

ORIGINAL ARTICLE

Safety and efficacy of desloratadine in chronic idiopathic urticaria in clinical practice: an observational study of 9246 patients

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Abstract

Background Post-marketing surveillance studies (PMSS) of medications are often mandated by authorities, provide crucial insights for health services and are useful to define the clinical profiles of therapies. Desloratadine, a non-sedating, second-generation H₁-receptor antagonist, is an effective and well-tolerated treatment for chronic idiopathic urticaria (CIU).

Methods A PMSS in CIU patients evaluated the tolerability and efficacy of desloratadine in clinical practice. At Visit 1 (baseline), demographic and CIU history were recorded and patients/physicians rated the severity of CIU symptoms, interference with sleep/daily activities and the general state of urticaria. Patients also noted the use and effectiveness of previous antihistamine therapy. At the end of treatment (Visit 2), CIU symptom severity and other disease criteria were re-assessed. Adverse events reported during or $\leq$ 30 days after treatment were collected.

Results A total of 9246 patients with CIU participated (63% female). Itching, number of wheals and the size of the largest wheal decreased significantly from baseline with desloratadine therapy ($P < 0.0001$). Improvements in CIU-impaired sleep and daily activities were reported by 67% and 71% of patients, respectively ($P < 0.0001$). In patients that received previous therapy with cetirizine, loratadine or fexofenadine alone, patients rated the onset of efficacy of desloratadine as faster in 55.5%, 54.7% and 57.6% of cases, respectively. The incidence of adverse events was low (0.5% of patients) and no serious adverse events were reported.

Conclusions This large PMSS confirms evidence from multiple placebo-controlled trials that desloratadine is effective and well tolerated in the treatment of CIU.

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Keywordschronic idiopathic urticaria, desloratadine, H₁-receptor antagonist, outcomes research, quality of life**Conflicts of interest**

None declared

Introduction

Chronic urticaria (CU) is defined as the spontaneous appearance of pruritic wheals for at least 6 weeks and is often recurrent over many years. When no clear aetiology can be determined, CU is traditionally termed chronic idiopathic urticaria (CIU). The epidemiology of CIU remains unclear. However, studies limited to individual regions or institutions suggest that CIU has a lifetime prevalence of 0.5–3% in the general population.^{1–3}

Pruritus and wheals are cardinal signs and symptoms of CIU and may be accompanied by the variable presence of angio-oedema; patients with active disease suffer decrements in sleep (due to itch) and daily activities (due in part to the unsightly nature of wheals). Together, the signs and symptoms of CIU are associated with decreased quality of life as measured by dermatology-specific questionnaires.^{4,5}

Traditionally, CIU was ascribed to cases of chronic wheals of unknown origin. In many cases, it is now recognized that CIU is caused by an autoimmune process, namely anti-IgE or anti-FcεRI autoantibodies.^{6,7} In non-autoimmune cases of CIU, the diagnosis may be one of exclusion after ruling out an extensive list of environmental, ingested or infective causes.⁶ It has been suggested recently in European Academy of Allergology and Clinical Immunology/GA2LEN and European Dermatology Forum guidelines that 'CIU' be replaced by 'CU'.^{7,8} This is due to the recognition of autoimmune pathophysiology in many cases and because the practical clinical management of CU and CIU is essentially the same.⁶

Non-sedating, second-generation H₁ receptor antagonists are first-line therapy for CIU.⁸ Desloratadine is a potent, selective,

non-impairing H₁-receptor antagonist that in three large placebo-controlled, randomized, multicentre trials has been shown to provide significant reductions in the severities of pruritus and wheal size/number in patients with CIU.^{9–11} These reductions were seen as early as the first day of treatment and lasted for up to 6 weeks of treatment. In parallel, improvements in CIU-impaired sleep and daily activities also occurred. A recent placebo-controlled trial has shown that desloratadine therapy was associated with significant improvements in quality of life as measured using two validated dermatology-specific questionnaires.¹²

Post-marketing surveillance studies (PMSS) of medications are growing in importance as such studies can verify the safety profile obtained in smaller placebo-controlled trials. Such studies also permit an assessment of the efficacy of a medication in the everyday clinical setting, which includes a more diverse group of patients than those subjects that take part in studies designed for drug registration and approval. Increasingly, in some countries, such PMSS are mandated by the government. In Germany, the performance of non-interventional studies is regulated by guidance from the German Society of Medical Statistics and by the Bundesinstitut für Arzneimittel und Medizinprodukte (the Federal Institute for Drugs and Medical Products).^{13,14} Following the approval of desloratadine in Germany, a PMSS of the use of desloratadine in CIU was undertaken under these guidelines. This study, involving 9246 patients in Germany, is the largest study of any type conducted to date in the setting of CIU.

