



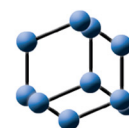
# NEW EMIRATES MEDICAL JOURNAL

## **An Algorithm Recommendation for Management of Allergic Rhinitis in the United Arab Emirates: A Consensus Statement from an Expert Panel**

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## REVIEW ARTICLE

### An Algorithm Recommendation for Management of Allergic Rhinitis in the United Arab Emirates: A Consensus Statement from an Expert Panel

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#### Abstract:

##### Background:

Allergic rhinitis (AR) is a common chronic health problem in the United Arab Emirates (UAE). Achieving adequate symptom control is pivotal to successful AR management, which may be attained following a stepwise treatment algorithm. Despite the availability of several guideline recommendations for the best management of AR, morbidity remains high in patients with AR, with treatment goals being far from reach.

##### Objective:

The objective of this consensus statement was to discuss the currently available knowledge on the treatment of AR and to provide an expert opinion on the use of MP-AzeFlu (azelastine HCl, AZE; 137 µg per spray) and INCS (fluticasone propionate, FP; 50 µg per spray) for the effective management of AR in the UAE.

##### Methods:

A consensus meet involving 13 otorhinolaryngologists and one pulmonologist was held in Dubai, UAE, to discuss the current understanding of the treatment and management of AR.

##### Results:

The panel advised to start AR pharmacotherapy with antihistamines (AH), leukotriene receptor antagonist (LTRA), INCS or MP-AzeFlu based on the visual analogue scale (VAS) score. In mild intermittent AR (VAS score <5/10), AH or LTRA is recommended as first-line therapy. However, in case of VAS score ≥5/10 or persistent AR, and treatment failure with AHs alone, INCS or MP-AzeFlu is recommended, followed by reassessment for 7 days to confirm a step-up or step-down therapy. Patients non-responsive to therapy were advised to step-up with MP-AzeFlu.

##### Conclusion:

The panel advocated a combination of intranasal second-generation AH and INCS in a single device (Dymista®) as first-line therapy for the management of AR. The algorithm provided herein can be applied in most healthcare settings by following a step-up or step-down strategy based on the VAS scores for AR control in the UAE.

**Keywords:** Allergic rhinitis, Azelastine HCl, Dymista, Fluticasone propionate, Treatment algorithm, Chronic health problem.

#### Article History

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## 1. INTRODUCTION

Despite the availability of numerous guideline recommendations for the best management of allergic rhinitis (AR), morbidity remains high in patients with AR, with treatment goals being far from reach. The reason could be the implementation of guidelines or social, organisational, economic and political context [1]. In addition, under-diagnosis and under-treatment of AR lead to increased morbidity [2, 3]. Studies have shown that patients with AR are not satisfied with current therapy mainly because of lack of efficacy and bothersome side effects [1, 4, 5]. Moreover, patients desire a new therapy that has a rapid onset of action, long-lasting effect, is well-tolerated and provides complete symptom relief [6]. Regardless of the availability of abundant treatment options, 60% of patients with AR responded that they were 'very interested' in finding a new medication and 25% were 'constantly' trying different medications to find the one that 'works' [4]. In the United Arab Emirates (UAE), a relatively higher proportion (54%) of patients were not satisfied with their current AR therapy [6]. In this regard, the steps for AR management should provide a modality of treatment that would narrow such a proportion of patients in the UAE region. Although several guidelines exist globally, there are no established guidelines in the Middle East for the best management of AR [7, 8]. Moreover, increased disease awareness within the community and evidence-based management is warranted. The objective of this study was to develop an algorithm based on the expert panel suggestion for the management of AR in the UAE.

## 2. METHODS

A consensus meet was held in Dubai, UAE, comprising a panel of 14 professional experts, including 13 ENT specialists and one pulmonologist who treat patients with AR in their routine clinical practice. The expert panel discussed the currently available knowledge on the treatment of AR, including clinical data, real-life experiences and feedback from healthcare practitioners (HCPs), and positioning of MP-AzeFlu (azelastine HCl, AZE; 137 µg per spray) and INCS (fluticasone propionate, FP; 50 µg per spray) in the international guidelines for the management of AR. On the basis of the discussion, a simplified AR treatment algorithm was developed, incorporating suggestions from the panel members.

