DRUGS IN CONTEXT
RIGOROUS • RAPID • RESPONSIVE

A continuous publication, open access, peer-reviewed journal

ACCESS ONLINE

CASE SERIES

Experience with bilastine in the management of urticaria: Original Real-world cases of Bilastine In Treatment (ORBIT) in Asia

Wai Kwong Cheong[1], Alson Wai Ming Chan[2], Chin Chwen Ch'ng[3], Wen Hung Chung[4], Ma Teresita Gabriel[5], Kiran Godse[6], Wat Mitthamsiri[7], Hao Trong Nguyen[8], Marysia Tiongco-Recto[9], Dinesh Nagrale[10]

[1]Specialist Skin Clinic & Associates Pte Ltd, Singapore; [2]Allergy Centre, Hong Kong Sanatorium & Hospital, Hong Kong; [3]Subang Jaya Medical Centre, Selangor, Malaysia; [4]Department of Dermatology, Chang Gung Memorial Hospital, Taipei, Taiwan; [5]Department of Dermatology, Research Institute for Tropical Medicine, Manila, Philippines; [6]Department of Dermatology, DY Patil University School of Medicine, Navi Mumbai, India; [7]Allergy and Clinical Immunology Division, Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand; [8]Ho Chi Minh City Hospital of Dermato-Venereology, Ho Chi Minh City, Vietnam ; [9]Allergy and Immunology, University of the Philippines – Philippine General Hospital, Manila, Philippines; [10]A. Menarini Asia-Pacific Pte Ltd, Singapore

Abstract

Urticaria is a disabling condition, resulting in an impaired quality of life and sleep disruption, and can have an adverse impact on work-related or school-related performance and attendance. It is defined according to the presence of unknown (chronic spontaneous urticaria) or known (inducible urticaria) eliciting factors. Guidelines recommend second-generation H_1-antihistamines for the first-line treatment of urticaria. Bilastine is indicated in adults, adolescents (aged ≥12 years) and children (aged ≥2 years (Mexico and some African countries), ≥4 years (Canada) or ≥6 years (Europe)) with a body weight of at least 20 kg for the symptomatic treatment of urticaria and allergic rhino-conjunctivitis. The aim of the Original Real-world cases of Bilastine In Treatment (ORBIT) study was to review real-world cases from across the Asia-Pacific region supported by evidence-based literature. Eight diverse, real-world, difficult-to-treat cases with urticaria in people aged 10–75 years are presented. Once-daily bilastine (20 mg (adults/adolescents) or 10 mg (children)) was found to be well tolerated and effective in the long-term management of chronic spontaneous urticaria and inducible urticaria.

Keywords: Asia, bilastine, case studies, chronic spontaneous urticaria, eczema/dermatitis, H_1-antihistamine, inducible urticaria, real-world evidence.

Citation

Cheong WK, Chan AWM, Ch'ng CC, Chung WH, Gabriel MT, Godse K, Mitthamsiri W, Nguyen HT, Tiongco-Recto M, Nagrale D. Experience with bilastine in the management of urticaria: Original Real-world cases of Bilastine In Treatment (ORBIT) in Asia. *Drugs Context*. 2022;11:2021-12-2. https://doi.org/10.7573/dic.2021-12-2

Introduction

Urticaria is a common, disabling dermatological disorder presenting as a red, itchy rash with characteristic wheals and/or angioedema. It results from increases in peripheral vasodilatation and vascular permeability and can be divided into three clinical phenotypes based on its duration (acute *versus* chronic) and on the presence or absence of inducing factors (inducible *versus* spontaneous).[1]

In affected individuals, the disabling nature of urticaria can impair quality of life (QoL), disrupt sleep and have a negative impact on performance at work or school. International guidelines define chronic spontaneous urticaria (CSU) as the spontaneous appearance of wheals and/or angioedema for >6 weeks due to known (e.g. autoreactivity) or unknown causes. Inducible urticaria is classified based on the relevance of eliciting factors and includes symptomatic dermographism, vibratory angioedema, and urticaria induced by cold, delayed pressure, solar, heat, cholinergic, contact or aquagenic stimuli.[2] The lifetime prevalence of urticaria has been reported to be almost 10%, with females being affected at least twice as often as males and the majority of patients being over 20 years of age. CSU occurs in approximately one-quarter of individuals.[1] Given the high prevalence and disabling nature of urticaria, the economic burden of chronic forms of the disease is substantial.[3]

As urticaria is predominantly mediated by histamine release, H_1-antihistamines are the mainstay of treatment for urticaria. However, first-generation H_1-antihistamines are limited by adverse effects, including anticholinergic effects, sedation,

drowsiness, fatigue, and impaired concentration and memory due to their central nervous system penetration, or can interact with alcohol and concomitant drugs.[4] In contrast, second-generation agents have improved peripheral histamine H_1-receptor selectivity, decreased lipophilicity (which minimizes central nervous system adverse effects) and antiallergic properties.[5] Guidelines recommend second-generation H_1-antihistamines for the first-line treatment of urticaria and continuous treatment with H_1-antihistamines is of paramount importance in the treatment of urticaria.[2]

Bilastine is a second-generation H_1-antihistamine indicated in adults, adolescents (aged ≥12 years) and children (aged ≥2 years (Mexico and some African countries), ≥4 years (Canada) or ≥6 years (Europe)) with a body weight of at least 20 kg for the symptomatic treatment of urticaria and allergic rhino-conjunctivitis.[6–9] Bilastine is highly selective for the H_1-histamine receptor with a well-documented efficacy and safety profile, which includes a rapid onset and prolonged duration of action, and less sedative potential than most other second-generation antihistamines.[10]

Although the global point prevalence of CSU is approximately 0.5–1.0%, data on the burden of urticaria in the Asia-Pacific region are limited.[10] In addition, there is a lack of real-world Asian experience with second-generation H_1-antihistamines such as bilastine. The main purpose of these case studies of urticaria is to capture the long-term use of bilastine in a range of patient types (CSU or inducible urticaria). The real-world cases discussed herein were presented by the panel members of the Original Real-world cases of Bilastine In Treatment (ORBIT) study and are supported by evidence-based literature.