Methods

This was an observational PMSS conducted in Germany in 965 dermatology, allergology and general practices. The study design and the performance of the study followed the German guidelines on observational studies.^{13,14} Patients attending their physician for regular consultations regarding CIU were eligible for enrolment. Patients aged ≥ 12 years had to meet the criteria for treatment with desloratadine as outlined in the package insert (e.g. a physician's diagnosis of CIU and no contraindications to therapy). The exclusion criteria were sensitivity, allergy or previous adverse reaction to desloratadine or its excipients. Pregnant or lactating women were also excluded and any pregnancy (or pregnancy of their partner) that occurred during the study was recorded. Patients did not undergo any programmed washout of concurrent medication or other clinical intervention other than the beginning of desloratadine therapy according to the physician's clinical decision.

All patients provided informed written consent to the study, which was performed according to the Declaration of Helsinki and the legal obligations under German National Law.

There were two study visits. Visit 1 was at enrolment (baseline) when desloratadine therapy was started and Visit 2 at the end of the prescribed desloratadine treatment period. At each visit, both patients and physicians completed specially designed case report forms.

Visit 1

At Visit 1, the day desloratadine therapy was prescribed and planned to begin, demographic information and medical history were recorded. The duration of CIU and the previous use of antihistamine treatment for CIU (the following could be indicated either individually or as multiple treatments: loratadine, cetirizine, fexofenadine or 'other'). Patients rated the efficacy of previous antihistamine therapy on a 4-point scale as excellent (1), good (2), moderate (3) or poor (4). The prescribed dose and planned duration of desloratadine treatment was also recorded before therapy began.

Measures of CIU disease activity were recorded before starting desloratadine using the following 4-point scales severity scales, similar to those used in randomized controlled trials:

Assessment of itching:

- 0 = none (no symptoms)
- 1 = mild (present, but nearly unapparent, easily tolerated)
- 2 = moderate (clearly apparent, unpleasant, but tolerable)
- 3 = severe (hard to tolerate)

Number of wheals:

- 0 = no wheals
- 1 = 1–6 wheals
- 2 = 7–12 wheals
- 3 = more than 12 wheals

Diameter of the largest wheal:

- 0 = no wheals
- 1 = diameter < 1.25 cm
- 2 = diameter from 1.25 cm to 2.5 cm
- 3 = diameter > 2.5 cm

Impairment of sleep (assessments refer to the time after midnight):

- 0 = none (no impairment)
- 1 = mild (not disturbing; sufficient sleep)
- 2 = moderate (definite sleep impairment, average duration and depth of sleep; awaking several times)
- 3 = severe (considerable impairment of sleep; poor sleep).

Impairment of daily activities (assessments refer to the time after midday):

- 0 = none (no impairment)
- 1 = mild (not disturbing; daily activities almost fully possible; nearly normal)
- 2 = moderate (definite impairment of daily activities)
- 3 = severe (considerable impairment of daily activities or daily activities impossible)

General state of urticaria:

- 0 = none (no apparent signs/symptoms)
- 1 = mild (definite presence of signs/symptoms, which are nearly unapparent and easy to tolerate)
- 2 = moderate (clear sensation of signs/symptoms, which are unpleasant but tolerable)
- 3 = severe (signs/symptoms are hard to tolerate; impairment of daily activities and/or sleep)

Visit 2

At the end of the desloratadine treatment period prescribed by the physician, the patient returned and the CIU severity was rated as at Visit 1 in terms of assessment of the severity of itching, number of wheals, diameter of the largest wheal, impairment of sleep and daily activities and the general state of urticaria. In addition, the following assessments of therapeutic efficacy were made:

Assessment of the therapeutic response:

- 1 = complete relief (free of all symptoms)
- 2 = significant relief (considerable improvement in signs/symptoms, which still exist but do not disturb the patient)
- 3 = moderate relief (signs/symptoms are present and may be disturbing although a clear improvement can be observed)
- 4 = poor relief (signs/symptoms are present; only a minimal improvement can be observed)
- 5 = therapeutic failure (no relief; symptoms are unchanged or increased compared to before the start of desloratadine treatment)

Onset of efficacy of desloratadine in comparison with previous antihistamine treatment:

- 1 = slower onset than previous antihistamine treatment
- 0 = equal onset
- 1 = faster onset than previous antihistamine treatment

Global assessment of efficacy of previous antihistamine therapy or current desloratadine therapy:

- 1 = excellent
- 2 = good
- 3 = moderate
- 4 = inadequate/poor

Global assessment of tolerability (separately rated by physician and patient):

- 1 = excellent
- 2 = good
- 3 = moderate
- 4 = inadequate/poor

Assessment of compliance (physician rating only):

- 1 = excellent
- 2 = good
- 3 = moderate
- 4 = inadequate/poor

Adverse events

The prescribing doctor recorded all adverse events that were reported during the study and up to 30 days after the end of treatment with desloratadine. All serious adverse events that were reported during this period were recorded on a specific form. Pregnancy occurring in a patient or partner of a patient was documented, for administrative purposes, as a serious adverse event.

Statistical analysis

Data entered on case report forms were coded into a database (Access, Microsoft Corp.) and assessed for inconsistencies using

an electronic checking system. Coding and data analyses were performed by DABIO, Höhenkirchen, Germany. The number of patients with valid data for each study parameter was calculated from the case report forms. For continuous data, such as, symptom scores, the number of valid entries, the mean, the standard deviation and minimum and maximum values were calculated. With respect to categorical data, frequencies and percentages were calculated. The main endpoints were: itching, number of wheals and diameter of the biggest wheal. All symptoms were assessed using scores. Additional variables were the global assessments of the efficacy and tolerability, the impairments of sleep and daily activities and the general state of urticaria. All variables were evaluated descriptively for both visits and tested by the Wilcoxon signed rank test. A subanalysis was performed to identify subgroups of patients that reported receiving previous treatment with only one antihistamine (loratadine, cetirizine, fexofenadine and other). In these subgroups, the onset of efficacy rating for desloratadine, compared with each individual antihistamine, was reported. The rating of efficacy of previous antihistamine treatment was also extracted for the subgroups of patients that reported treatment with a single antihistamine.

Results

Demographics and disease characteristics

In total, 9246 patients with CIU took part in the study, of whom 5717 (62.5%) were female. The mean age was 43.2 years (range 2–101 year); the mean height was 171 cm (range: 104–205 cm); and mean weight was 71.1 kg (range: 20–178 kg; mean body mass index: 24.3; range 12–50). Concomitant diseases were present in 24.7% ($n = 2288$) of patients, which had been diagnosed on average 10.6 years previously. The most frequent concomitant diseases were atopic eczema ($n = 343$), hypertension ($n = 240$), allergic rhinitis/pollen allergy ($n = 238$), diabetes mellitus ($n = 151$) and asthma ($n = 87$). Of these patients, 1389 were receiving concomitant medical therapy, which included oral corticosteroids in 333 patients, topical corticosteroids in 808 patients, another antihistamine in 105 and other (unspecified) medications in 230 cases.

The mean duration of CIU was 24.9 months (range: 1–600 months). CIU had been treated previously with an antihistamine in 53.6% ($n = 4957$) of cases. Overall 32.7%, 28.0%, 15.8%, and 30.7% of the patients, respectively, reported taking cetirizine, loratadine, fexofenadine, or 'another' antihistamine. In general the efficacy of this previous antihistamine therapy was rated as good in less than a third of cases (29.2%) and moderate in 52.7% of cases.

Efficacy

The average duration of desloratadine treatment (period between Visit 1 and Visit 2) was 40.4 days (range: 1–238 days). Physicians rated compliance with desloratadine therapy as being excellent in 72.2% of cases, while a small minority of patients had poor compliance (0.6%).

