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for allergic rhinitis include pollen and pollution, which affect the patient outdoors.

As pharmaceutical companies develop more advanced treatments for this therapy area, or look towards lifecycle management of existing branded treatments to protect against generic entrants, patient preferences must be taken into account. The patient is increasingly influential in determining which products will be prescribed, and in some countries these products are available over the counter. In recent years sufferers have had no choice but to use aqueous sprays for topical application, but new research reveals that patients want an alternative.5

AN ALTERNATIVE TO THE AQUEOUS PUMP SPRAY

Nasal metered dose inhalers (MDIs) were commonly used to treat allergic rhinitis until the phase-out of chlorofluorocarbon (CFC) propellants in favour of the “ozone-friendly” hydrofluoroalkane (HFA) propellants following the signing of the Montreal Protocol.6 Nasal MDIs were not included alongside pulmonary MDIs in the “essential use” exemption. Leading nasal MDI products included Rhinocort (from AstraZeneca UK Ltd), developed and manufactured by 3M Drug Delivery Systems in partnership with AstraZeneca, as well as Nasacort (from sanofi-aventis, France), and others.

Given the complexity of reformulation using HFA propellants for the first time, developers opted to reformulate instead into simple aqueous systems. However, anecdotal evidence from patients suggests that many believed aerosols to be more effective than the aqueous sprays that replaced them, and they lamented their demise, hoping for a return to the market of key aerosol brands.7

The unpleasant experiences associated with aqueous sprays can be overcome using MDI devices, whereby medication is delivered in the form of a quickly evaporating “no-drip” spray. In addition, new technologies such as ergonomic designs and dose counters can be incorporated to add further differentiation and command a price premium.

3M has developed one such nasal MDI device and this is shown in Figure 1. MDI devices can add differentiation using human design factors in contrast to the purely functional and relatively generic designs of most aqueous pump sprays. A range of currently marketed aqueous pump sprays is shown in Figure 2.

When considering MDIs for nasal use, one question that can arise is whether an MDI is at risk of causing irritation of the nasal cavity, due to the velocity of the plume and also the use of ethanol in some formulations. In fact, nasal MDIs have been demonstrated to be safe and well tolerated in a range of clinical trials, including studies performed on an HFA formulation of triamcinolone acetonide (Nasacort HFA, sanofi-aventis) 8 and an HFA formulation of ciclesonide (Omnaris HFA, Sunovion). 9 Of course, the historical success of nasal MDIs also inspires confidence, particularly when one considers that the newer HFA propellants give a “warm” plume in comparison with the “cold Freon effect” of the old CFC propellants.

A second question is the risk of unintended deposition in the lung due to the high velocity delivery of small particles. In fact, it has been demonstrated that no significant deposition occurs in the lung when a nasal MDI is administered 10 and this finding is supported by recent studies demonstrating the safety of several corticosteroid nasal MDIs. 11,12

There is evidence that MDIs may be more effective than aqueous pump sprays. The successful nasal retention of drug delivered via an MDI has been demonstrated as shown in Figure 3, which illustrates that only 18% and 15.4% of the dose for the one-position and two-position studies, respectively, had been cleared after 30 minutes, with 64.5% and 65.3% of the respective doses remaining in situ.10

This contrasts with the almost total clearance of droplets delivered by an aqueous pump
spray in an average of 30 minutes. The high velocity of an MDI spray deposits drug primarily in the anterior region of the nasal cavity where there are fewer nasal cilia available for clearance, and the small particles delivered by an MDI are less partial to clearance versus the large droplets from an aqueous pump spray. This superior retention also means that MDIs are more suited to patients with runny noses.

More recently, studies have evaluated the risk of sub-therapeutic dosing with the “force-dependent” aqueous pump spray format, which has been shown to deliver large variances in delivered dose with different patient groups, a drawback that is not seen with the MDI format, long recognised for its excellent dose consistency.

DEVELOPMENTS IN THE TOPICAL ALLERGIC RHINITIS MARKET

As nasal corticosteroids go off-patent and generics enter the market, pharmaceutical companies are reformulating their products to add additional indications or to improve patient benefits, for example once-a-day dosing, and patient-friendly devices. One such recent product introduction is Veramyst (GlaxoSmithKline, UK), which utilises a “side-actuated” device incorporating a viewing window to enable the patient to determine how much medication is left in the bottle.

An alternative to this basic viewing window is a dose counter – a technology which can be incorporated into a nasal MDI and which is already widely used in the respiratory category. 3M’s Nasal MDI device is available with an integrated dose counter based on 3M technology which has been FDA-approved in conjunction with an MDI product.

3M’s research with patients shows that the introduction of a dose counter gives them a feeling of security, enabling them more accurately to monitor doses remaining in their device and to renew prescriptions without the inconvenience of running out of medication.