Methods

The ORBIT study presents real-world cases using bilastine for the long-term management of urticaria in both adult and paediatric populations. Long-term treatment was defined as ≥3 months of treatment with bilastine 20 mg and 10 mg in adults and children, respectively. This article includes eight 'difficult-to-treat' cases from the Southeast Asia region that were presented and discussed at a STAR-D Advisory Board meeting held on 29 May 2021 in Singapore (Appendix 1). Cases were from Hong Kong, India, Malaysia, the Philippines (two cases), Taiwan, Thailand and Vietnam.

Inclusion criteria

Difficult-to-treat adult and paediatric cases with urticaria treated with bilastine 20 mg once daily (OD; adults) or 10 mg OD (children) were included. Bilastine treatment used the Bilaxten® branded drug and not generic versions and was prescribed as per label.

Diagnosis

Cases were diagnosed and classified according to international guidelines as CSU (based on the absence of known external physical stimuli) or inducible urticaria.[2]

Literature review

To provide an overview of relevant clinical studies of bilastine for the treatment of urticaria, a literature review was conducted on 13 August 2021 using the search terms "bilastine" and "urticaria". Publications that included combined allergic rhino-conjunctivitis and urticaria patient populations were excluded, as were publications including indications for which bilastine is not currently approved.

Role of the Expert Panel

The authors of this article comprised an Expert Panel of allergologists and dermatologists from the Asia-Pacific region who regularly treat patients with dermatological disorders such as urticaria (including urticarial vasculitis and pruritus due to various causes, such as atopic dermatitis) in everyday clinical practice. All have experience with using second-generation H_1-antihistamines, including bilastine, and they were asked to present real-life case studies covering urticarial conditions of special interest. The panel members used a template for their case studies.

During a 1-day authorship meeting, the panel presented their cases, followed by a group discussion, after which the authors decided which of the real-world cases using bilastine were to be included in the manuscript. The publication was developed, reviewed by the panel members and prepared for publication.

Results

Literature review

A total of 62 publications were retrieved and assessed for relevance, with 3 within-label publications included. Results of relevant clinical studies of bilastine for the treatment of urticaria are summarised in Table 1. A large randomized, double-blind, placebo and active treatment controlled trial of CSU patients reported comparable efficacy and safety for bilastine 20 mg OD and levocetirizine 5 mg OD, including significant improvement in the primary efficacy outcome, the total symptom score.[11] Similarly, in a parallel group, a randomized controlled trial (RCT) of CSU patients in India, both bilastine 20 mg OD and levocetirizine 5 mg OD significantly improved efficacy outcomes from baseline, including the primary efficacy outcome of 7-day Urticaria Activity Score.[12] In this study, reported treatment-emergent adverse events included somnolence, which was significantly more common with levocetirizine than bilastine (63% *versus* 12.9%; p=0.002).[12] In a Japanese randomized, placebo-controlled trial of adult patients with CSU, bilastine (20 or 10 mg OD) significantly

improved efficacy outcomes, including the primary efficacy outcome (change from baseline in total symptom score), when compared to placebo.[13] All studies reported a good safety profile and tolerability for bilastine (Table 1).

Case reports

The real-world cases presented here used bilastine in long-term urticaria management. The patients were between the ages of 10 and 75 years and 50% (*n*=4) were female. Cases included 1 paediatric case (aged 10 years), 5 cases aged between 20 and 61 years, and 2 cases aged ≥65 years. Seven patients were diagnosed with CSU (Cases 1–3, 5–8) and 1 (Case 4) with cholinergic urticaria (Table 2).

In 4 cases with CSU (Cases 2, 3, 5, 8), antihistamine-induced somnolence was an issue with prior treatment (before using bilastine). In this sense, Case 3, who was initially treated with first-generation (chlorpheniramine) and second-generation (levocetirizine, ketotifen) H_1-antihistamines, exhibited drowsiness and a sense of dissociation, which made her unable to concentrate on her daytime work. Case 5, a 20-year-old student, was initially treated with hydroxyzine (a first-generation antihistamine) and, due to her daytime sedation, was unable to concentrate during lectures and her memory was impaired. In Case 8, an elderly man treated with cetirizine (second-generation antihistamine) suffered from drowsiness and had difficulty waking up in the morning. Finally, the paediatric patient (Case 2) was treated with first-generation (chlorpheniramine) and second-generation (cetirizine) antihistamines and had somnolence associated with sleep disturbances and tiredness during the day, which impacted on his school work. Following treatment with bilastine, problems with antihistamine-induced somnolence were resolved in all cases, whilst urticaria was well controlled.