Itching/pruritus. The severity of itching at the end of desloratadine treatment demonstrated a significant decrease as compared with Visit 1 ($P < 0.0001$). At Visit 1, most patients (79.1%) suffered from moderate or severe itching. By the end of the desloratadine treatment period, 86.1% of patients rated itching severity as none or mild (Fig. 1a). Overall, 83.4% of patients experienced a decrease in the severity of itching during desloratadine therapy compared with 15.3% that had no change in itching and only 1.3% in whom itching worsened.

Number of wheals. The number of wheals score decreased significantly during treatment with desloratadine ($P < 0.0001$). At the start of the study, 67.5% of patients had at least 7 wheals, while only 5.3% had no wheals. At the end of the study, this situation had altered markedly, with 54.8% reporting no wheals, 32.1% reporting 1–6 wheals, 8.4% with 7–12 wheals and 4.7% with > 12 wheals (Fig. 1b). Overall, 79.2% of patients had an improvement in wheal number score, compared with 19.5% that had no change, and 1.3% of patients that experienced an increased number of wheals.

Size of the largest wheal. As with the number of wheals score, desloratadine treatment was associated with a significant decrease in the size of the largest wheal score ($P < 0.0001$). At the beginning of the study, only 5.1% of patients had no size-scored wheals, while after desloratadine therapy 54.7% of subjects reported no wheals. Similarly, the percentage of patients reporting at least one wheal > 2.5 cm in diameter fell from 22.2% at baseline to 4.0% after desloratadine therapy (Fig. 1c). In total, 71.9% of patients reported a decrease in the size of their largest wheal during desloratadine therapy, while 26.8% of patients reported no change and 1.3% reported an increase in the size of their largest wheal.

General state of urticaria. There was a statistically significant improvement in the general state of urticaria following desloratadine therapy as rated by physicians. At Visit 1, 19.6% had severe CIU, 54.4% moderate CIU, 24.4% mild CIU and 1.5% with no evidence of active disease. At the end of desloratadine therapy, only 2.3% of patients still had severe CIU, 11.3% had moderate CIU, 43.2% had mild CIU and the percentage of patients with no active disease had risen to 43.2% (Fig. 1d). The improvement in the general state of urticaria during desloratadine therapy was statistically significant ($P < 0.0001$).

Effect on sleep and daily activities. At Visit 1, only 19.8% of patients reported no CIU-related disturbance. At the end of desloratadine therapy, the percentage of patients with no sleep disturbance due to CIU had risen markedly to 70.3%. Overall, 67.3% of patients had improvement in sleep disturbance score with desloratadine therapy, while only 1.3% experienced a worsening of their sleep disturbance (Fig. 2a; $P < 0.0001$).

