

Role of bilastine in the management of allergic rhinitis and urticaria: an Asia-Pacific consensus statement

Ralph Mösges^{1,*}, Dennis Lip Yen Lee², Jovilia Abong³, Bella Siasoco³, Steven KW Chow⁴, Jern-Lin Leong⁵, Harvinder Singh⁶, S Kuljit⁷, and Benjamin Campomanes⁸

¹Institute of Medical Statistics, Informatics and Epidemiology, University Hospital of Cologne, 50931 Cologne, Germany

²Department of Ear, Nose, and Throat, United Christian Hospital and Department of Otorhinolaryngology, Head and Neck Surgery, Chinese University of Hong Kong, Hong Kong, China

³University of the Philippines College of Medicine and Philippine General Hospital, 1000 Manila, Philippines

⁴The KL Skin Centre, Pantai Hospital, 59100 Kuala Lumpur, Malaysia

⁵Ascent Ear Nose Throat Specialist Group, Mount Elizabeth Medical Centre, Singapore 228510, Singapore

⁶Hospital Raja Permaisuri Bainun (Ipoh General Hospital), 30990 Ipoh, Malaysia

⁷Department of Otorhinolaryngology, Prince Court Medical Centre, 50450 Kuala Lumpur, Malaysia

⁸Department of Otorhinolaryngology-Head & Neck Surgery, University of Santo Tomas, 1008 Manila, Philippines

The prevalence of allergic diseases is increasing globally, most particularly in middle- to low-income countries. This article examines the burden of allergic rhinitis and chronic urticaria in the Asia-Pacific region, unmet clinical needs, and the potential role of bilastine in the management of these conditions. An International Advisory Group meeting was convened in association with the Asian Pacific Society of Respiriology Annual Congress in November 2014, followed by a literature review, and consensus-based outcomes from the meeting and literature review are described. Regional estimates of the prevalence of allergic rhinitis range from 10% to 50%, while little is known regarding the burden of urticaria in the Asia-Pacific region. A survey of allergy patients in the region identified fast, complete, and long-lasting symptom relief as the medication attributes most important to patients. International treatment guidelines for allergic rhinitis and urticaria advocate the first-line use of second-generation, no-sedating H₁-antihistamines, such as bilastine, over their first-generation counterparts and a range of these agents are available to Asia-Pacific patients. The newer agents possess many of the properties of an "ideal" antihistamine (once daily administration, rapid and complete symptom relief, limited potential for drug-drug interactions, minimal side effects). The burgeoning prevalence of allergic diseases in the Asia-Pacific region and the uncontrolled symptoms that these patients experience demand a new antihistamine that offers the highest number of positive features according to the international guidelines.

Key words: Rhinitis; Allergic; Urticaria; Histamine Antagonists; Asia; Consensus; Bilastine

Correspondence: Ralph Mösges
Institute of Medical Statistics, Informatics and Epidemiology,
University Hospital of Cologne Lindenburger Allee 42, 50931
Cologne, Germany
Tel: +49-221-478-3456
Fax: +49-221-478-3465
E-mail: ralph@moesges.de

This is an Open Access article distributed under the terms of the Creative Commons Attribution. Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Received: September 16, 2015

Accepted: December 31, 2015

Copyright © 2016. Asia Pacific Association of Allergy, Asthma and Clinical Immunology.

INTRODUCTION

There is growing evidence that the prevalence of allergic diseases is increasing globally [1], including in the Asia-Pacific region [2-5]. Estimates suggest that 20% to 30% of the world's population suffers from some form of allergic disease [1]. Allergy is a common and often unrecognized cause of respiratory illness among primary care patients. For example, data from China show that more than 50% of primary care patients with cough have a history of atopic illness [6]. Yet, cross-country studies show a consistent trend towards underdiagnosis of allergic diseases [7].

Although the causes of the worldwide "allergy epidemic" are not known, the growth in allergy prevalence is mainly centered in middle to low-income countries [2], which suggests that economic development may be driving the increase. In the Asia-Pacific region, this theory is borne out by data showing that allergy rates are higher in urban than in rural parts of Asian countries [8-11]. There is now emerging evidence of an interaction between irritants and allergens, whereby inhaled pollutants increase sensitization to allergens, and enhance airway hyperresponsiveness in susceptible people [12]. This may occur because pollutants compromise the barrier function of airway epithelial cells, or because they enhance the immune response to airborne allergens [12, 13]. The ability of pollutants to stimulate a nonallergic hypersensitivity reaction may explain the relationship between urbanization and rhinitis incidence in Asia and elsewhere [1, 8-11]. Climate change may also impact on the development of allergic disease, and the combination of declining air quality and increasing global temperatures is likely to be driving the increase in allergy prevalence in developing and developed countries alike [1].

Allergic diseases may include asthma, rhinitis, anaphylaxis, food allergy, eczema, urticaria and angioedema [1], and many patients with one type of atopic disorder often have another [14]. For example, up to 80% to 90% of patients with asthma also have allergic rhinitis, and 40% of patients with allergic rhinitis have asthma [1]. Almost half of patients (48%) with chronic urticaria also experience allergic rhinitis [15].

Allergic rhinitis and urticaria are common histamine-induced allergies that respond to treatment with antihistamines [16]. Although not life-threatening, the consequences of these conditions are not trivial. Patients with allergic rhinitis or urticaria report impaired quality of life [17-21]. Both of these conditions impact on patients' sleep [18, 20], and affect their daily activities

such as work/school performance [19, 21]. Moreover, physicians frequently underestimate the impact of allergic conditions on the health and quality of life of afflicted patients [1].

International evidence-based guidelines have been published for the management of allergic rhinitis [22] and chronic urticarial [23]. However, the extent to which these are applicable or followed in the Asia-Pacific region is unknown. In November 2014, an Advisory Group Meeting, sponsored by Menarini, was convened in association with the Asia-Pacific Society of Respiriology Annual Congress in Bali, Indonesia. The aim of this Meeting was to identify unmet clinical needs in the management of allergic rhinitis and chronic urticaria in the region, and the role that bilastine may play in addressing these unmet needs. Unmet needs in Asia-Pacific were identified at the meeting by questionnaire. Once identified, literature searches relating to these unmet clinical needs were conducted, and an overview developed from those results, which was circulated electronically among all consensus group members. The current article describes the consensus-based outcomes of that meeting and the subsequent literature review.