Somnolence, due to poor sleep quality caused by itching, was a major concern for Case 1, which reduced his ability to concentrate, causing problems at work and was responsible for two near misses with other motor vehicles. In common with the four cases outlined above (Cases 2, 3, 5, 8), one reason for selecting bilastine was its lack of, or minimal, sedative effects. Case 1 had a good response to treatment with bilastine and was able to return to work.

Other reasons for selecting bilastine in this case series included its good safety and tolerability profile, including in elderly patients with/without renal insufficiency (Case 8), cost-effectiveness, fast action and absence of immunosuppressive effects. In the paediatric case (Case 2), an additional cited benefit of bilastine (10 mg) was its easy-to-use orodispersible tablet formulation, which, unlike most antihistamine liquid formulations, does not require refrigeration for storage and there is no requirement for age-adjusted or weight-adjusted dosing (thus avoiding possible dosing errors).

Table 1. Bilastine in clinical studies of CSU.

Study	Patients	Treatment	Results
Zuberbier et al. 2010[11]	CSU (*n*=525)	Bilastine 20 mg OD (*n*=173), levocetirizine 5 mg OD (*n*=165) or placebo OD (*n*=184) for 28 days	• Bilastine improved TSS, DLQI, general discomfort and sleep disruption compared with placebo ($p<0.001$ for all) • Bilastine had comparable efficacy to levocetirizine • Bilastine and levocetirizine were safe and well tolerated
Podder et al. 2020[12]	Moderate to severe CSU (*n*=58)	Bilastine 20 mg OD (*n*=31) or levocetirizine 5 mg OD (*n*=27) for 42 days	• Both bilastine and levocetirizine significantly improved changes from baseline in UAS7, DLQI and Urticaria-Induced Global Discomfort at day 42 ($p<0.001$ for all) • UAS7 at day 42 was significantly lower with bilastine compared with levocetirizine ($p=0.03$) • Somnolence was more common with levocetirizine than bilastine (63% *versus* 12.9%, $p=0.002$)
Hide et al. 2017[13]	CSU (*n*=304)	Patients randomized to receive bilastine 20 mg OD (*n*=101), bilastine 10 mg OD (*n*=100) or placebo OD (*n*=103) for 2 weeks	• Bilastine 20 mg and 10 mg improved TSS, rash score, itch score and DLQI compared with placebo ($p<0.001$ for all) • Bilastine was safe and well tolerated

CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; OD, once daily; TSS, total symptom score; UAS7, 7-day Urticaria Activity Score.

Table 2. Cases[a] of CSU and inducible urticaria treated with bilastine.

Presentation	Previous treatment and diagnosis	Treatment decision	Clinical outcome
Case 1: 35-year-old man complaining of an itchy skin rash for the previous 6 months			
Itchy skin lesions reported during the previous 6 months manifested as a rash, which was worst around the waistline and exacerbated by scratching and occurred nightly and resolved by morning. The itching worsened (but not consistently) after eating seafood and some canned foods and during hot weather. There was no angioedema or symptoms such as fever, mouth ulcers or joint pain. More recently, the intensity of the itch had increased, resulting in sleep disturbances and tiredness, with blood-stained bedsheets from scratching. This was reducing his ability to concentrate, resulting in problems at work because of an increase in the number of errors he was making. Worryingly, there were two occasions when he was nearly involved in motor vehicle accidents as a result of tiredness/ poor concentration. Lately, a recurring erythematous urticarial rash with wheals on the forearms and thighs had developed and tests revealed no signs of thyroid or autoimmune disease, or infection, whereas a dermographism friction test was positive	The employer's physician had previously prescribed intramuscular steroids (4 occasions); oral cetirizine 10 mg OD (morning dose); oral chlorpheniramine 4 mg OD (evening dose) and betamethasone valerate cream; while these had provided some relief, sleeping continued to be a problem. A complete blood count and ESR were normal and a diagnosis of CSU was made with the challenge of improving sleep quality and the patient's ability to concentrate	Bilastine 20 mg OD was chosen as the treatment of choice because it is non-sedating and cost-effective and has a good safety/tolerability profile with no immunosuppressive effects	The patient responded well to treatment with an UAS <10 on week 2 of treatment and was able to go back to work. No AEs to bilastine were observed and, after 8 months of treatment, all antihistamines were tapered off
Case 2: 10-year-old boy who developed recurrent hives over the past 3–4 years			
A 10-year-old boy was referred to the allergy centre (a tertiary referral centre) with recurrent hives (urticaria), which occurred almost daily for 3–4 years. The wheals were variable in size and shape and occurred on various parts of the body. They were very itchy and generally resolved spontaneously within 1–2 hours. Empirical elimination diet failed to identify any usual food trigger. His condition was severe, affecting his school attendance and causing frequent sleep awakening (3–4 times per week). There was no family history of atopy	The patient had been managed by several GPs over a few years. Investigations including complete blood count, serum total IgE and specific IgE for common allergens were unremarkable A diagnosis of chronic urticaria was made and the patient was still having recurrences 2–3 times per week despite treatment with oral first-generation or second-generation antihistamines such as chlorpheniramine 2–4 mg TDS and cetirizine 5 mg once or twice daily. Compliance with oral therapy was poor and the patient complained of sleepiness (even after changing to cetirizine) with feelings of daytime malaise and sleepiness (hangover). He frequently missed morning or afternoon doses and suffered from recurrent breakthrough hives	The treatment was subsequently changed to bilastine 10 mg OD; since then, it demonstrated good efficacy and had a more prolonged effect without breakthrough hives using once-daily dosing and his compliance improved. The tablet formulation was perceived by his parents as more convenient to use (easier to take orally and does not require refrigeration)	The patient responded well to bilastine. There has been no more recurrence of urticaria from day 3 onwards. He can attend school daily without complaint from teachers regarding his urticaria; can sleep well and is more confident with classmates and friends. There is no need for empirical food avoidance and he is more willing to participate in outdoor sporting activities

