# allergic rhinitis

BACK

***Jean Bousquet, David Price, Massimo Triggiani, Ludger Klimek***

## In reality, allergic rhinitis is poorly managed (1-7)

Although intranasal corticosteroids (INS) are the most effective allergic rhinitis (AR) treatment[8;9], not all patients achieve optimal symptom relief whilst taking them[10]. Treatment practices as in real life and the degree of pharmacologic insufficiency in AR have recently been assessed in the UK and Italy. In the UK, a resource utilisation survey of 1000 AR patients in 2011 showed that 70.5% of patients with moderate/severe disease reported using at least 2 AR medications (either prescription or over-the-counter) searching for better and faster nasal and ocular symptom relief. However, these patients continued to experience both nasal and ocular breakthrough symptoms[2]. Another large UK retrospective observational study, looking only at prescription data, revealed that during the 2010 hayfever season INS monotherapy proved insufficient for approximately one quarter of seasonal AR (SAR) patients (25.9%) and nearly half of perennial AR (PAR) patients (43.6%) who visited their doctor[1]. Approximately 1 in 3 AR patients (30.7%) who started the season on INS monotherapy required an additional GP visit, some re-consulting 2 and even 3 times. A shift to multi-therapy prescription was the consequence, which rose from 33.5% for SAR patients and 23.1% for PAR patients at season start to approximately 1 in every 2 patients by season end (SAR: 45.3%; PAR: 52.0%). The Italian survey of 100 GPs, 100 pharmacists and 552 AR patients revealed that the situation is no better there[3-7]. Many GPs (49%) and pharmacists (87%) were unaware of the ARIA guidelines, a fact that was evidenced by an over-reliance on anti-histamines (GPs: 37%; pharmacists: 56%) regardless of disease severity, a reluctance to switch therapy to more effective ones and a high incidence of co-prescribing behaviour (27% of GPs)[3-6]. Almost half of patients were not satisfied with their AR therapy, with 55% of them reporting multiple therapy usage[7].

> *There is a clear pharmacologic unmet need in AR. INS provide sub-optimal control for many of our SAR and PAR patients, necessitating additional GP visits and encouraging therapy addon (most commonly an oral anti-histamine), even though this is not officially recommended by ARIA, nor supported by the majority of scientific literature[11;12]. We know that patients frequently self-medicate at the pharmacy, so GPs may be unaware of what medications their patients are taking. There is a need to simplify rhinitis treatment with a more effective option with proven superiority over current firstline therapies, INS and antihistamines. [Prof David Price, UK]*

*AR patients expect a lot from their treatment. Future guidelines and*



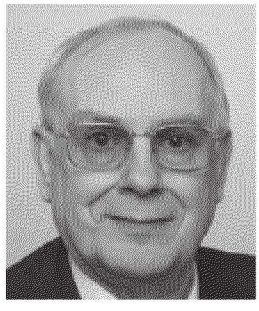
*code ATC R01AD58) developed to fill the therapeutic gap in AR. The innovation of Dymista® derives from the incorporation of two potent drugs from different medication classes with complementary effects (i.e. azelastine hydrochloride [AZE] and fluticasone propionate[FP]), in a novel, patented formulation and an improved device. It is considered by myself, and others, as the drug of choice for AR[13-15].*
*[Prof Massimo Triggiani, Italy]*

Dymista® is indicated for the relief of symptoms of moderate/severe SAR and PAR if monotherapy with either intranasal antihistamines or INS is not considered sufficient[16].

# Only Dymista® provides fast and clinically relevant symptom relief(14)

The efficacy of Dymista® versus intranasal AZE and FP has been investigated in moderate/severe SAR patients in randomized double blind trials as well in real life studies in more than 6000 patients[13-15;17]. Dymista® was twice as effective as either commercially available first-line therapy, in reducing the overall nasal and ocular symptom score (rT7SS: reflective total of 7 symptom scores) (Figure 1)[14]. While this information is necessary for drug registration, it is unclear what it means to patients. To that end, Dymista®'s efficacy was assessed in more clinically-relevant ways, using a timeto-response sensitivity analysis and by assessing symptom relief according to most bothersome symptom (i.e. nasal congestion). Reponse was defined as ≥ 30, 50, 60, 75 or 90% change from baseline in reflective total nasal symptom score (rTNSS). More Dymista® patients achieved each response (up to and including 90% response) and days faster than AZE or FP. One in two Dymista® patients (49.1%) first experienced a 50% reduction in their nasal symptoms and did so up to six days earlier than FP (p=0.0284) and AZE (p=0.0223) and up to 10 days ahead of placebo (p<0.0001)(14). A response ceiling of 60% rTNSS was identified, at or above which FP could no longer be differentiated from placebo. Dymista® breached this INS response ceiling and did so up to 7 and 8 days faster than FP (p=0.0496) and AZE (p=0.0404), respectively. Putting these results into the context of a typical 12.5 day symptom episode[18]; a similar proportion of patients treated with FP, AZE or PLA achieved a 60% response within this SAR episode window (i.e. approx. 20-25% of patients). However, this level had already been achieved by Dymista® on Day 5, increasing to 1 in 3 patients by the end of a typical symptom episode (Figure 2). Furthermore, Dymista® was three times as effective as FP (p=0.0018) in relieving nasal congestion in congestion-predominant patients and five times as effective as AZE (p=0.0001) (Figure 3). FP and AZE were no better than placebo for these patients[14].