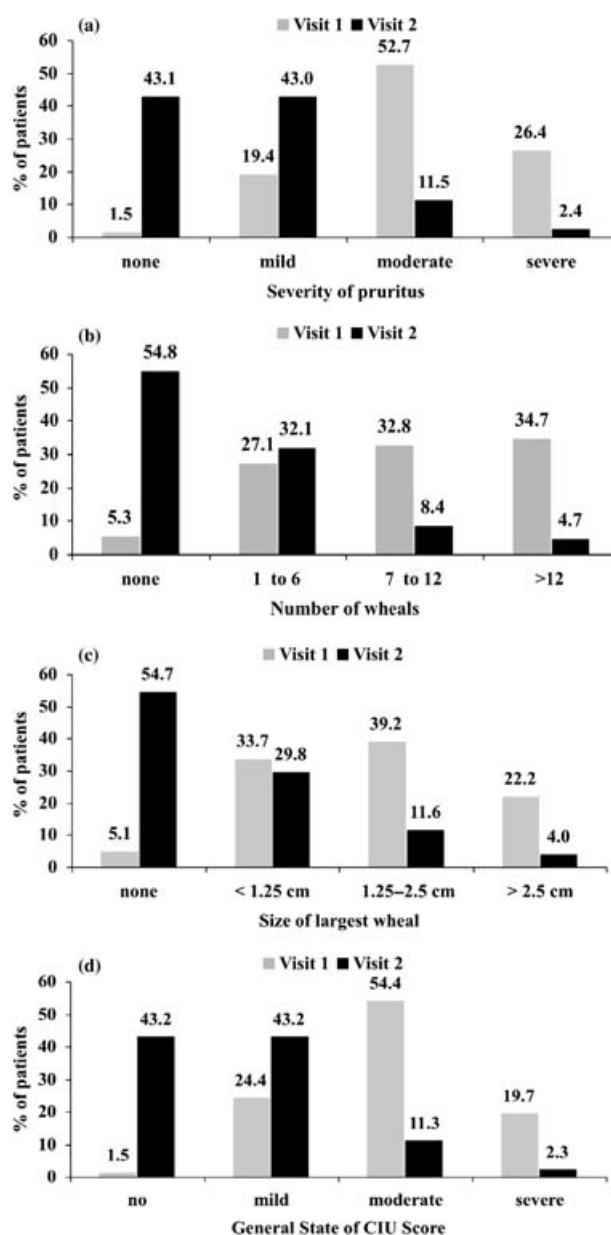


Figure 1 CIU signs and symptom scores at baseline (Visit 1) and at the end of desloratadine treatment (Visit 2). Panels show changes in the severity of (a) itching, (b) number of wheals, (c) size of largest wheal and (d) general state of urticaria. Numbers above columns denote percentage of patients per category. All decreases in the severities of signs and symptoms of CIU with desloratadine therapy were statistically significant ($P < 0.0001$).

At baseline, CIU-related disturbance in daily activities was frequent and only 14.1% of patients reported no disturbance of their daily activities. Desloratadine therapy was associated with a lessening of daily activity disturbance due to CIU; at the end of therapy, 67.2% of patients reported no disturbance of daily activities. In particular, the percentage of patients with moderate

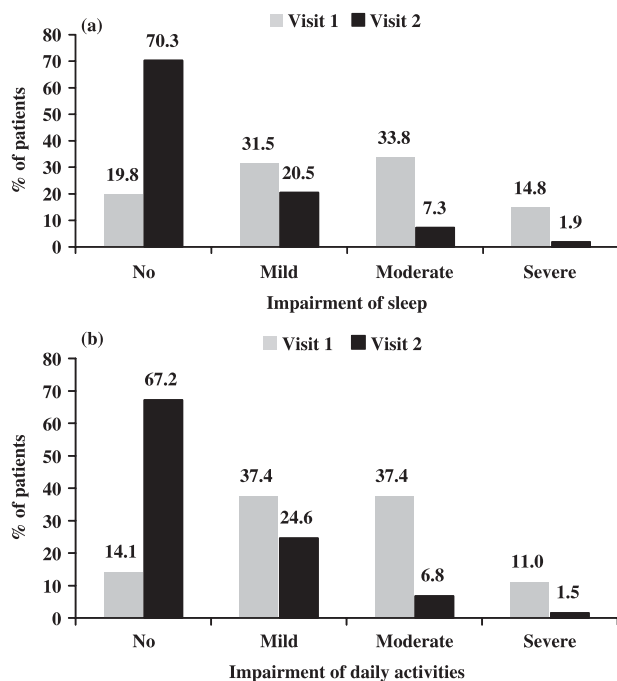


Figure 2 Effect of desloratadine therapy on CIU-related disturbances in (a) sleep and (b) daily activities. Numbers above columns denote percentage of patients per category. Overall decreases from baseline in the severities of sleep and daily activity disturbances were statistically significant ($P < 0.0001$).

disturbance of daily activities decreased from 37.4% at baseline to 6.8% after desloratadine therapy. The improvement from baseline in CIU-related disturbance of daily activities was statistically significant ($P < 0.0001$), with 71.0% experiencing less disturbance as compared with 1.5% with more disturbance (Fig. 2b).

Assessment of response to therapy. At the end of desloratadine treatment, the therapeutic response was rated by the physician. In 42.7% of cases, there was complete relief of signs and symptoms of CIU, whereas a further 45.6% had a significant relief of symptoms (Fig. 3). The remaining patients had moderate relief.

Global assessments of efficacy and tolerability. Patients and physicians separately judged the efficacy of desloratadine at the end of treatment. Overall, 46.3% of physicians and 46.9% of patients judged the efficacy of desloratadine as being excellent. Desloratadine therapy was rated having good efficacy by a further 37.3% of physicians and 35.2% the patients. Only 4.4% of physicians and 6.1% of patients rated the efficacy of desloratadine as being poor.