(Continued)

Table 2. (*Continued*)

Presentation	Previous treatment and diagnosis	Treatment decision	Clinical outcome
Case 3: 54-year-old woman with poorly controlled chronic urticaria and intolerance to sedating antihistamines			
The woman presented with poorly controlled chronic urticaria lasting for ≥1 year	During the previous 12 months, she was treated with multiple antihistamines, including levocetirizine 5 mg, diphenhydramine 25 mg and ketotifen 1 mg BID but, due to the side effects of drowsiness and sense of dissociation, she was unable to concentrate on her daytime work. She then stopped the daytime dose of antihistamines, taking them only at night, but the symptoms of wheals and intractable pruritus appeared during antihistamine tapering	Due to her concerns of antihistamine-induced drowsiness, she was prescribed bilastine 20 mg OD combined with fexofenadine 180 mg OD and ketotifen 1 mg OD taken at night. Her symptoms of wheals and pruritus were significantly improved and she tolerated the new medications well	One month after controlling her chronic urticaria, ketotifen was successfully discontinued without recurrence of urticaria. Her symptoms continued to be well controlled for ≥3 months by combination bilastine plus fexofenadine. She then discontinued fexofenadine and continued with single-agent bilastine. Her urticaria was well controlled by single dose bilastine and she went into remission 4 months later
Case 4: 33-year-old woman with cholinergic urticaria			
The patient was very active and loved to go to the gym and jog daily. She presented with a 3-month history of recurrent wheals, which occurred almost daily, appearing after exercise and associated with moderate to severe pruritus	Initial treatments included loratadine, cetirizine and prednisone, which slightly improved her condition but were associated with slight weight gain. The patient consulted the clinic because of the persistence of the lesions. At presentation, there were multiple wheals on the trunk with areas of excoriation and erythematous maculopapular lesions on the upper extremities (Figure 1A). A complete blood count and ESR were normal, DLQI was 13, indicative of a large negative impact on QoL and UAS7[b] was 28 (severe disease) The final diagnosis was cholinergic urticaria caused by elevated body temperature and sweating as a result of exercise	The treatment challenge was to achieve total clearance of lesions using a fast-acting antihistamine to enable the patient to engage in sports activities while being symptom free. The therapy had to be non-sedating, fast acting and well tolerated without causing dry mouth or weight gain. Based on these requirements, the patient was treated with bilastine 20 mg OD for 4 months	The patient was symptom free from day 1 of treatment for 4 months (Figure 1B). She was able to exercise without any recurrence of cholinergic urticaria. Both UAS7[a] and DLQI were 0 after 1 week and this was sustained for 4 months. No side effects, such as sedation, dizziness or weight gain, occurred. It is now >1 year since the patient discontinued all drugs, and she remains symptom free and continues regular exercising (gym and daily jogging)

(Continued)

Table 2. (*Continued*)

Presentation	Previous treatment and diagnosis	Treatment decision	Clinical outcome
Case 5: 20-year-old woman with intensely itchy rash			
A 20-year-old female student complained of an intensely itchy rash affecting her torso, arms and legs (especially her thighs) for the past 7 weeks. The lesions appeared abruptly without any aggravating factors and lasted for 6–8 hours and then were replaced by new lesions at other sites. There was no history of atopy. Her general health was good but the rash was causing her distress. There was no other significant medical history. The patient was using an over-the-counter traditional topical Ayurvedic medication whenever the lesions appeared	A general examination was within normal limits. Individual lesions varied from 2–25 mm in diameter and were dispersed over the back, chest, arms, thighs and legs. The lesions were red, raised (some with white centres) and in irregular patches; they were typically urticarial; UAS7[b] score was 28 (severe disease) and the Urticaria Control Test[c] score was 10 (poorly controlled urticaria). A complete blood count, C-reactive protein and complement C4 and C1 inhibitor levels were normal, whereas IgE levels were slightly elevated The patient was prescribed hydroxyzine 25 mg BID for a week, with calamine lotion for application BID. Symptoms improved with a reduction in rash and itching after 1 week, but the patient complained of daytime sedation and she was unable to concentrate during lectures. Additionally, she was forgetting things easily. The QoL of the patient was negatively affected	The treatment challenge was to maintain the positive effects associated with antihistamine therapy whilst avoiding the sedative effects associated with hydroxyzine. She was counselled and the decision was made to switch treatment to bilastine (a non-sedating antihistamine) 20 mg OD for 1 week. At this stage, the rash was well controlled and the patient did not complain of sedation. The patient was advised to continue with bilastine for another week	Bilastine was effective in reducing the symptoms of CSU and, as a result of its non-sedating properties, it is likely to improve adherence to therapy
Case 6: 61-year-old woman with atopic (allergic rhinitis) with new-onset urticaria			
A Thai woman with allergic rhinitis for more than 20 years (skin tests were positive to mixed mould, mixed grass smut and cockroach), benign thyroid nodule with euthyroid status (not treated), presented with new onset urticaria 2–4 times per week for about 2 months and no obvious precipitating factor. She previously had recurrent acute urticaria (frequency: twice a year to once weekly) for several years	Her previous treatment for allergic rhinitis and intermittent urticaria was specific AIT with mixed grass, mixed mould and cockroach antigens (already in maintenance phase), fluticasone furoate nasal spray 2 puffs/nostril/d, montelukast 10 mg/d, ranitidine 300 mg/d, 10% urea cream and irregularly switching/mixing of antihistamines, including desloratadine 5–10 mg OD, levocetirizine 5–10 mg OD and bilastine 20 mg OD. She regularly received AIT but poorly complied with other medicines because of fear of long-term AEs (these never occurred except for occasional somnolence). Fluticasone furoate nasal spray was stopped once symptoms improved at the patient's request and antihistamine usage was self-adjusted. Her fear of long-term AEs explained the frequent switching/mixing of antihistamines	About 12 months prior, the urticaria was well controlled with bilastine 20 mg OD, desloratadine 5 mg OD, ranitidine 300 mg OD and 10% urea cream. Earlier attempts made to step down therapy by stopping ranitidine resulted in recurrence of the urticaria and montelukast was reintroduced to her treatment regimen	Currently, during the COVID-19 pandemic, patients with stable disease are advised to remain home and report their status via phone or internet messaging services. All required medicines are delivered. The patient reported that her symptoms remain controlled with bilastine, desloratadine, montelukast, urea cream regimen, without daytime somnolence