BURDEN OF ILLNESS IN ASIA-PACIFIC

Allergic rhinitis

In Asia-Pacific, the prevalence of allergic rhinitis is variously reported as ranging from around 8–10% of the population (in Korea) to more than 50% (among adults in Vietnam and Thailand), depending on the method of assessment [9, 24-32]. The allergies in Asia-Pacific survey reported an adult prevalence of 9%, with 63% of patients having seasonal or intermittent allergies [33]. Studies consistently report that dust mites are the most common causative allergen in the region [34-37].

Patients with allergic rhinitis experience the three cardinal symptoms of sneezing, nasal obstruction, and rhinorrhea as a result of IgE-mediated inflammation of the nasal mucosa [38]. In addition, patients with allergic rhinitis can experience troublesome nonnasal symptoms, such as headache, thirst, and difficulty sleeping [17], as well as cough, snoring, wheezing, sinus pressure, sore throat, and ocular symptoms such as itchy, red or watery eyes [33, 39]. More than 70% of people with allergic rhinitis in Asia-Pacific suffer from sleep problems, which they rate as extremely troublesome, and many experience daytime fatigue related to sleep disturbance [33]. Comorbid asthma is common

in allergic rhinitis, and many patients also experience sinusitis, depression and anxiety [39].

As described earlier, allergic rhinitis impairs quality of life [17, 21], and interferes with daily activities [33]. Patients with allergic rhinitis miss a substantial number of days of work or school because of their symptoms [33, 40, 41], and are less productive when at work because of their symptoms [33]. Direct and indirect costs of illness are high [40–42], to the health system as well as the patient, because many patients use over-the-counter products in addition to prescription medicines to manage their symptoms [41, 43]. An analysis of allergy-related medical costs among children in Thailand found that rhinitis was associated with higher per-patient costs than asthma [42].

Urticaria

Data on the current burden of urticaria in the Asia-Pacific region have yet to be reported. The lifetime prevalence may be as high as 23% [1]. Principal signs and symptoms are the development of wheals and/or angioedema. A single lesion usually lasts no more than 24 hours, but each episode is usually characterized by multiple lesions coming and going [1]. When severe (>50 lesions in 24 hours or large confluent areas of wheals), patients often experience intense pruritus, which can affect normal daily activity and sleep [23].

Urticaria may be classified as acute (episode lasting <6 weeks) or chronic (lasting ≥6 weeks). There is a high prevalence of emotional distress in patients with chronic urticarial [44].

The most common age for development of urticaria is early adulthood, a peak time for education, career development and starting a family; therefore, urticaria has the potential to negatively impact productivity at a crucial time in people's lives [1]. Because of the clear impact of urticaria on patient quality of life [19, 20, 45], guidelines recommend that physicians caring for patients with urticaria routinely assess their quality of life using a validated patient outcome measure such as the chronic urticaria questionnaire on quality of life [46].

PHARMACOLOGICAL TREATMENT: GUIDELINE RECOMMENDATIONS

Allergic rhinitis

The most widely used guidelines for allergic rhinitis are the Allergic Rhinitis and its Impact on Asthma (ARIA) evidence-based

guidelines, which were last updated in 2010 [22]. Pharmacological treatment recommendations are summarized in Table 1 [22].

The ARIA group grades their recommendations as “strong” (i.e., most individuals should receive this intervention, and adherence to this guideline could be used as a quality criterion or performance indicator), or “conditional” (i.e., applying to most individuals but recognizing that different choices will be appropriate for different patients) [22]. Most ARIA recommendations on pharmacological therapy are conditional, but several are strong recommendations. These include the recommendation that, for first-line treatment, patients receive new-generation oral H₁-antihistamines that do not cause sedation or interact with cytochrome P450 enzymes [22]. In these guidelines, new-generation oral H₁-antihistamines are recommended over old-generation oral H₁-antihistamines [22].

Urticaria

Joint guidelines for the management of urticaria have been developed by the Asian Academy of Dermatology and Venereology (AADV), European Academy of Allergy and Clinical Immunology (EAACI), the Global Allergy and Asthma European Network (GA²LEN), the European Dermatology Forum (EDF) and the World Allergy Organization (WAO) [23]. These guidelines were last updated in 2013 [23].

The goal of treatment in urticaria is complete symptom control [23]. Similar to ARIA, these guidelines strongly recommend that modern second-generation H₁-antihistamines are preferred over first-generation H₁-antihistamines in the treatment of urticaria, based on a high level of evidence [23]. In addition, the EAACI/GA²LEN/EDF/WAO guidelines recommend that modern second-generation H₁-antistamines be used first-line for the treatment of urticaria, and be taken continuously at the lowest effective dose rather than on-demand [23].

Another key recommendation in the EAACI/GA²LEN/EDF/WAO guidelines is that the dose of modern second-generation H₁-antistamines can be increased up to 4 folds, and this approach is preferred to combining different H₁-antistamines at the same time [23]. If patients have persistent symptoms despite a 4-fold increase in the dose of second-generation antihistamine, then a trial of add-on therapy (with omalizumab or cyclosporine) is recommended, rather than trying to increase the dose of antihistamine further [23]. Montelukast is an alternative third-line agent, but this is a weak recommendation based on a low level of evidence [23]. A short course of oral corticosteroids may

Table 1. Allergic Rhinitis and its Impact on Asthma recommendations for the pharmacological treatment of allergic rhinitis [22]