## 3. RESULTS

### 3.1. Burden of AR in the Middle East

AR, a common chronic health problem in developing countries, affects up to 36% of the population in the Middle East [9 - 11]. A recent nationwide cross-sectional study in Saudi Arabia revealed that at least two-thirds of patients with AR suffer from moderate to severe symptoms and intermittent patterns of the disease [12]. Further, the prevalence of physician-diagnosed AR in Middle East countries, including Egypt, Lebanon, Saudi Arabia and the UAE was 10%, and in the UAE, it was 9% [6]. In the UAE, nasal congestion (40%)

and sneezing (38%) were the most commonly reported symptoms during the worst month among patients suffering from AR. The Allergies in the Middle East Survey (AIMES) revealed that 58% of the population with AR in the Middle East had an impact on their daily private and professional life [6]. Among those, 49% of the UAE population reported AR symptoms-related absenteeism, reduced productivity or both AR symptoms [6], particularly nasal congestion, affect the quality of life [13, 14], emotional well-being [14, 15], productivity [16 - 18] and sleep [14, 19].

### 3.2. Management of AR – Recommendations from the Expert Panel

Achieving adequate symptom control is pivotal to successful AR management, which may be attained following the stepwise treatment algorithm. Based on the severity and duration of specific symptoms and the presence of any comorbidities, the panel outlined a simplified algorithm by incorporating recently available treatment options for the management of AR in the UAE (Fig. (1)). For example, step 1 would be initiated for a patient with mild intermittent symptoms, with treatment progressing through each succeeding step if symptoms remain uncontrolled.

### 3.3. Treatment Options

#### 3.3.1. Oral/topical non-sedating Antihistamines

In step 1, the panel recommended non-sedating intranasal (IN) or oral antihistamines (AHs) as first-line therapy for mild intermittent AR with VAS score <5/10. INAH (e.g., azelastine and olopatadine) with a rapid onset of action (within 15 mins) was reported to be more efficacious than oral AH [20, 21]. AH-responsive patients should continue therapy during periods of allergen exposure. The panel advised to step-up the therapy in patients with uncontrolled symptoms and who are non-responsive to therapy.

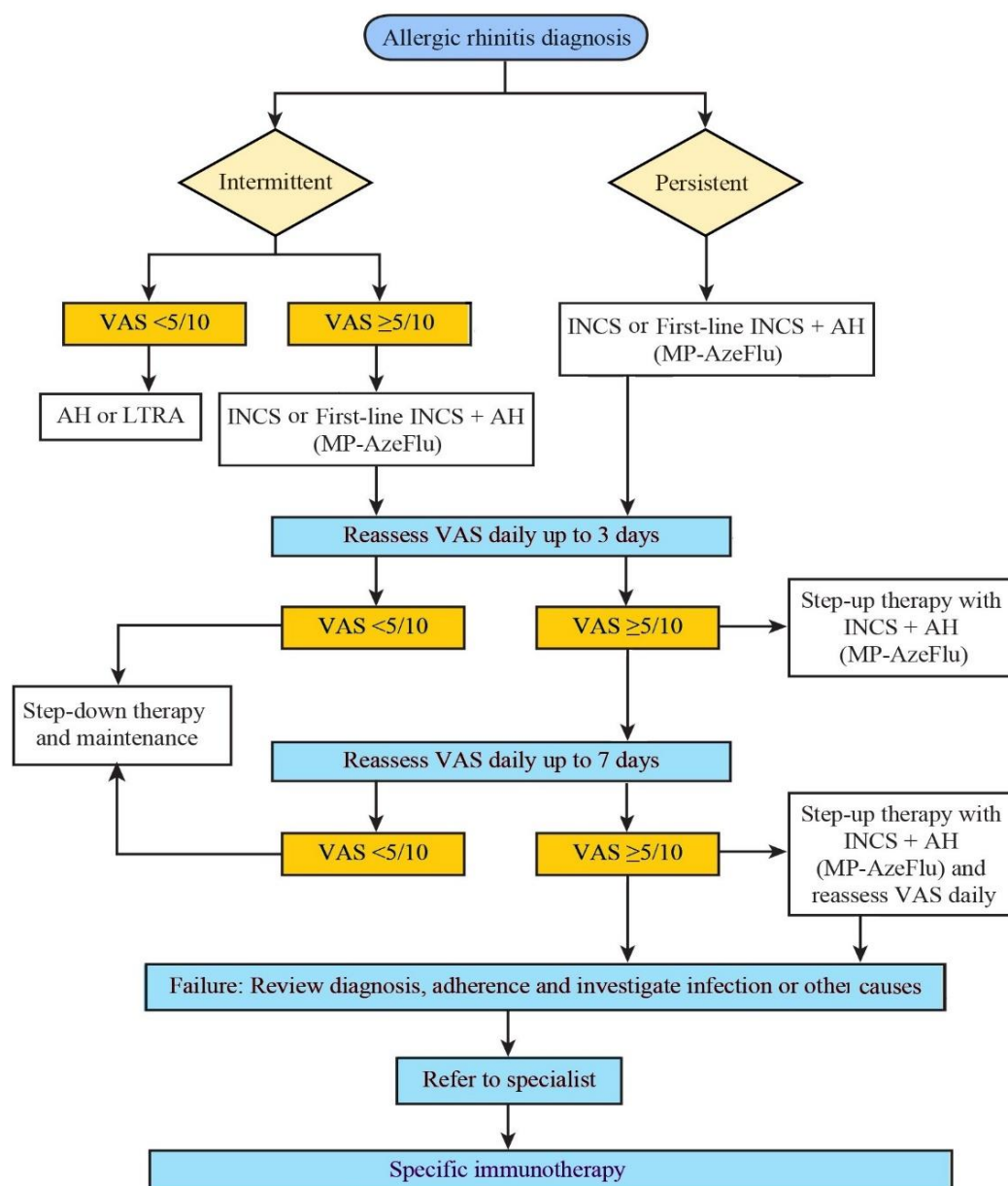
#### 3.3.2. Leukotriene Receptor Antagonists