(Continued)

Table 2. (*Continued*)

Presentation	Previous treatment and diagnosis	Treatment decision	Clinical outcome
Case 7: An elderly man with recalcitrant CSU unresponsive to second-generation antihistamines			
A 65-year-old man had a 10-year history of urticaria with intermittent episodes of hives and angioedema Two months before hospital administration, the patient developed widespread urticaria with almost daily symptoms	Previous treatments by the patient's GP included oral corticosteroids, fexofenadine, levocetirizine, desloratadine and ebastine; however, on this latest occurrence, the patient was unresponsive or only partly responsive to combinations of the afore-mentioned antihistamines; UAS7[a] score was 36, which is indicative of severe disease Investigations: full blood count, renal function, liver function and thyroid function tests were all considered to be within the normal range; UAS7[a] score was 28, indicating severe disease The final diagnosis was CSU	Treatment considerations were the patient's age and selection of a therapy that could safely and effectively maintain long-term control of CSU. Safety considerations included a low risk of blood–brain barrier penetration to avoid CNS AEs and, for efficacy, selection of an antihistamine for which the patient had not previously exhibited resistance. Bilastine 20 mg OD was selected since it has low CNS penetration potential, has proven safety in elderly patients and exhibited efficacy in patients with CSU refractory to other antihistamines	To date, bilastine has provided good control of CSU with only mild pruritus and few wheals remaining and no AEs
Case 8: Chronic rash in an elderly man with multiple comorbidities			
A 75-year-old man who, over the last 12 months, had been treated for recurrent rashes that were pruritic, evanescent, with erythematous wheals on the extremities and occasional angioedema, but no other clinical symptoms. He was a retired banker who was unable to play golf due to discomfort of the rashes. He also had difficulty waking up in the morning due to antihistamines and was an ex-smoker Six months prior to the current consultation, he complained of fatigue, increased dryness of the skin and a slight decrease of urine output. More recently (3 weeks prior to the consultation), daily wheals with increased severity of pruritus were noted and these were causing problems with sleeping. Cetirizine at bedtime was prescribed and there was improvement of cutaneous symptoms. However, this was associated with increased drowsiness, difficulty waking up and decreased urine output	At the current consultation, a broad range of laboratory tests were performed and he was diagnosed with the following medical disorders: CSU, diabetes mellitus type 2, uncontrolled hypertension, hyperlipidaemia, paroxysmal atrial fibrillation, stage 3 chronic kidney disease and benign prostatic hypertrophy	With regard to the choice of antihistamine for treating this patient, some of the key considerations were sedation, poor renal function, cardiotoxicity and benign prostatic hypertrophy. Based on its excellent safety profile, with minimal to no sedative effects, absence of cardiovascular risk and the fact that it can be administered to subjects independently of glomerular filtration rate in a safe and efficacious manner, bilastine was chosen as the most suitable antihistamine for this patient	Bilastine 20 mg OD before breakfast for the past 6 months produced good control of symptoms of CSU and improved the patient's QoL, including being able to resume playing golf

(Continued)

Table 2. (*Continued*)

Presentation	Previous treatment and diagnosis	Treatment decision	Clinical outcome
Medical history: the patient was being treated for type 2 diabetes, hypertension, paroxysmal AF, hyperlipidaemia and benign prostatic hypertrophy. However, he did not suffer from any allergic diseases or asthma			

Case 1 described by Chin Chwen Ch'ng (Malaysia); Case 2 by Alson Wai Ming Chan (Hong Kong); Case 3 by Wen Hung Chung (Taiwan); Case 4 by Ma. Teresita Gabriel (Philippines); Case 5 by Kiran Godse (India); Case 6 by Wat Mitthamsiri (Thailand); Case 7 by Hao Trong Nguyen (Vietnam); and Case 8 by Marysia Tiongco-Recto (Philippines).