The majority of patients and physicians rated the global tolerability of desloratadine as being excellent (82.0% of physicians and 77.0% of patients). Few physicians (0.4%) and patients (0.7%) rated the tolerability of desloratadine as being poor.

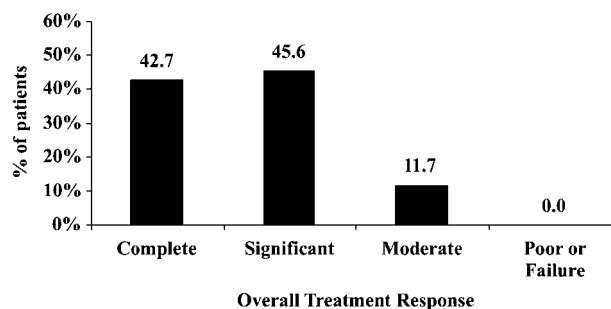


Figure 3 Overall assessment of therapeutic response to desloratadine therapy at the end of treatment (Visit 2). Numbers above columns denote percentage of patients per category.

Comparison of desloratadine with previous antihistamine therapy.

A subgroup analysis revealed that 4457 patients had reported previous treatment with only one antihistamine (cetirizine, loratadine, fexofenadine or 'other'). Of these patients, 1375 reported receiving previous treatment with cetirizine alone, 1179 with loratadine alone, 643 with fexofenadine alone, and 1260 with another antihistamine. Overall, the previous treatment was rated as poor by 14.9% of patients, moderate by 52.3%, good by 30% and excellent by 2.7%. In the individual subgroups, ratings were broadly similar. In the loratadine-treated subgroup, for example, efficacy was rated as excellent by 4.3%, good by 43.5%, moderate by 42.5% and poor by 9.5% of patients. When rated using the same 4-point scale, these patients rated the overall efficacy of desloratadine higher than that of their previous antihistamine: 41.2% (excellent), 37.6% (good), 14.6% (moderate) and 6.6% poor (Fig. 4). The subsequent efficacy ratings for desloratadine in patients that received previous treatment with other antihistamines were similar to the group overall. For instance, in patients that had received loratadine pretreatment, desloratadine was rated as excellent or good by 83.2%, while only 4.5% rated desloratadine as poor. Furthermore, in the 112 patients that reported loratadine as having poor efficacy, 64.2% subsequently rated the efficacy of desloratadine as being excellent or good, while of 615 patients that rated their previous loratadine treatment as poor/moderate, 79.2% reported desloratadine as having excellent/good efficacy. Only 19 patients reported poor efficacy for both loratadine and desloratadine.

Similar to the case with loratadine above, 62.5% of patients that received cetirizine as their only previous treatment for CIU rated its efficacy as poor/moderate. Subsequent desloratadine therapy was rated as excellent (40.7%) or good (38.1%). Again, few patients rated the efficacy of desloratadine as poor (6.5%). Overall fewer patients had received fexofenadine as a pretreatment ($n = 643$) compared with loratadine or cetirizine. Efficacy of fexofenadine therapy was rated as poor by 13.4%, moderate by 58.5%, good by 25.8% and excellent by 2.3% of patients. Subsequent

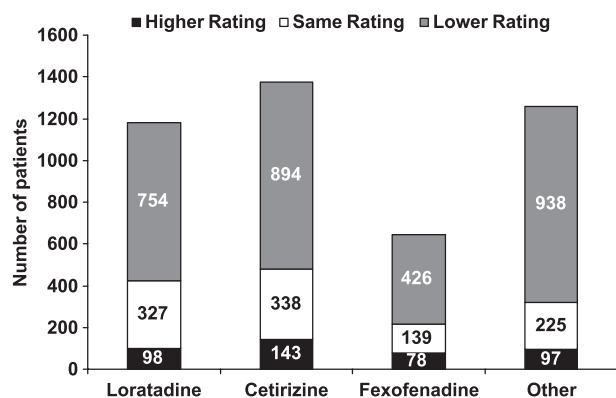


Figure 4 Proportions of the study population that reported a higher, equal or lower rating for efficacy of desloratadine in the treatment of CIU compared with previous monotherapy with loratadine, cetirizine, fexofenadine or other antihistamine.

desloratadine therapy was generally rated more favourably, with 38.6% rating efficacy as excellent, 38.1% as good, 15.2% as moderate and poor by 8.1% of patients. The proportions of patients that reported a higher rating for desloratadine efficacy than for their pretreatment efficacy were similar across those that reported receiving loratadine, cetirizine, fexofenadine or other therapies (Fig. 4). Overall, 68.0% gave a higher rating of desloratadine efficacy than their previous treatment, while 22.9% gave the same rating and 9.1% gave a lower rating.