- Dymista® is three times more effective than FP and five times more effective than AZE for nasal congestion relief in patients who are most bothered by this symptom[14].
- AR is well-controlled by Dymista® in real-life[17].



*There is a real need to describe response to treatment in way that is relevant to both patients and physicians. Patients simply would like to know how quickly they will feel better, while physicians would like to explain the degree of improvement their patients may expect from a new treatment compared to the treatment they are currently using, and also whether it will be effective for all 'patient types,' like those patients who present with the most bothersome symptom of congestion. The efficacy of Dymista® has been assessed in a way which answers these questions; bridging the gap between clinical trial results, physician understanding and patient expectations. The responder analysis tells patients that they may expect to feel a substantial response on Dymista® almost a week faster than on an INS or antihistamine. Crucially for physicians, the responder analysis defines the level of response NOT achievable by currently considered first-line AR treatments (i.e. ≥60% rTNSS response). This newly identified INS efficacy threshold helps to explain symptom breakthrough in INS-treated patients, and may help to guide prescription choices. INS should no longer be considered the most effective symptomatic treatment for AR as they cannot provide sufficient symptom control in many moderate/severe AR patients. Finally, the predominant symptom analysis reassures physicians that they now have something in their treatment arsenal which can effectively tackle the most bothersome symptom of congestion more effectively than ever before. Dymista® will simplify the way we manage AR. It provides the best response, in the shortest time for more patients and for all patient types. [Prof Jean Bousquet, France]*

# Effectiveness of Dymista® in real life is better than the efficacy observed in controlled studies(14;15;17)

The efficacy of Dymista® has been well-established in randomized controlled trials (RCTs), where it was shown to provide complete/near-to-complete symptom relief in 1 of 6 moderate/severe SAR patients and in 7 of 10 mild-to-moderate PAR patients, many days faster than an INS[14;15]. The effectiveness of Dymista® has also been assessed in real life in a German, multi-centre, prospective, 14-day (approx.) non-interventional study, including 1781 patients with moderate/severe AR[17]. Eligible patients were prescribed Dymista® according to SPC, and evaluated their AR symptom severity on a simple 100 mm visual analogue scale (VAS), from 0 mm (not at all bothersome) to 100 mm (very bothersome) in the morning prior to Dymista® use and on Days 0, 1, 3, 7 and last day. Patients' perceived level of disease control was assessed on Day 3. Dymista® reduced the VAS score from 75.4 mm (SD 17.2) at baseline

21.3 mm (SD 18.3) by the last visit, a shift of 54.1 mm (SD 24.62) (Figure 4).



*response to treatment under usual conditions of care. Randomized controlled trials (RCTs) are necessary for drug registration, but their strict inclusion and exclusion criteria for entry, mean that patients included in them are often not representative of the general population. Real life studies include a broad patient population, often those actively excluded from RCTs (such as smokers and those with co-morbidities), and a free ecology of care, thus maximising applicability of findings to every day practice. The Dymista® non-interventional study is important as it used a simple VAS to assess effectiveness, is the first to describe a patientreported VAS score cut-off value for 'well-controlled' disease (i.e. ≤ 36 mm) and to show that on average patients shift from uncontrolled to well-controlled disease after just 7 days treatment. This VAS has recently been proposed by ARIA as the new control language of AR and will form the basis for the new AR guideline, simplifying the treatment algorithm, encouraging compliance, ensuring open and effective communication between all stakeholders and will facilitate tailoring of AR medication to patients' needs. [Prof David Price, UK]*

*The true test of any new pharmacologic AR treatment is how it performs in a real-world setting; whether (or not) it fulfils the promise observed in RCTs, and Dymista® certainly lives up to the expectations! My patients who received Dymista® reported a rapid onset of action, a clinically-relevant response from the first day of treatment and the feeling of 'well-controlled' disease within the first few days. The effect was apparent in my SAR and PAR patients (and those with both SAR & PAR), in adolescents, adults and the elderly, irrespective of symptom severity at first clinic visit, and was sustained for the duration of treatment. My personal experience is now confirmed in a real life study. Dymista® delivers what AR patients want – faster and more complete symptom control. The vast majority of AR patients who visit their physician have moderate/severe disease and have been, or are currently, on treatment. Dymista® offers these patients, for the first time, the chance to be completely symptom free, the chance to enjoy the 'feeling' of not having AR. Results from controlled clinical trials led experts to describe Dymista® as the drug of choice for AR. The results observed in real life further endorse this opinion and position Dymista® as the drug of choice in real life too. [Prof Ludger Klimek, Germany]*

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