PATIENT ASSESSMENTS OF AQUEOUS PUMP SPRAY DEVICES

3M Drug Delivery Systems conducted qualitative research with 64 sufferers of seasonal and/or perennial allergic rhinitis, half of the sample in the US and half in the UK. The commonly available aqueous pump sprays were deemed a necessary evil rather than a fully accepted form of treatment.

In preparation for using an aqueous spray, users describe a feeling of having to “steel themselves” for the shock of the administration, and they have to have tissues handy in order to deal with the embarrassing nasal run-off post-administration. During use, they describe shock as the product ‘hits’; an unpleasant sensation in the sinuses; an unpleasant taste sometimes accompanied by irritation in the throat due to post-nasal drip; and finally the need for privacy to deal with the aftermath. Post-administration, the patient attempts to retain the product in the nostrils by holding the breath, trying not to swallow or blow the nose.

Patients questioned the efficacy of aqueous sprays as a result of the nasal run-off. The functionality of aqueous spray devices was also queried – particularly the force-dependent nature of actuation, which means that an inaccurate dose can be administered.

During development of the 3M Nasal MDI some of the industry’s cutting-edge processes and technologies were used to produce moulded samples to facilitate pharmaceutical data generation, and allow patient focus groups to interact with the device. Some of the technologies used included rapid prototyping, rapid tool manufacture and chromatographic evaluations (colour-coded deviation display). These processes have allowed 3M to provide moulded samples from the initial generation of CAD in weeks instead of months. Patients liked the idea of the new 3M Nasal MDI device, which they perceived as overcoming most of the problems associated with aqueous pump spray products.

The main perceived benefit of the 3M Nasal MDI was the “dryness” of the spray and the elimination of the unpleasant sensations and taste associated with the “wet” aqueous sprays. This meant that users would no longer feel embarrassed to use their spray in public, and would be more likely to carry it around and use it when needed. In addition, the styling of the device was appreciated, being described as compact and portable, and the “twist-and-lock” cover was particularly appealing as an aid to hygiene. Finally, the device was perceived to be more effective than an aqueous pump spray device due to the metered dose mechanism, which patients understood meant a consistent and correct dose with every administration.

ADDITIONAL CONSIDERATIONS FOR DEVELOPERS

In addition to the voice of the patient, there are other considerations for the pharmaceutical company considering the development of a topical allergic rhinitis product.

The MDI device is a low-risk choice, given that it is familiar to regulators, physicians and patients alike due to its more than 50 years track record in pulmonary drug delivery, and previous use in the nasal drug delivery marketplace. Further, business considerations such as the ability to create a fast line extension of a successful inhaled corticosteroid in the respiratory market make the MDI an attractive proposition.

Unit cost of product is always a consideration, and the low cost of MDIs, particularly on a cost-per-dose basis, means they will remain an attractive delivery system.

MOVING TOWARDS PATIENT-FOCUSED DEVICES

The patient’s voice has become increasingly important in pharmaceutical device development, and developers acknowledge that the patient’s interface with the device is crucial to its success. Evolution in device design will be driven by more informed consumers, confident to demand products to meet their needs and fit their lifestyles. Allergic rhinitis patients demand attributes for topical products that are currently not met by aqueous pump sprays.

In the current economic climate, a convincing business case must be made for device developments. Drug delivery innovators such as 3M believe that pharmaceutical products should not be any less consumer-researched and design-optimised than other consumer products, and that a “device-edge” is possible and worthwhile in the attractive allergic rhinitis market.

CONCLUSION

Nasal MDIs were the leading delivery systems for topical allergic rhinitis medications until the CFC phaseout. In recent years, allergy sufferers requiring topical application have had no choice but to use aqueous pump sprays to treat their rhinitis. Research amongst patients demonstrates that they want an alternative.

Whilst there will undoubtedly be a place in the worldwide marketplace for low-cost aqueous spray devices for generic applications, it is...
clear that the voice of the patient will increasingly be heard in nasal device development. Patient and physician choice is set to expand further as improvements in the aqueous spray format are brought to market and, in addition, differentiated MDI devices are welcomed into this market once more.

*Boots Hayfever Relief Nasal Spray is a trademark of Boots Company plc; Nasacort® Allergy Nasal Spray is a registered trademark of sanofi-aventis; Flonase Allergy™ Nasal Spray is a registered trademark of GlaxoSmithKline; Nasonex® is a trademark of Merck & Co; Beconase® Hayfever relief for Adults is a registered trademark of GlaxoSmithKline; and Rinholast® Nasal Spray is a registered trademark of Meda Pharmaceuticals Ltd.

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In fifty years, we’ve created a lot of firsts, including the first pressurized metered-dose inhaler (pMDI). Today, we offer the most complete range of pMDI solutions supported by our unparalleled global expertise to help move products to market more efficiently.

- In-house services streamline development, registration and commercialization
- Patient-centered designs and breakthrough technologies combine to help ensure technical success
- Expanded manufacturing services, including pressure-fill capabilities, provide reliable delivery from clinical to commercial scale

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