A leukotriene receptor antagonist (LTRA) is usually less or equally effective as oral AH; however, it is less effective than INCS [22], and thus, clinicians should not routinely offer LTRA as the sole primary therapy for patients with AR, but it can be combined with nasal steroids, especially in patients with concomitant asthma [23].

#### 3.3.3. Intranasal Corticosteroids

In step 2, for moderate-severe intermittent (VAS score ≥5/10) and persistent AR and treatment failures with AHs alone, INCSs are recommended as first-line therapy. For patients who do not tolerate INCSs or prefer not to use them, adding LTRA to an oral or topical AH may be considered [24, 25]. Responsive patients should be instructed to continue therapy during periods of allergen exposure. Treatment should be re-assessed within 7 days to confirm a step-up or step-down approach. Those non-responsive to the therapy should be stepped up with MP-AzeFlu [26]. Its lower viscosity, smaller droplet size, larger volume (137 µL) and wider spray angle ensure optimal coverage of, and retention on, the nasal mucosa, contributing to its efficacy [27].

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**Fig. (1).** Treatment algorithm for the management of AR in the UAE.

Abbreviations: AH, antihistamines; LTRA, leukotriene receptor antagonists; INCS, intranasal corticosteroids; VAS, visual analog scale.

### 3.3.4. Recently-approved AR Treatment

In step 3, the panel recommended MP-AzeFlu as the first-line treatment for the management of persistent and moderate-severe intermittent AR. MP-AzeFlu was reported to be safe and tolerable [28] with rapid onset of action (5 min) [29]. In terms of reaching minimal clinically important difference (MCID) for symptom relief, INAH + INCS (single-device MP-AzeFlu) demonstrated superiority compared with either monotherapy (AZE or FP) [30]. In the pivotal randomised, double-blind, parallel-group, placebo-controlled, two-week, multicentre

studies (MP4002, MP4004, and MP4006) [28, 31], MP-AzeFlu was superior to both intranasal AH and INCS. MP-AzeFlu provided clinical benefits beyond what is achieved with 2 currently available first-line intranasal monotherapies, making it the ideal treatment consideration for AR. Real-world and non-interventional studies have also confirmed the efficacy of MP-AzeFlu across all age groups, with responder rates higher than those observed in controlled clinical trials, supporting MP-AzeFlu's position as the drug of choice for the treatment of AR [32 - 34].



