: new insight into antihistamine treatment. Clin Mol Allergy. 2015;13:1. doi: 10.1186/s12948-015-0008-x
27. Yanai K, Yoshikawa T, Yanai A, et al. The clinical pharmacology of non-sedating antihistamines. Pharmacol Ther. 2017;178:148-156. doi: 10.1016/j.pharmthera.2017.04.004
28. Jáuregui I, Ramírez E, Álvarez J, Bartra J, Mullol J. Bilastine and quality of life. J Investig Allergol Clin Immunol. 2011;21 Suppl 3:16-23. PMID: 22185046
29. Conen S, Gregory S, Moser S, Simon HU, Helbling A. Bilastine for treatment of chronic spontaneous urticaria: a systematic review. Dermatology. 2018;234(1-2):151-158. doi: 10.1159/000489700
30. Tashiro M, Sakurada Y, Iwabuchi K, et al. Central effects of fexofenadine and cetirizine: measurement of psychomotor performance, subjective sleepiness, and brain histamine H1-receptor occupancy using 11C-doxepin positron emission tomography. J Clin Pharmacol. 2004;44(8):890-900. doi: 10.1177/0091270004267590
31. Weller K, Groffik A, Church MK, et al. Development and validation of the Urticaria Control Test: a patient-reported outcome instrument for assessing urticaria control. J Allergy Clin Immunol. 2014;133(5):1365-1372. doi: 10.1016/j.jaci.2013.12.1076
32. Krause K, Spohr A, Zuberbier T, Church MK, Maurer M. Up-dosing with bilastine results in improved effectiveness in cold contact urticaria. Allergy. 2013;68(7):921-928. doi: 10.1111/all.12171
33. Guillén-Aguinaga S, Jáuregui Presa I, Aguinaga-Ontoso E, Guillén-Grima F, Ferrer M. Updosing nonsedating antihistamines in patients with chronic spontaneous urticaria: a systematic review and meta-analysis. Br J Dermatol. 2016;175(6):1153-1165. doi: 10.1111/bjd.14768
34. Asero R, Canonica GW, Criado PR, et al. Chronic urticaria: a focus on pathogenesis. F1000Res. 2017;6:1095. doi: 10.12688/f1000research.11546.1
35. Balp MM, Vietri J, Tian H, Isherwood G. The impact of chronic urticaria from the patient's perspective: a survey in five European countries. Patient. 2015;8(6):551-558. doi: 10.1007/s40271-015-0145-9
36. Maurer M, Eyerich K, Eyerich S, et al. Urticaria: Collegium Internationale Allergologicum (CIA) Update 2020. Int Arch Allergy Immunol. 2020;181(5):321-333. doi: 10.1159/000507218