Recommendation	Strength	Evidence quality
Oral antihistamines		
Recommend use of new-generation oral H ₁ -antihistamines that do not cause sedation and do not interact with CYP450	Strong	Low
Suggest use of new-generation oral H ₁ -antihistamines that do cause sedation and/or interact with CYP450	Conditional	Low
New-generation oral H ₁ -antihistamines are recommended over old-generation oral H ₁ -antihistamines	Strong	Low
New-generation oral H ₁ -antihistamines are recommended over intranasal H ₁ -antihistamines in adults with persistent or seasonal AR, and in children with intermittent or persistent AR	Conditional	Very low
New-generation oral H ₁ -antihistamines are recommended over oral leukotriene receptor antagonists in patients with seasonal AR, and in preschool children with persistent AR	Conditional	Low
Do NOT use oral H ₁ -antihistamines to treat wheezing in preschool children with other allergic diseases	Conditional	Very low
Intranasal antihistamines		
Suggest use of intranasal H ₁ -antihistamines for symptoms of seasonal allergic rhinitis in adults and children, but NOT for persistent allergic rhinitis	Conditional	Very low
Suggest use of intranasal H ₁ -antihistamines over intranasal chromones in patients with AR	Conditional	Low
Oral leukotriene receptor antagonists		
Can use oral leukotriene receptor antagonists in adults and children with season AR and in preschool children with persistent AR, but NOT in adults with persistent AR	Conditional	High
Intranasal glucocorticosteroids		
Recommend use of intranasal glucocorticosteroids in adults	Conditional	Moderate
Suggest use of intranasal glucocorticosteroids in children	Conditional	Low
Suggest use of intranasal glucocorticosteroids over oral H ₁ -antihistamines in adults with seasonal AR	Conditional	Low
Suggest use of intranasal glucocorticosteroids over oral H ₁ -antihistamines in children with seasonal AR	Conditional	Very low
Recommend use of intranasal glucocorticosteroids over intranasal H ₁ -antihistamines in patients with AR	Strong	High
Recommend use of intranasal glucocorticosteroids over oral leukotriene receptor antagonists in patients with seasonal AR	Strong	Low
Intranasal chromones		
Suggest use of intranasal chromones in patients with AR	Conditional	Moderate
Intranasal ipratropium bromide		
Suggest use of intranasal ipratropium bromide to treat rhinorrhea in patients with persistent AR	Conditional	Moderate
Decongestants		
Suggest a very short course (≤ 5 days) of intranasal decongestant in combination with other treatments in adult patients with AR and severe nasal obstruction, but do NOT use in preschool children	Conditional	Very low
Do NOT use oral decongestants regularly in patients with AR	Conditional	Low
Suggest NOT to use a combination of an oral H ₁ -antihistamine and oral decongestant compared with an oral H ₁ -antihistamine alone	Conditional	Moderate
Ocular treatments		
Suggest use of an intraocular H ₁ -antihistamine in patients with AR and symptoms of conjunctivitis	Conditional	Low
Suggest use of an intraocular chromone in patients with AR and symptoms of conjunctivitis	Conditional	Low

CYP450, cytochrome P450; AR, allergic rhinitis.

be also used third-line or for acute exacerbations, but long-term treatment with systemic steroid is not recommended [23].

The AADV consensus guidelines (2012) are in general agreement with the EAACI/GA²LEN/EDF/WAO guidelines in stating that second-generation H₁-antihistamines should be used first-line in most patients [47]. However, they also note that up dosing of H₁-antihistamines can be undertaken in smaller dose increments in Asian patients, because they are generally of smaller build [47].

APPLICABILITY OF ANTIHISTAMINE TREATMENT RECOMMENDATIONS IN ASIA-PACIFIC

The clinical attributes of allergy medications that are important to patients include good efficacy, a rapid onset of action, a long duration of action, and a lack of unwanted effects [48]. Second generation H₁-antihistamines are recommended first-line because of their proven efficacy and good tolerability, in particular a low rate of sedative effects [48].

In the Asia-Pacific allergies survey, the medication attributes rated as most important were fast onset (30%), complete (26%), and long-lasting (25%) symptom relief [33]. Specifically, 72% of patients expected relief within 3 hours, and 21% expected symptom relief to last for >24 hours [33].

As new agents become available, the clinical profile of these agents approaches those defined by the EAACI and ARIA as the attributes of the 'ideal' antihistamine [49, 50]. Most are taken once daily; the exception is fexofenadine, which is cleared more quickly from the body because it is actively secreted into the intestine and urine [48]. Cetirizine, and to a lesser extent levocetirizine, have the potential to cause sedating effects, because they are capable of crossing the blood-brain barrier [48].

The consensus group believes that physicians in Asia-Pacific have access to a range of suitable second-generation H₁-antihistamine options and are therefore well placed to follow international guideline recommendations for first-line treatment of allergic rhinitis and urticaria.

ROLE OF BILASTINE IN ALLERGY MANAGEMENT

Bilastine, a novel second-generation H₁-antihistamine,

is approved for the symptomatic treatment of allergic rhinoconjunctivitis and urticaria in adults and children over 12 years of age. Current AR and urticaria guidelines recommend second-generation antihistamines as first-line therapy for both conditions [22, 23], and bilastine has the highest number of positive attributes of such agents using the criteria defined by the EAACI/GA²LEN/WAO guidelines [23]. Bilastine has a favourable pharmacokinetic profile, being rapidly absorbed resulting in an onset of clinical effect within one hour of administration, and has a long duration of action, exceeding 24 hours, which allows for once-daily dosing [49]. In a comparison versus cetirizine, bilastine had a significantly greater beneficial effect on wheals and flares at the earliest postdose measurement (89% vs. 44%, $p = 0.011$ and 85% vs. 45%, $p = 0.016$, respectively, at 1.5 hours after administration), suggesting a faster onset of antihistaminergic action [51]. The duration of action of bilastine has also proven to be significantly longer than that of fexofenadine [52]. The route of bilastine elimination is independent of the liver, and therefore this agent has limited potential for metabolic drug-drug interactions [49].

In clinical trials, bilastine has shown efficacy equivalent to cetirizine and desloratadine in allergic rhinitis [53-55], and equivalent to levocetirizine in urticarial [56], and was shown to improve the quality of life of patients with allergic rhinitis [54] or chronic urticarial [56]. The cumulative quality of life data from the major bilastine clinical trials demonstrate significant improvements with bilastine relative to placebo in patients with allergic rhinitis or urticaria, with quality of life improvements consistent with symptom relief in these conditions [57].

An important advantage of bilastine is that it has a very favourable tolerability profile with minimal effect on sedation, psychomotor performance and driving competence [58, 59]. Bilastine is truly nonsedative. A study using positron emission tomography found that bilastine 20 mg occupied almost none of the cerebral H₁-receptors, compared with about 54% occupancy with hydroxyzine 25 mg ($p < 0.01$) [60]. This means that bilastine has one of the lowest reported rates of central nervous system H₁-receptor occupancy of the available antihistamines [60]. In addition, and unlike cetirizine, bilastine does not augment the CNS effects of alcohol [61].

In addition to being nonsedative, bilastine is not associated with weight gain, anticholinergic effects, or cardiac side effects [49]. Even at supratherapeutic doses, bilastine has no significant effect on QT interval, even when administered with ketoconazole

[62]. In comparative analyses, bilastine was associated with significantly lower rates of somnolence and fatigue relative to cetirizine [55]. These features mean that bilastine has many of the characteristics of the optimal H₁-antihistamine as recommended for first-line treatment of allergic rhinitis or urticaria in current international guidelines [23, 49].