In view of the high global burden and human suffering due to the chronic nature of respiratory diseases, World Health Organization (WHO) launched the WHO Global Alliance against Chronic Respiratory Diseases (GARD) to understand local needs and to identify implementation steps. GARD ensured that guidelines were adaptable in the local settings to manage the respiratory disease better and to modify the levels of major risk factors in the population [35, 36]. A new ARIA initiative, the Mobile Airways Sentinel Network (MASK) (MACVIA-ARIA Sentinel Network), has been developed and implemented in over 70 countries worldwide [37]. This initiative focuses on the implementation of multi-sectoral care pathways for personalized and predictive medicine using emerging mobile technologies with real-life data in rhinitis by a multidisciplinary group and patients. It uses a VAS to assess symptom control and work productivity as well as a clinical decision support system [38]. Further analysis of this data revealed that such novel methods may highlight new concerns that may not seem feasible by classical methods [38, 39]. Such health apps have the potential to profoundly affect the management of AR since patients' behaviour with respect to treatment adherence and practices is recorded in real time [7]. The expert panel recommended to establish a mobile phone application similar to MASK as implemented in European countries to collect the most accurate and appropriate local data to facilitate the development of steps of management in accordance with the local concerns.

### 3.4. Step-up and Step-down Strategy to Control AR Symptoms

Measures of AR control include symptom score assessment, patients' self-administered VAS and a recent modification of the Allergic Rhinitis and its Impact on Asthma (ARIA) severity classification [40 - 42]. Based on the VAS cut-off values from allergy-related literature [42 - 44], a step-up/step-down approach to AR pharmacotherapy was proposed by the panel. In the algorithm developed, the panel advised starting the treatment with AH, LTRA, INCS or MP-AzeFlu based on the VAS score. In case of intermittent AR with VAS score  $<5/10$ , AH or LTRA should be given. However, in case of a VAS score  $\geq 5/10$  or persistent AR, INCS or MP-AzeFlu is recommended as the first-line treatment. The physician may consider reverting to a lower step if the patients respond to the treatment. The step-up/down therapy depends on the magnitude of current symptoms, compliance issues, potential adverse effects, costs and exposure factors.

#### 3.4.1. Step-up Approach

As explained earlier, for mild AR symptoms, non-sedating IN or oral AH should be given to the patients. For moderate-severe intermittent AR or persistent AR, INCS or MP-AzeFlu should be given. Step-up with MP-AzeFlu should be considered when the symptoms appear uncontrolled (VAS  $\geq 5/10$ ) after a 3-day assessment and when AH or LTRA failed in controlling symptoms. VAS should be reassessed for up to 7 days to confirm the symptoms control and using the step-up approach. In addition, if a rapid onset of action is preferred by the patients, MP-AzeFlu should be recommended as first-line treatment.

#### 3.4.2. Step-down Approach

A step-down approach can be used in case of intermittent AR or no allergen exposure. In patients with persistent AR, a longer course of treatment is often needed (maintenance or step-up treatment). VAS should be reassessed for up to 3 days to check again whether VAS score is  $<5/10$  or  $\geq 5/10$ . In case of VAS score  $<5/10$ , continue the treatment if symptomatic or step-down treatment if no symptoms are present. If VAS score  $\geq 5/10$ , step-up treatment with MP-AzeFlu as second-line treatment, followed by reassessment of VAS up to 7 days to confirm control by using a step-up approach. Specialist referral should be considered if there is a failure to reduce the VAS score to  $<5/10$  after 10 to 14 days.

### 3.5. Referral after Failure to Control Symptoms after Second-line MP-AzeFlu

Improper use of medication is considered one of the main reasons for lack of efficacy; therefore, patients should be trained in advance to ensure the correct use of medication [6]. In the event of treatment failure with MP-AzeFlu as second-line therapy, the panel advised checking for the correct use of medication, compliance and whether the correct diagnosis was made, and recommended further investigations. In addition, discussing potential side effects of the medications with the patient before taking the nasal spray may reassure patients, so they become more compliant. The use of MP-AzeFlu may be an additional treatment option prior to immunotherapy. Immunotherapy may be appropriate for some patients with persistent symptoms. However, many patients are polysensitized and will remain symptomatic despite immunotherapy; these patients should receive symptomatic treatment in addition to immunotherapy. Relapse following successful immunotherapy treatment may occur; for these patients, further treatment options, including symptomatic treatment, may be considered. Although biological therapies have the potential to provide individualised treatment for refractory AR, endotyping inflammatory reactions and lack of known biomarkers remain the major challenges for recommending biologics in the care pathway of AR [45]. Nonetheless, positioning MP-AzeFlu as first line with an integrated check of compliance and technique has the potential to avert costly add-on treatments, repeat visits and possibly the need for immunotherapy or surgery.