[a]Due to the retrospective nature of the cases, detailed information may not be available for some of the cases.

[b]UAS7 is an objective scoring system used for grading of the number of hives and degree of pruritus and is based on scoring wheals and itch separately on a scale of 0–3 over 7 days; the final score is calculated by adding together daily scores (up to 6) for 7 days and provides a weekly average score up to maximum score of 42 (most severe disease).

[c]The Urticaria Control Test assesses control of the disease in CSU patients with 4 questions; a low total score reflects poor disease control and a score <12 indicates poorly controlled urticaria.

AEs, adverse effects; AIT, allergen immunotherapy; BID, twice daily; CNS, central nervous system; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; ESR, erythrocyte sedimentation rate; OD, once daily; QoL, quality of life; TDS, three times daily; UAS, Urticaria Activity Score.

In terms of elderly patients with CSU, Case 7 had recalcitrant disease unresponsive to second-generation antihistamines (fexofenadine, levocetirizine, desloratadine, ebastine) and Case 8 had multiple comorbidities (type 2 diabetes, hypertension, hyperlipidaemia, paroxysmal atrial fibrillation, stage 3 chronic kidney disease (CKD), benign prostatic hypertrophy). Both cases responded well to bilastine 20 mg OD, and Case 8 saw a marked improvement in QoL, including being able to resume playing golf following resolution of symptoms.

Case 6 was a 61-year-old woman with a history of allergic rhinitis and with new-onset urticaria. Her symptoms were well controlled by bilastine in combination with desloratadine, montelukast (leukotriene receptor antagonist) and urea cream without daytime somnolence.

Case 4 was diagnosed with cholinergic urticaria caused by exercise-induced elevated body temperature and sweating and which had a considerable negative impact on her QoL. Bilastine treatment produced a rapid improvement in symptoms (Figure 1), enabling her to resume regular exercise and was associated with a marked improvement in QoL.

Discussion

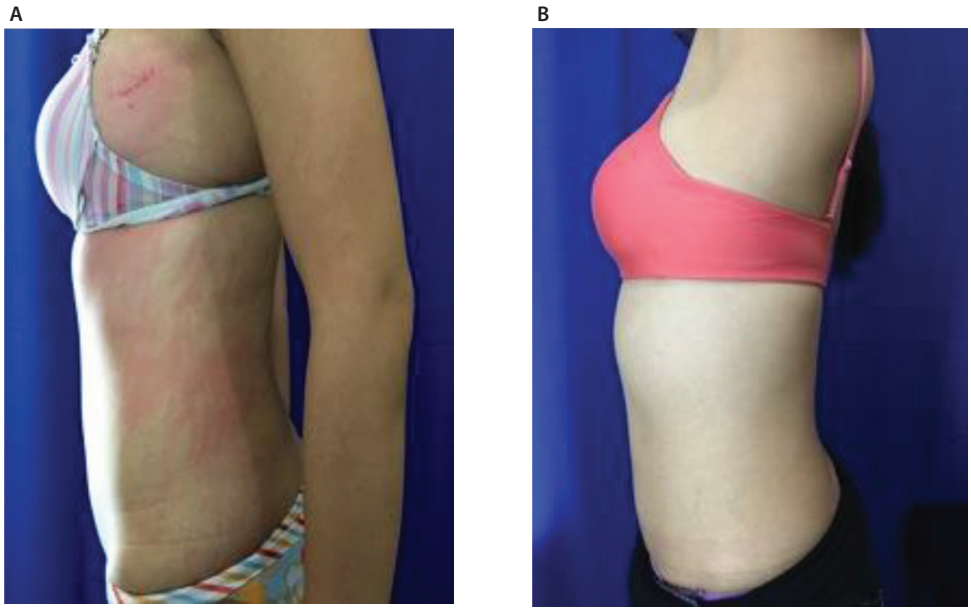
The real-world cases presented here used bilastine in long-term urticaria management in patients aged from 10 to 75 years who required treatment with a second-generation antihistamine. Bilastine (20 mg OD for adults; 10 mg OD for the child) was found to be well tolerated and effective in all patients.

Reasons for selecting bilastine in these diverse cases included its well-documented good safety and tolerability profile; this was particularly important for one elderly patient with multiple comorbidities, such as type 2 diabetes, hypertension, hyperlipidaemia, paroxysmal atrial fibrillation, stage 3 CKD and benign prostatic hypertrophy. Other benefits included a lack of (or minimal) sedative effects, fast action, absence of immunosuppressive effects and cost-effectiveness. These reasons for selecting bilastine in real-world cases are in agreement with the consensus views of a panel of experts from the Asia-Pacific region who identified bilastine as the preferred choice for urticaria (and allergic rhino-conjunctivitis) due to its high efficacy and safety, together with suitability for special patient populations and the lack of sedative effects.[14]

Based on brain H_1-receptor occupancy findings, antihistamines are classified into non-sedating (<20%), less-sedating (20–50%) and sedating (≥50%) agents.[15] Amongst second-generation H_1-antihistamines, bilastine and fexofenadine are classified as 'non-brain-penetrating antihistamines'.[15] There were no reports of sedation with bilastine in the presented cases, which enabled patients to resume normal working activities or studies. Due to the absence of sedating effects, evidence supports bilastine as being the optimal treatment option for patients who require an antihistamine that does not affect fine motor skills (e.g. driving),[16,17] as exemplified by Case 1 herein.