UNMET NEEDS IN ALLERGY MANAGEMENT IN ASIA-PACIFIC

The consensus group identified a number of barriers to the optimal management of allergic conditions in Asia-Pacific. These include underdiagnosis and undertreatment of allergies, diverse treatment practices, patient perceptions of allergy treatment options, and physicians' attitudes to guidelines and treatments.

Diverse treatment practices

Anecdotal evidence suggests that allergic rhinitis and urticaria are managed differently in different countries with variable use of international guidelines [63]. Specialist care of allergy patients differs between countries. For example, in Singapore, adults requiring specialist care for allergic disease tend to be referred to rheumatologists with a subinterest in allergy, whereas in Malaysia, referral is mainly to otolaryngologists or dermatologists. While some variation between countries is unavoidable in health care, a more consistent approach to allergy management within countries should be the goal. Consistent and structured approaches to disease management in allergic conditions can reduce morbidity, improve patient well-being and reduce costs to both the healthcare system and the patient [1]. In addition, treatment according to accepted guidelines results in better symptom control and improved quality of life for patients with allergy compared with treatment based on physician free choice [63].

Suboptimal use of evidence-based guidelines in allergy is also a concern. For example, sedating antihistamines are frequently used in Malaysia. The reason for this is not clear, but it may involve primary care physicians' lack of awareness of current recommendations, patients self-medicating with over-the-counter treatments, or patients/physicians opting for this treatment because of issues related to cost.

A recent initiative in Europe has been the development of integrated care pathways (ICPs) to standardize the management

and referral of patients with chronic respiratory disease, including allergic rhinitis, with or without concomitant asthma [64]. It is hoped that, by providing a common framework for guideline-directed care in these conditions, not only will the evidence-based management of patients improve, but there will be a reduction in the healthcare burden associated with these diseases, e.g., fewer emergency room visits or hospitalizations, less patient disability, and reduced costs [64].

Physicians need to be aware of the potential adverse effects of first-generation H₁-antihistamines, including CNS effects and anticholinergic effects (e.g., dry mouth, urinary retention), when making prescribing choices [48]. If first-generation H₁-antihistamines are prescribed, patients need to be fully aware of the potential CNS side effects of these agents, and the impact they may have on their ability to drive and to use machinery.

In addition, there is variable use of up dosing of second-generation H₁-antihistamines as recommended in the international urticaria guidelines [23], probably because this practice is not used in the management of other allergic conditions.

Patient perceptions of treatment

Asia-Pacific data show that the most common reasons for patients to be dissatisfied with treatment for allergic rhinitis are inadequate efficacy and bothersome side effects [21]. Moreover, these are also reasons cited for nonadherence, along with symptom relief that does not last 24 hours and safety concerns with intranasal corticosteroids [65]. Poor adherence or inadequate treatment efficacy may explain why, in the Asia-Pacific allergies survey, only 42% of patients with allergic rhinitis reported that their symptoms were completely or well controlled [33].

For urticaria patients, a GA²LEN Task Force report indicates that <50% of patients respond to standard doses of second-generation H₁-antistamines [66], supporting the EAACI/EDF/GA²LEN/WAO recommendation that the dose be increased up to 4 folds to achieve relief [23]. If physicians are unwilling to updose H₁-antihistamines for these patients, many will be dissatisfied with treatment.

Taken together, these data suggest that much can be done to improve the treatment (and treatment satisfaction) of allergy patients in Asia-Pacific. Choosing a treatment with a rapid onset of action, good efficacy and tolerability, and proven effects on quality of life would help to improve patient satisfaction with treatment in the region.

CONSENSUS GROUP RECOMMENDATIONS

The Consensus Group encourages and endorses regional initiatives to raise awareness of allergic diseases as a common cause of respiratory problems among patients attending primary care physicians [1, 6]. They also endorse all regional activities that will optimize treatment outcomes for allergy patients in Asia-Pacific through physician education, guideline adherence, and improved awareness of burden of illness. Consideration should be given to the development of ICPs, similar to those being introduced in Europe, in the Asia-Pacific region, on either a national or a regional basis.

The Consensus Group recommends that further research be undertaken, specifically in Asia-Pacific, into various aspects of allergic disease, including patient attitudes to treatment and factors affecting adherence in both urticaria and allergic rhinitis. The data on the relationship between pollutants and allergy, and the differences between 'true' allergic rhinitis and a non-IgE-mediated hypersensitivity phenotype (also called local allergic rhinitis), highlight the need for more research into the classification of rhinitis subtypes, which may eventually help physicians to better tailor treatment for individual patients. Unlike most other forms of nonallergic rhinitis, which are treated with topical corticosteroids, local allergic rhinitis can respond to oral antihistamines [67].

They also endorse all efforts to improve the use of guideline-recommended therapies for allergic rhinitis and urticaria in the Asia-Pacific region. The Consensus Group recommends that more effort is made by regional organizations to raise awareness and drive medical education on guidelines for optimal disease management in allergic rhinitis and urticaria. This education should reinforce the importance of using second-generation H₁-antihistamines in preference to first-generation agents, because of their improved CNS safety profile. There are no significant barriers to the optimal prescription of nonsedating H₁-antihistamines in Asia-Pacific, and therefore the Consensus Group recommends that more activities are undertaken at a regional and national level to raise awareness of international guidelines, and to encourage adherence to these guidelines through continuing medical education, and quality assurance endeavours.

The Consensus Group also urges physicians, when prescribing, to keep in mind those treatment-related factors that are likely to

achieve the greatest patient adherence: convenient treatment regimen, rapid symptom relief, long-lasting effects, and a good tolerability profile. The availability of newer second-generation H₁-antihistamines, such as bilastine, allows the use of agents that have these features and which closely meet the criteria for the ideal agent outlined by the EAACI and ARIA [50].

CONCLUSIONS

Because of the growing prevalence of allergic disease in Asia-Pacific, more research is needed in the region on the experience and attitudes of patients with allergies, and on the prevalence of urticaria, in order to fully define the burden of illness in the region. Currently, these conditions are underdiagnosed and undertreated, and much can be done at a regional and national level to improve awareness of the burden of illness, and adherence to international guidelines, in order to optimize treatment for patients. One of the key guideline recommendations is for nonsedating antihistamines to be used first-line in the treatment of allergic rhinitis and urticaria. Physicians in Asia-Pacific have access to a range of suitable second-generation H₁-antihistamine options and are therefore well placed to follow international guideline recommendations for first-line treatment of allergic rhinitis and urticaria. International guidelines have defined a number of features for the ideal antihistamine. Of the available agents, bilastine has the highest number of these features, with good efficacy, excellent tolerability, rapid onset and long duration of action, as well as being truly nonsedative, with minimal CNS penetration.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Menarini Asia-Pacific Holdings Pte Ltd for providing logistic support and funding for the consensus meeting, and for commissioning MIMS Pte Ltd to provide writing assistance and editorial support. The views expressed in this manuscript are solely those of the authors.