Onset of efficacy. In 60% of cases, the onset of efficacy of desloratadine was rated as being faster than previous antihistamine medication, whereas 5.7% judged the onset of desloratadine as being slower.

A subgroup analysis was also performed on the patients that reported receiving cetirizine, loratadine, fexofenadine or 'other' antihistamine monotherapy as previous treatment ($n = 4242$). The proportions of patients that rated desloratadine as having a faster onset of action than cetirizine (55.5%), loratadine (54.7%), and fexofenadine (57.6%) were similar (Fig. 5). Few patients rated the onset of efficacy with desloratadine as being slower than that of loratadine (3.6%), cetirizine (7.9%), fexofenadine (7.4%), or other therapies (6.2%).

Adverse events

The incidence of adverse events in this PMSS was low, with 62 events reported in 43 patients (0.5% of patients). No serious adverse events and no pregnancies were reported. The most frequent adverse events were headache (0.13% of cases), fatigue (0.11%), and dry mouth (0.06%). Most of the adverse events were mild (19 of 62) or moderate (27 of 62) in intensity. Forty-five adverse events in 31 patients were judged a possibly or probably related to desloratadine therapy; potentially treatment-related fatigue/somnolence was reported in only 0.05% of cases. In 22

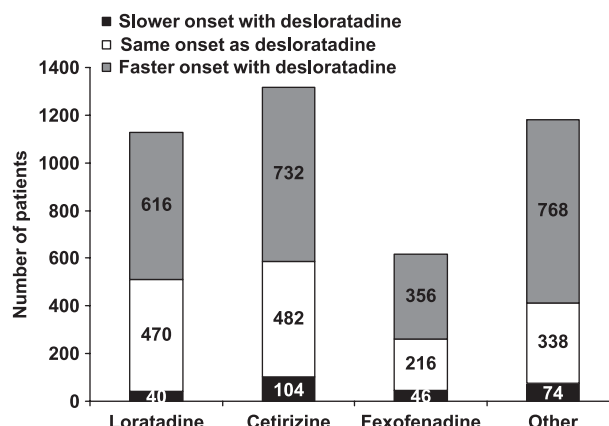


Figure 5 Assessment of onset of efficacy of desloratadine as compared directly with pretreatment in subgroups of patients that reported only pretreatment with loratadine, cetirizine, fexofenadine or other antihistamine alone. Patients rated desloratadine as having a faster (grey), equal (white) or slower (black) onset than their pretreatment antihistamine.

patients with adverse events, desloratadine therapy was stopped; the most frequently causes were fatigue ($n = 7$), headache ($n = 7$), nausea ($n = 3$), dry mouth ($n = 2$) and dizziness ($n = 2$).

Discussion

PMSS are increasingly important in order to provide health services with a validation of the clinical utility of marketed therapies and also to provide a clearer view of the clinical safety and efficacy profile of a drug in the general population. The present study on desloratadine in CIU was performed in Germany, under the guidance for non-interventional studies of the German Society of Medical Statistics and by the Bundesinstitut für Arzneimittel und Medizinprodukte (the Federal Institute for Drugs and Medical Products).^{13,14} The performance of this observational study under tightly defined methodological criteria provides for a robust and high-quality data set; the results obtained from this process are not only confirmatory of placebo-controlled data but extend our understanding of the clinical characteristics of desloratadine in CIU.