Bilastine was not only effective in relieving the symptoms of CSU but also improved the QoL of patients, as shown in Cases 4, 5 and 8. Similar results were reported in a parallel group RCT of patients with CSU in India.[12] Bilastine 20 mg OD or levocetirizine

Figure 1. A 33-year-old woman with cholinergic urticaria (Case 4). A) At presentation B) After bilastine 20 mg once-daily treatment.



5 mg OD significantly improved changes from baseline in 7-day Urticaria Activity Score, Dermatology Life Quality Index and urticaria-induced global discomfort at day 42 ($p<0.001$ for all).[12]

Bilastine (10 mg OD) was well tolerated and effective in the single paediatric case (Case 2) as well as in two elderly patients (Cases 7, 8) described in this case series. In a large phase III RCT, bilastine 10 mg OD had a safety and tolerability profile similar to that of placebo in children with allergic rhino-conjunctivitis or chronic urticaria.[18] Moreover, in elderly patients with allergic rhino-conjunctivitis and/or urticaria, bilastine has a favourable safety profile.[19] Furthermore, bilastine has no reported cardiotoxic effects and it is known to be well tolerated in renal insufficiency.[10,20] These were important considerations for the elderly patient who had multiple comorbidities (Case 8), including paroxysmal atrial fibrillation, stage 3 CKD, type 2 diabetes, hypertension and hyperlipidaemia.

Conclusions

In this small but diverse group of patients with urticaria considered by the Expert Panel to be difficult to treat, bilastine (administered as per the approved product labelling) was well tolerated and effective in the long-term management of CSU and a case of inducible urticaria.

Contributions: All authors contributed equally to the preparation of this manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Disclosure and potential conflicts of interest: WKC has served as an advisory board member for A. Menarini and been a speaker for and received honoraria from Johnson & Johnson, Novartis and A. Menarini. HTN served as an advisory board member and speaker, receiving honoraria from Novartis, Janssen and A. Menarini. MTR disclosed non-financial interests for A. Menarini for acting as an advisory board member and speaker, has received support from A. Menarini for registration at conventions, and is the immediate Past President of the Philippine Society of Allergy, Asthma and Immunology (unpaid). CCC received an honorarium from A. Menarini. MTG received honoraria from A. Menarini for lectures and has acted in an unpaid role on an advisory board for A. Menarini. KG has received honoraria from A. Menarini and received support from A. Menarini for the present manuscript. WM received support from A. Menarini for writing the present manuscript, has received honoraria from A. Menarini for lectures and panel discussion, and from GlaxoSmithKline, Organon and AstraZeneca for lectures, and has received registration support from GlaxoSmithKline and Organon for attending virtual academic meetings. AWMC and WHC had no conflicts of interest to disclose. DN is an employee of A. Menarini. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: https://www.drugsincontext.com/wp-content/uploads/2022/03/dic.2021-12-2-COI.pdf

Acknowledgements: The authors thank A. Menarini for providing financial support for the Asia-Pacific STAR-D Specialist Taskforce on Allergy/Dermatology initiative and medical writing support provided by David P Figgitt, PhD, ISMPP CMPP™ and Steve Clissold, PhD, ISMPP CMPP™, Content Ed Net (Singapore).

Funding declaration: Funding was received from A. Menarini, including financial support for the Asia-Pacific STAR-D Specialist Taskforce on Allergy/Dermatology initiative and medical writing support.

Article URL: https://www.drugsincontext.com/experience-with-bilastine-in-the-management-of-urticaria-original-real-world-cases-of-bilastine-in-treatment-orbit-in-asia

Correspondence: Wai Kwong Cheong, Specialist Skin Clinic & Associates Pte Ltd, Singapore. Email: cheong.wkwong@gmail.com

Provenance: Submitted; externally peer reviewed.

Submitted: 23 December 2021; **Accepted:** 19 January 2022; **Publication date:** 15 March 2022.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT.

BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 252 7720 07.

For all manuscript and submissions enquiries, contact the Editorial office editorial@drugsincontext.com

For all permissions, rights and reprints, contact David Hughes david.hughes@bioexcelpublishing.com