REFERENCES

1. Pawankar R, Canonica GW, Holgate ST, Lockey RF, Blaiss MS. WAO

- white book on allergy: update 2013. Milwaukee (WI): World Allergy Organization; 2013.
2. Bjorksten B, Clayton T, Ellwood P, Stewart A, Strachan D; ISAAC Phase III Study Group. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. *Pediatr Allergy Immunol* 2008;19:110-24.
3. Park HS, Choi GS, Cho JS, Kim YY. Epidemiology and current status of allergic rhinitis, asthma, and associated allergic diseases in Korea: ARIA Asia-Pacific workshop report. *Asian Pac J Allergy Immunol* 2009;27:167-71.
4. Wu WF, Wan KS, Wang SJ, Yang W, Liu WL. Prevalence, severity, and time trends of allergic conditions in 6-to-7-year-old schoolchildren in Taipei. *J Investig Allergol Clin Immunol* 2011;21:556-62.
5. Zhao J, Bai J, Shen K, Xiang L, Huang S, Chen A, Huang Y, Wang J, Ye R. Self-reported prevalence of childhood allergic diseases in three cities of China: a multicenter study. *BMC Public Health* 2010;10:551.
6. Hong Q, Bai C, Wang X. Characteristics of Chinese patients with cough in primary care centre. *J Transl Med* 2011;9:149.
7. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J* 2004;24:758-64.
8. Chang JW, Lin CY, Chen WL, Chen CT. Higher incidence of *Dermatophagoides pteronyssinus* allergy in children of Taipei city than in children of rural areas. *J Microbiol Immunol Infect* 2006;39:316-20.
9. Lam HT, Van Tuong N, Ekerljung L, Ronmark E, Lundback B. Allergic rhinitis in northern vietnam: increased risk of urban living according to a large population survey. *Clin Transl Allergy* 2011;1:7.
10. Ma Y, Zhao J, Han ZR, Chen Y, Leung TF, Wong GW. Very low prevalence of asthma and allergies in schoolchildren from rural Beijing, China. *Pediatr Pulmonol* 2009;44:793-9.
11. Sriyaraj K, Priest N, Shutes B. Environmental factors influencing the prevalence of respiratory diseases and allergies among schoolchildren in Chiang Mai, Thailand. *Int J Environ Health Res* 2008;18:129-48.
12. Devalia JL, Rusznak C, Davies RJ. Allergen/irritant interaction: its role in sensitization and allergic disease. *Allergy* 1998;53:335-45.
13. D'Amato G, Cecchi L, D'Amato M, Liccardi G. Urban air pollution and climate change as environmental risk factors of respiratory allergy: an update. *J Investig Allergol Clin Immunol* 2010;20:95-102.
14. Annesi-Maesano I, Beyer A, Marmouz F, Mathelier-Fusade P, Vervloet D, Bauchau V. Concurrent allergic diseases: a cross-sectional study in a French population. *Allergy* 2006;61:390-1.
15. Zazzali JL, Broder MS, Chang E, Chiu MW, Hogan DJ. Cost, utilization, and patterns of medication use associated with chronic idiopathic urticaria. *Ann Allergy Asthma Immunol* 2012;108:98-102.
16. Blaiss MS, Montanaro A. Allergic rhinitis and chronic urticaria: management of histamine-induced disorders. *Prim Issue* 2009;11:24-34.
17. Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of life in allergic rhinitis and asthma. A population-based study of young adults. *Am J Respir Crit Care Med* 2000;162(4 Pt 1):1391-6.
18. Pherwani AV, Bansode G, Gadhia S. The impact of chronic urticaria on the quality of life in Indian patients. *Indian J Dermatol* 2012;57:110-3.
19. Liu JB, Yao MZ, Si AL, Xiong LK, Zhou H. Life quality of Chinese patients with chronic urticaria as assessed by the dermatology life quality index. *J Eur Acad Dermatol Venereol* 2012;26:1252-7.
20. Kang MJ, Kim HS, Kim HO, Park YM. The impact of chronic idiopathic urticaria on quality of life in Korean patients. *Ann Dermatol* 2009;21:226-9.
21. Katelaris CH, Lai CK, Rhee CS, Lee SH, Yun WD, Lim-Varona L, Quang VT, Hwang J, Singh H, Kim J, Boyle JM, Dhong HJ, Narayanan P, Vicente G, Blaiss M, Sacks R. Nasal allergies in the Asian-Pacific population: results from the Allergies in Asia-Pacific Survey. *Am J Rhinol Allergy* 2011;25 Suppl 1:S3-15.
22. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, van Wijk RG, Ohta K, Zuberbier T, Schunemann HJ; Global Allergy and Asthma European Network; Grading of Recommendations Assessment, Development and Evaluation Working Group. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol* 2010;126:466-76.
23. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, Church MK, Ensina LF, Gimenez-Arnau A, Godse K, Gonçalo M, Grattan C, Hebert J, Hide M, Kaplan A, Kapp A, Abdul Latiff AH, Mathelier-Fusade P, Metz M, Nast A, Saini SS, Sanchez-Borges M, Schmid-Grendelmeier P, Simons FE, Staubach P, Sussman G, Toubi E, Vena GA, Wedi B, Zhu XJ, Maurer M; European Academy of Allergy and Clinical Immunology; Global Allergy and Asthma European Network; European Dermatology Forum; World Allergy Organization. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. *Allergy* 2014;69:868-87.
24. Ahn K, Kim J, Kwon HJ, Chae Y, Hahm MI, Lee KJ, Park YM, Lee SY, Han M, Kim WK. The prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in Korean children: Nationwide cross-sectional survey using complex sampling design. *J Korean Med Assoc* 2011;54:769-78.
25. Li F, Zhou Y, Li S, Jiang F, Jin X, Yan C, Tian Y, Zhang Y, Tong S, Shen X. Prevalence and risk factors of childhood allergic diseases in eight