The clinical profile of desloratadine in CIU has been studied comprehensively in three prospective, randomized, placebo-controlled clinical trials.^{9–11} These studies, all of 6 weeks duration, demonstrated consistent improvements in pruritus and wheal size/severity, which are the cardinal symptoms and signs of CIU. The effects of desloratadine in these three studies were seen after the first dose, and continued during prolonged daily treatment. Also, reductions in symptom severity were accompanied by improvements in CIU-impaired sleep and daily activity. The current study is the largest trial to date involving the treatment of patients with CIU. In a population of more than 9000 CIU patients treated in general and specialist practices, desloratadine

treatment for a mean duration of approximately 40 days (duration between Visit 1 and Visit 2) was rated as being well tolerated, had a low incidence of adverse events (0.5% of patients), and significantly reduced itch and wheal size/number. Potentially treatment-related fatigue/somnolence was reported in only 0.05% of cases. A large majority of patients experienced a reduction in symptom severity and a lessening in CIU-impaired sleep and daily activities. Generally, less than 2% of patients experienced a worsening of their symptoms during desloratadine therapy.

CIU is typically a disease that can last for years, a fact that is reinforced by the findings of the current study. As such, patients will often require treatment with antihistamines on multiple occasions. In this study about half of the patients had taken an antihistamine previously and in many cases patients reported having received only one type of antihistamine. Although this treatment with other antihistamines occurred at variable times in the past, analysis of data from these subgroups of patients that received previously only cetirizine, loratadine or fexofenadine as monotherapy demonstrated that patients rated desloratadine as having a more rapid onset of efficacy in 54.7–57.6% of cases. Further subanalyses support these findings, with ratings for the effectiveness of desloratadine being consistently higher than those reported for previous monotherapy with cetirizine, loratadine and fexofenadine. Taken together with the efficacy and tolerability data from this study and the extensive placebo-controlled data sets, these results underline that desloratadine has a highly favourable profile for use as a first-line therapy in CIU in the clinical setting.

PMSS such as this one are generally performed to identify safety issues that arise in the general target population but were not identified in regulatory placebo-controlled trials that typically have more restrictive exclusion criteria. Many examples of unexpected adverse events have arisen in the postmarketing setting across a variety of therapeutic areas, often in the absence of mandatory PMSS data collection. In particular, postmarketing safety assessment is important in highly prevalent conditions like allergies, cardiovascular diseases and diabetes mellitus. The second-generation antihistamine class was one of the first to experience marketing withdrawals due to rare but potentially fatal adverse events that were noted first in the general population. Both terfenadine and astemizole were shown to be associated with important drug–drug interactions that led to increased risk of serious cardiac arrhythmias; although extremely rare, these adverse events led to the withdrawal of terfenadine and astemizole from the market by many health authorities. More recently, a number of high-profile drug withdrawals due to unexpected adverse events that were not noted in phase III trials has occurred with drugs used to treat diabetes mellitus, hyperlipidaemia, arthritis and irritable bowel syndrome among others. PMSS can help to identify such problems, or can support the safety profile obtained in phase III studies. In the case of desloratadine, the current study is the largest reported in the setting of CIU, and the adverse events

reported were infrequent and were in keeping with those noted in the summary of product characteristics. Bachert *et al.* reported a PMSS that studied the safety and efficacy profiles of desloratadine in patients with seasonal allergic rhinitis.¹⁵ That study involved 47 953 patients treated with desloratadine for a mean duration of 38 days, and confirmed the tolerability and efficacy of desloratadine in the setting of allergic rhinitis. In particular, the results of Bachert *et al.* and the current PMSS confirm that desloratadine is associated with a low rate of somnolence/fatigue when used in the clinical setting in a combined population of more than 57 000 patients.¹⁵

With open-label trials, one must always consider the caveat of a lack of a placebo-controlled group. However, against a background of three large placebo-controlled clinical trials that demonstrate the safety and efficacy of desloratadine in CIU, this issue is less pressing.^{9–11} In addition to these studies, other peer reviewed data on the use of desloratadine in CIU in the clinical setting, or in prospective trials, provide further confirmation of the clinical safety and efficacy of desloratadine in patients with CIU.^{16–18}

In conclusion, desloratadine was effective and well-tolerated when used in clinical practice in more than 9000 patients with CIU in Germany. Desloratadine was associated with a low incidence of adverse events and was rated as having excellent or good tolerability by a large majority of patients and physicians. Desloratadine treatment was associated with decreases in CIU signs and symptoms such as itching and wheal size/number, and the overall response to therapy was rated highly by patients and physicians. Compared with previous antihistamine therapy, a majority of patients rated desloratadine as having a more rapid onset of action. This large PMSS confirm the efficacy and safety profile of desloratadine as derived from multiple randomized placebo-controlled trials.

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