References

1. 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. https://doi.org/10.1016/j.waojou.2021.100533
2. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA^{2}LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy*. 2018;73(7):1393–1414. https://doi.org/10.1111/all.13397
3. Maurer M, Abuzakouk M, Bérard F, et al. The burden of chronic spontaneous urticaria is substantial: real-world evidence from ASSURE-CSU. *Allergy*. 2017;72(12):2005–2016. https://doi.org/10.1111/all.13209
4. Church MK, Church DS. Pharmacology of antihistamines. *Indian J Dermatol*. 2013;58(3):219–224. https://doi.org/10.4103/0019-5154.110832
5. Kavosh ER, Khan DA. Second-generation H1-antihistamines in chronic urticaria: an evidence-based review. *Am J Clin Dermatol*. 2011;12(6):361–376. https://doi.org/10.2165/11591130-000000000-00000
6. eMC. Ilaxten 20 mg tablets: SmPC. May 2021. https://www.medicines.org.uk/EMC/medicine/24461/SPC/Ilaxten+20+mg+tablets/#gref. Accessed December 23, 2021.
7. eMC. Ilaxten 10 mg orodispersible tablets. May 2021. https://www.medicines.org.uk/emc/product/11727/smpc#gref
8. Leceta A, García A, Sologuren A, Campo C. Bilastine 10 and 20 mg in paediatric and adult patients: an updated practical approach to treatment decisions. *Drugs Context*. 2021;10:2021-5-1. https://doi.org/10.7573/dic.2021-5-1
9. Miravo Healthcare. Miravo Healthcare™ announces receipt of health Canada notice of compliance for the pediatric use of Blexten®. August 12, 2021. https://www.miravohealthcare.com/fr/news/miravo-healthcare-announces-receipt-of-health-canada-notice-of-compliance-for-the-pediatric-use-of-blexten/. Accessed December 20, 2021.
10. Wang XY, Lim-Jurado M, Prepageran N, Tantilipikorn P, Wang de Y. Treatment of allergic rhinitis and urticaria: a review of the newest antihistamine drug bilastine. *Ther Clin Risk Manag*. 2016;12:585–597. https://doi.org/10.2147/TCRM.S105189
11. 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. https://doi.org/10.1111/j.1398-9995.2009.02217.x
12. Podder I, Das A, Ghosh S, Biswas D, Sengupta S, Chowdhury SN. Effectiveness, safety, and tolerability of bilastine 20 mg vs levocetirizine 5 mg for the treatment of chronic spontaneous urticaria: a double-blind, parallel group, randomized controlled trial. *Dermatol Ther*. 2020;33(6):e13946. https://doi.org/10.1111/dth.13946
13. Hide M. Yagami A, Togawa M, Saito A, Furue M. 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. https://doi.org/10.1016/j.alit.2016.08.004

14. Recto MT, Gabriel MT, Kulthanan K, et al. Selecting optimal second-generation antihistamines for allergic rhinitis and urticaria in Asia. *Clin Mol Allergy*. 2017;15:19. https://doi.org/10.1186/s12948-017-0074-3
15. Kawauchi H, Yanai K, Wang D-Y, Itahashi K, Okubo K. Antihistamines for allergic rhinitis treatment from the viewpoint of nonsedative properties. *Int J Mol Sci*. 2019:20(1):213. https://doi.org/10.3390/ijms20010213
16. Jáuregui I, Ramaekers JG, Yanai K, et al. Bilastine: a new antihistamine with an optimal benefit-to-risk ratio for safety during driving. *Expert Opin Drug Saf*. 2016;15(1):89–98. https://doi.org/10.1517/14740338.2016.1112786
17. Demonte A, Guanti MB, Liberati S, et al. Bilastine safety in drivers who need antihistamines: new evidence from high-speed simulator driving test on allergic patients. *Eur Rev Med Pharmacol Sci*. 2018;22(3):820–828. https://doi.org/10.26355/eurrev_201802_14318
18. Novák Z, Yáñez A, Kiss I, et al. Safety and tolerability of bilastine 10 mg administered for 12 weeks in children with allergic diseases. *Pediatr Allergy Immunol*. 2016;27(5):493–498. https://doi.org/10.1111/pai.12555
19. Sologuren A, Viñas R, Cordón E, et al. Open-label safety assessment of bilastine in elderly patients with allergic rhinoconjunctivitis and/or urticaria. *Allergy Asthma Proc*. 2018;39(4):299–304. https://doi.org/10.2500/aap.2018.39.4136
20. Lasseter KC, Sologuren A, La Noce A, Dilzer SC. Evaluation of the single-dose pharmacokinetics of bilastine in subjects with various degrees of renal insufficiency. *Clin Drug Investig*. 2013;33(9):665–673. https://doi.org/10.1007/s40261-013-0110-0

Regional Specialist Taskforce on Allergy – Dermatology (STAR-D) Meeting, Singapore, 29th May 2021

Advisors

Dr Wai Kwong CHEONG (Chairperson) – Specialist Skin Clinic & Associates Pte Ltd, Singapore
Dr Alson Wai Ming CHAN – Allergy Centre, Hong Kong Sanatorium Hospital, Hong Kong
Dr Kingsley Hau Ngai CHAN – Dermamier Skin & Laser Center, Hong Kong
Dr Chin Chwen CH'NG – Subang Jaya Medical Centre, Selangor, Malaysia
Professor Wen-Hung CHUNG – Department of Dermatology, Chang Gung Memorial Hospital, Taipei, Taiwan
Dr Ma. Teresita GABRIEL – Department of Dermatology, Research Institute for Tropical Medicine, Manila, Philippines
Dr Kiran GODSE – Department of Dermatology, D.Y. Patil School of Medicine, Mumbai, India
Associate Professor Anne GOH – KK Women's and Children's Hospital, Singapore
Professor Kanokvalai KULTHANAN – Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
Dr Wat MITTHAMSIRI – Allergy and Clinical Immunology Division, Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand
Dr Hao Trong NGUYEN – Ho Chi Minh City Hospital of Dermato-Venereology, Ho Chi Minh City, Vietnam
Dr Nirmala PONNUTHURAI – Hospital Tunku Azizah, Kuala Lumpur, Malaysia
Associate Professor Noemie SALTA-RAMOS – Fatima University Medical Center, Manila, Philippines
Professor Marysia TIONGCO-RECTO – Allergy and Immunology, University of the Philippines - Philippine General Hospital, Philippines
Professor Siriwan WANANUKUL – Chulalongkorn University, Bangkok, Thailand
Dr Kent Chee Keen WOO – Gleneagles Hospital, Kuala Lumpur, Malaysia