- metropolitan cities in China: a multicenter study. *BMC Public Health* 2011;11:437.
26. Seong HU, Cho SD, Park SY, Yang JM, Lim DH, Kim JH, Son BK. Nationwide survey on the prevalence of allergic diseases according to region and age. *Pediatr Allergy Respir Dis* 2012;22:224-31.
27. Shen J, Ke X, Hong S, Zeng Q, Liang C, Li T, Tang A. Epidemiological features of allergic rhinitis in four major cities in Western China. *J Huazhong Univ Sci Technolog Med Sci* 2011;31:433-40.
28. Teeratakulpisarn J, Paironkul S, Heng S. Survey of the prevalence of asthma, allergic rhinitis and eczema in schoolchildren from Khon Kaen, Northeast Thailand. an ISAAC study. *International Study of Asthma and Allergies in Childhood. Asian Pac J Allergy Immunol* 2000;18:187-94.
29. Teeratakulpisarn J, Wiangnon S, Kosalaraksa P, Heng S. Surveying the prevalence of asthma, allergic rhinitis and eczema in school-children in Khon Kaen, Northeastern Thailand using the ISAAC questionnaire: phase III. *Asian Pac J Allergy Immunol* 2004;22:175-81.
30. Uthaisangsook S. Prevalence of asthma, rhinitis, and eczema in the university population of Phitsanulok, Thailand. *Asian Pac J Allergy Immunol* 2007;25:127-32.
31. Wang ZH, Lin WS, Li SY, Zhao SC, Wang L, Yang ZG, Chen J, Zhang ZF, Yu JZ. Research on prevalence and related factors in allergic rhinitis. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2011;46:225-31.
32. Zhao J, Bai J, Shen KL, Xiang L, Huang Y, Huang S, Chen AH, Wang JS, Ye RW. Questionnaire-based survey of allergic diseases among children aged 0 - 14 years in the downtown of Beijing, Chongqing and Guangzhou. *Zhonghua Er Ke Za Zhi* 2011;49:740-4.
33. Meltzer EO, Blaiss MS, Naclerio RM, Stoloff SW, Derebery MJ, Nelson HS, Boyle JM, Wingertzahn MA. Burden of allergic rhinitis: allergies in America, Latin America, and Asia-Pacific adult surveys. *Allergy Asthma Proc* 2012;33 Suppl 1:S113-41.
34. Andiappan AK, Puan KJ, Lee B, Nardin A, Poidinger M, Connolly J, Chew FT, Wang DY, Rotzschke O. Allergic airway diseases in a tropical urban environment are driven by dominant mono-specific sensitization against house dust mites. *Allergy* 2014;69:501-9.
35. Lam HT, Ekerljung L, Bjerg A, Van T Tng N, Lundbäck B, Ronmark E. Sensitization to airborne allergens among adults and its impact on allergic symptoms: a population survey in northern Vietnam. *Clin Transl Allergy* 2014;4:6.
36. Prasarnphanich T, Sindhurat S. Sensitization to common indoor allergens and its association with allergic diseases in Thai female high-school students. *Pediatr Allergy Immunol* 2005;16:402-7.
37. Sun BQ, Zheng PY, Zhang XW, Huang HM, Chen DH, Zeng GQ. Prevalence of allergen sensitization among patients with allergic diseases in Guangzhou, Southern China: a four-year observational study. *Multidiscip Respir Med* 2014;9:2.
38. Pawankar R, Bunnag C, Khaltayev N, Bousquet J. Allergic rhinitis and its impact on asthma in Asia Pacific and the ARIA update 2008. *World Allergy Organ J* 2012;5(Suppl 3):S212-7.
39. Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. *Allergy* 2007;62 Suppl 85:17-25.
40. Blaiss MS. Allergic rhinitis: direct and indirect costs. *Allergy Asthma Proc* 2010;31:375-80.
41. Nathan RA. The burden of allergic rhinitis. *Allergy Asthma Proc* 2007;28:3-9.
42. Ngamphaiboon J, Kongnakorn T, Detzel P, Sirisomboonwong K, Wasiaik R. Direct medical costs associated with atopic diseases among young children in Thailand. *J Med Econ* 2012;15:1025-35.
43. Stull DE, Gavriel S. Use of, satisfaction with, and willingness to switch prescription and over-the-counter treatments for chronic urticaria: an online survey. *Patient* 2009;2:151-7.
44. Staubach P, Dechene M, Metz M, Magerl M, Siebenhaar F, Weller K, Zezula P, Eckhardt-Henn A, Maurer M. High prevalence of mental disorders and emotional distress in patients with chronic spontaneous urticaria. *Acta Derm Venereol* 2011;91:557-61.
45. Yun J, Katelaris CH, Weerasinghe A, Adikari DB, Ratnayake C. Impact of chronic urticaria on the quality of life in Australian and Sri Lankan populations. *Asia Pac Allergy* 2011;1:25-9.
46. Baiardini I, Braidò F, Bindeslev-Jensen C, Bousquet PJ, Brzoza Z, Canonica GW, Compalati E, Fiocchi A, Fokkens W, Gerth van Wijk R, Gimenez-Arnau A, Godse K, Grattan C, Grob JJ, La Grutta S, Kalogeromitros D, Kocatürk E, Lombardi C, Mota-Pinto A, Ridolo E, Saini SS, Sanchez-Borges M, Senna GE, Terreehorst I, Todo Bom A, Toubi E, Bousquet J, Zuberbier T, Maurer M. Recommendations for assessing patient-reported outcomes and health-related quality of life in patients with urticaria: a GA(2) LEN taskforce position paper. *Allergy* 2011;66:840-4.
47. Chow SK. Management of chronic urticaria in Asia: 2010 AADV consensus guidelines. *Asia Pac Allergy* 2012;2:149-60.
48. Church DS, Church MK. Pharmacology of antihistamines. *World Allergy Organ J* 2011;4(3 Suppl):S22-7.
49. Bousquet J, Ansotegui I, Canonica GW, Zuberbier T, Baena-Cagnani CE, Bachert C, Cruz AA, González SN, Kuna P, Morais-Almeida M, Mullol J, Ryan DP, Sánchez-Borges M, Valiente R, Church MK. Establishing the place in therapy of bilastine in the treatment of allergic rhinitis according to ARIA: evidence review. *Curr Med Res Opin* 2012;28:131-9.

50. Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham SR, Fokkens W, Lockey R, Meltzer EO, Mullol J, Naclerio RM, Price D, Simons FE, Vignola AM, Warner JO; European Academy of Allergy and Clinical Immunology (EAACI); Allergic Rhinitis and its Impact on Asthma (ARIA). Requirements for medications commonly used in the treatment of allergic rhinitis. *European Academy of Allergy and Clinical Immunology (EAACI), Allergic Rhinitis and its Impact on Asthma (ARIA)*. *Allergy* 2003;58:192-7.
51. Church MK. Comparative inhibition by bilastine and cetirizine of histamine-induced wheal and flare responses in humans. *Inflamm Res* 2011;60:1107-12.
52. Horak F, Ziegelmayer P, Ziegelmayer R, Lemell P. The effects of bilastine compared with cetirizine, fexofenadine, and placebo on allergen-induced nasal and ocular symptoms in patients exposed to aeroallergen in the Vienna Challenge Chamber. *Inflamm Res* 2010;59:391-8.
53. Bachert C, Kuna P, Sanquer F, Ivan P, Dimitrov V, Gorina MM, van de Heyning P, Loureiro A; Bilastine International Working Group. Comparison of the efficacy and safety of bilastine 20 mg vs desloratadine 5 mg in seasonal allergic rhinitis patients. *Allergy* 2009;64:158-65.
54. Kuna P, Bachert C, Nowacki Z, van Cauwenberge P, Agache I, Fouquert L, Roger A, Sologuren A, Valiente R; Bilastine International Working Group. Efficacy and safety of bilastine 20 mg compared with cetirizine 10 mg and placebo for the symptomatic treatment of seasonal allergic rhinitis: a randomized, double-blind, parallel-group study. *Clin Exp Allergy* 2009;39:1338-47.
55. Sastre J, Mullol J, Valero A, Valiente R; Bilastine Study Group. Efficacy and safety of bilastine 20 mg compared with cetirizine 10 mg and placebo in the treatment of perennial allergic rhinitis. *Curr Med Res Opin* 2012;28:121-30.
56. Zuberbier T, Oanta A, Bogacka E, Medina I, Wesel F, Uhl P, Antepara I, Jauregui I, Valiente R; Bilastine International Working Group. 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;65:516-28.
57. Jauregui I, Bartra J, del Cuvillo A, Dávila I, Ferrer M, Montoro J, Mullol J, Sastre J, Valero A. Bilastine and quality of life. *J Invest Allergol Clin Immunol* 2011;21 Suppl 3:16-23.
58. Bousquet J, Schünemann HJ, Samolinski B, Demoly P, Baena-Cagnani CE, Bachert C, Bonini S, Boulet LP, Bousquet PJ, Brozek JL, Canonica GW, Casale TB, Cruz AA, Fokkens WJ, Fonseca JA, van Wijk RG, Grouse L, Haahtela T, Khaltaev N, Kuna P, Lockey RF, Lodrup Carlsen KC, Mullol J, Naclerio R, O'Hehir RE, Ohta K, Palkonen S, Papadopoulos NG, Passalacqua G, Pawankar R, Price D, Ryan D, Simons FE, Togias A, Williams D, Yorgancioglu A, Yusuf OM, Aberer W, Adachi M, Agache I, Ait-Khaled N, Akdis CA, Andrianarisoa A, Annesi-Maesano I, Ansotegui IJ, Baiardini I, Bateman ED, Bedbrook A, Beghe B, Beji M, Bel EH, Ben Kheder A, Bennoor KS, Bergmann KC, Berrissoul F, Bieber T, Bindslev Jensen C, Blaiss MS, Boner AL, Bouchard J, Braidio F, Brightling CE, Bush A, Caballero F, Calderon MA, Calvo MA, Camargos PA, Caraballo LR, Carlsen KH, Carr W, Cepeda AM, Cesario A, Chavannes NH, Chen YZ, Chiriac AM, Chivato Pérez T, Chkhartishvili E, Ciprandi G, Costa DJ, Cox L, Custovic A, Dahl R, Darsow U, De Blay F, Deleanu D, Denburg JA, Devillier P, Didi T, Dokic D, Dolen WK, Douagui H, Dubakiene R, Durham SR, Dykewicz MS, El-Gamal Y, El-Meziane A, Emuzyte R, Fiocchi A, Fletcher M, Fukuda T, Gamkrelidze A, Gereda JE, González Diaz S, Gotua M, Guzmán MA, Hellings PW, Hellquist-Dahl B, Horak F, Hourihane JO, Howarth P, Humbert M, Ivancevich JC, Jackson C, Just J, Kalayci O, Kaliner MA, Kalyoncu AF, Keil T, Keith PK, Khayat G, Kim YY, Koffi N'goran B, Koppelman GH, Kowalski ML, Kull I, Kvedariene V, Larenas-Linnemann D, Le LT, Lemièr C, Li J, Lieberman P, Lipworth B, Mahboub B, Makela MJ, Martin F, Marshall GD, Martinez FD, Masjedi MR, Maurer M, Mavale-Manuel S, Mazon A, Melen E, Meltzer EO, Mendez NH, Merk H, Mihaltan F, Mohammad Y, Morais-Almeida M, Muraro A, Nafti S, Namazova-Baranova L, Nekam K, Neou A, Niggemann B, Nizankowska-Mogilnicka E, Nyembue TD, Okamoto Y, Okubo K, Orru MP, Ouedraogo S, Ozdemir C, Panzner P, Pali-Schöll I, Park HS, Pigearias B, Pohl W, Popov TA, Postma DS, Potter P, Rabe KF, Ratomaharo J, Reitamo S, Ring J, Roberts R, Rogala B, Romano A, Roman Rodriguez M, Rosado-Pinto J, Rosenwasser L, Rottem M, Sanchez-Borges M, Scadding GK, Schmid-Grendelmeier P, Sheikh A, Sisul JC, Solé D, Sooronbaev T, Spicak V, Spranger O, Stein RT, Stoloff SW, Sunyer J, Szczeklik A, Todo-Bom A, Toskala E, Tremblay Y, Valenta R, Valero AL, Valeyre D, Valiulis A, Valovirta E, Van Cauwenberge P, Vandenplas O, van Weel C, Vichyanond P, Viegi G, Wang DY, Wickman M, Wöhrl S, Wright J, Yawn BP, Yiallourou PK, Zar HJ, Zernotti ME, Zhong N, Zidarn M, Zuberbier T, Burney PG, Johnston SL, Warner JO; World Health Organization Collaborating Center for Asthma and Rhinitis. Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. *J Allergy Clin Immunol* 2012;130:1049-62.
59. Conen S, Theunissen EL, Van Oers AC, Valiente R, Ramaekers JG. Acute and subchronic effects of bilastine (20 and 40 mg) and hydroxyzine (50 mg) on actual driving performance in healthy volunteers. *J Psychopharmacol* 2011;25:1517-23.
60. Farre M, Perez-Mana C, Papaseit E, Menoyo E, Perez M, Martin