## 4. DISCUSSION

This study provided a simplified algorithm for the management of AR and a consensus on the positioning of MP-AzeFlu as the first-line therapy for the management of moderate to severe AR on the basis of clinical evidence and existing treatment algorithms used by clinicians. The panel discussed the relative efficacy of MP-AzeFlu, FP, AZE, speed of onset of action, guidelines, and various statements by the experts for AR pharmacotherapy. MP-AzeFlu's position as the drug of choice for the treatment of moderate to severe AR is well supported by the safety and efficacy evidence. Moreover, considering the positioning of MP-AzeFlu in different international guidelines, the panel advocated the combination monotherapy of INCS + AH as the first-line treatment for the management of AR in the UAE. The rapid onset of action of

INCS/AZE (single device) for both nasal and ocular symptom relief [29, 31], reducing inflammatory markers, and the use of a single spray may improve compliance and treatment outcomes by avoiding administration and delivery issues [46, 47].

The real-life evidence on the efficacy and safety of MP-AzeFlu supports its early incorporation as first-line treatment into the regimen of AR management [33]. Contrary to the UK consensus panel recommendation of MP-AzeFlu as the first-line treatment in the secondary care option [48], it can be used as first-line treatment in the primary care itself, which can further help to limit the cost of providing effective AR management by avoiding the need for unnecessary repeat healthcare visits and costly referrals to secondary care in the majority of AR cases. The current algorithm is similar and agrees with the recent GARD guidelines, which support the combination of an INCS with an INAH (MP-AzeFlu) for SAR and PAR as a first-line treatment regimen. A joint task force by the American Academy of Allergy, Asthma, and Immunology (AAAAI) and the American College of Allergy, Asthma, and Immunology (ACAAI) and ARIA guidelines recommended a combination of an INCS and an INAH for initial treatment of moderate to severe seasonal allergic SAR in persons aged 12 years or older [8, 49, 50]. Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI) recommended the use of oral AH or INCS if symptoms are mild-moderate or severe. If treatment fails, combination therapy (MP-AzeFlu) should be used [51]. In the 2016 ARIA guidelines, it was reported that at the initiation of treatment (approximately the first 2 weeks), a combination of INCS with INAH (MP-AzeFlu) might act faster than INCS alone and thus may be preferred by patients with SAR and PAR [8]. The new 2019 ARIA guidelines were updated with GRADE-based guidelines integrating real-world evidence (RWE) provided by mobile technology and additive studies (allergen chamber studies). Although the 2019 ARIA algorithm followed previous recommendations without any change in the step-up and step-down approach, the panel advocated the need for further validation of different steps of algorithm using RWE [7]. The guideline also proposed to consider studies that assessed the onset of action of AR medications, especially the allergen exposure chamber studies. Several nasal drugs were tested in the pollen exposure chambers of Ontario [29, 52 - 54] and Vienna [55 - 57]. Rapid onset of action of azelastine and its combinations, including MP-AzeFlu, was observed in the Ontario chamber studies. Therefore, MP-AzeFlu is the first-line choice even in treatment-naïve patients.

## CONCLUSION

This guideline provides a simplified step-up or step-down approach for AR treatment in UAE that can improve the management and control of AR symptoms, compliance and patient satisfaction. Moreover, this approach can increase adherence to the treatment and reduce the cost of AR management.

## LIST OF ABBREVIATIONS

AR = Allergic Rhinitis

HCPs = Healthcare Practitioners

LTRA = Leukotriene Receptor Antagonist

GARD = Global Alliance against Chronic Respiratory Diseases

## CONSENT FOR PUBLICATION

Not applicable.

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## CONFLICT OF INTEREST

Yousef El-Hefny, Bassam Almahboub, Ayman Al-Fraihat, Ricardo Persaud, Abdul Juratli, Faheem Tadros, Abdul Aljassim, Bernard Hoffmann, Khairullah Alabdali, Khalid Elmesallamy, Mahdi Shkoukani, Taher Mohamed and Mohamed Alrakhawy declared no conflict of interest. Anastasios Hantzakos is a Member of the advisory board for Dymista and the advisory board for Dupixent.

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