- S, Bullich S, Rojas S, Herance JR, Trampal C, Labeaga L, Valiente R. Bilastine vs. hydroxyzine: occupation of brain histamine H1-receptors evaluated by positron emission tomography in healthy volunteers. *Br J Clin Pharmacol* 2014;78:970-80.
61. García-Gea C, Martínez J, Ballester MR, Gich I, Valiente R, Antonijoan RM. Psychomotor and subjective effects of bilastine, hydroxyzine, and cetirizine, in combination with alcohol: a randomized, double-blind, crossover, and positive-controlled and placebo-controlled Phase I clinical trials. *Hum Psychopharmacol* 2014;29:120-32.
62. Tyl B, Kabbaj M, Azzam S, Sologuren A, Valiente R, Reinbolt E, Roupe K, Blanco N, Wheeler W. Lack of significant effect of bilastine administered at therapeutic and supratherapeutic doses and concomitantly with ketoconazole on ventricular repolarization: results of a thorough QT study (TQTS) with QT-concentration analysis. *J Clin Pharmacol* 2012;52:893-903.
63. Bousquet J, Lund VJ, van Cauwenberge P, Bremard-Oury C, Mounedji N, Stevens MT, El-Akkad T. Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled trial. *Allergy* 2003;58:733-41.
64. European Innovation Partnership on Active and Healthy Ageing, Action Plan B3; Mechanisms of the Development of Allergy, WP 10; Global Alliance against Chronic Respiratory Diseases, Bousquet J, Addis A, Adcock I, Agache I, Agusti A, Alonso A, Annesi-Maesano I, Anto JM, Bachert C, Baena-Cagnani CE, Bai C, Baigenzhin A, Barbara C, Barnes PJ, Bateman ED, Beck L, Bedbrook A, Bel EH, Benezet O, Bennoor KS, Benson M, Bernabeu-Wittel M, Bewick M, Bindslev-Jensen C, Blain H, Blasi F, Bonini M, Bonini S, Boulet LP, Bourdin A, Bourret R, Bousquet PJ, Brightling CE, Briggs A, Brozek J, Buhl R, Bush A, Caimmi D, Calderon M, Calverley P, Camargos PA, Camuzat T, Canonica GW, Carlsen KH, Casale TB, Cazzola M, Cepeda Sarabia AM, Cesario A, Chen YZ, Chkhartishvili E, Chavannes NH, Chiron R, Chuchalin A, Chung KF, Cox L, Crooks G, Crooks MG, Cruz AA, Custovic A, Dahl R, Dahlen SE, De Blay F, Dedeu T, Deleanu D, Demoly P, Devillier P, Didier A, Dinh-Xuan AT, Djukanovic R, Dokic D, Douagui H, Dubakiene R, Eglin S, Elliot F, Emuzyte R, Fabbri L, Fink Wagner A, Fletcher M, Fokkens WJ, Fonseca J, Franco A, Frith P, Furber A, Gaga M, Garcés J, Garcia-Aymerich J, Gamkrelidze A, Gonzales-Diaz S, Gouzi F, Guzmán MA, Haahtela T, Harrison D, Hayot M, Heaney LG, Heinrich J, Hellings PW, Hooper J, Humbert M, Hyland M, Iaccarino G, Jakovenko D, Jardim JR, Jeandel C, Jenkins C, Johnston SL, Jonquet O, Joos G, Jung KS, Kalayci O, Karunanithi S, Keil T, Khaltayev N, Kolek V, Kowalski ML, Kull I, Kuna P, Kvedariene V, Le LT, Lodrup Carlsen KC, Louis R, MacNee W, Mair A, Majer I, Manning P, de Manuel Keenoy E, Masjedi MR, Melen E, Melo-Gomes E, Menzies-Gow A, Mercier G, Mercier J, Michel JP, Miculinic N, Mihaltan F, Milenkovic B, Molimard M, Momas I, Montilla-Santana A, Morais-Almeida M, Morgan M, N'Diaye M, Nafti S, Nekam K, Neou A, Nicod L, O'Hehir R, Ohta K, Paggiaro P, Palkonen S, Palmer S, Papadopoulos NG, Papi A, Passalacqua G, Pavord I, Pigearias B, Plavec D, Postma DS, Price D, Rabe KF, Radier Pontal F, Redon J, Rennard S, Roberts J, Robine JM, Roca J, Roche N, Rodenas F, Roggeri A, Rolland C, Rosado-Pinto J, Ryan D, Samolinski B, Sanchez-Borges M, Schünemann HJ, Sheikh A, Shields M, Siafakas N, Sibille Y, Similowski T, Small I, Sola-Morales O, Sooronbaev T, Stelmach R, Sterk PJ, Stiris T, Sud P, Tellier V, To T, Todo-Bom A, Triggiani M, Valenta R, Valero AL, Valiulis A, Valovirta E, Van Ganse E, Vandenplas O, Vasankari T, Vestbo J, Vezzani G, Viegi G, Visier L, Vogelmeier C, Vontetsianos T, Wagstaff R, Wahn U, Wallaert B, Whalley B, Wickman M, Williams DM, Wilson N, Yawn BP, Yiallourou PK, Yorgancioglu A, Yusuf OM, Zar HJ, Zhong N, Zidarn M, Zuberbier T. Integrated care pathways for airway diseases (AIRWAYS-ICPs). *Eur Respir J* 2014;44:304-23.
65. Katelaris CH, Sacks R, Theron PN. Allergic rhinoconjunctivitis in the Australian population: burden of disease and attitudes to intranasal corticosteroid treatment. *Am J Rhinol Allergy* 2013;27:506-9.
66. Maurer M, Weller K, Bindslev-Jensen C, Gimenez-Arnau A, Bousquet PJ, Bousquet J, Canonica GW, Church MK, Godse KV, Grattan CE, Greaves MW, Hide M, Kalogeromitros D, Kaplan AP, Saini SS, Zhu XJ, Zuberbier T. Unmet clinical needs in chronic spontaneous urticaria. A GA²LEN task force report. *Allergy* 2011;66:317-30.
67. Rondon C, Campo P, Togias A, Fokkens WJ, Durham SR, Powe DG, Mullol J, Blanca M. Local allergic rhinitis: concept, pathophysiology, and management. *J Allergy Clin Immunol* 2012;129:1460-7.