Inhaled Medicines: Product Differentiation by Device

Given the availability of many similar inhaled medicines and the shortcomings of existing devices, there are several opportunities for companies to gain market share by product differentiation with an improved inhaler device.

By Lisette Oversteegen at Datamonitor

Lisette Oversteegen has worked at Datamonitor since October 2005 where she has focused on the field of respiratory diseases, including asthma, COPD, allergic rhinitis and cystic fibrosis. She is now a Senior Respiratory Analyst, but also writes market analyses in areas such as infectious and autoimmune diseases. Prior to Datamonitor, Lisette completed a Master’s degree in Public Health at Maastricht University, the Netherlands, specialising in work and health, and a Bachelor’s degree in Occupational Therapy at Amsterdam University.

The respiratory disease market is becoming increasingly saturated for most drug classes, such as inhaled steroids and bronchodilators. Since this trend will continue in the near future, choice of device – rather than choice of drug – is set to become one of the driving forces behind pulmonary disease management. The development of novel devices with improved features is therefore becoming increasingly important for companies in order to differentiate their product offering. This article gives an overview of the key trends in portable inhaler devices (excluding nebulisers and nasal sprays) used in the treatment of respiratory diseases like asthma and chronic obstructive pulmonary disease (COPD).

Respiratory sales in the six major markets – US, France, Germany, Italy, Spain and the UK – have grown rapidly over the past few years due to the launch of new products, including several successful combination products. Within the asthma/COPD market in 2007, about two-thirds of the total sales came from drugs delivered in portable inhaler devices, while tablets and nebulised products accounted for a much smaller proportion of sales (see Figure 1).

Inhaled Medicines: An Overview

The use of inhaled medications for the treatment of pulmonary diseases became well established in the second half of the 20th century, when the advantages of administering drugs directly to the lungs had become evident. These include the fact that the inhaled route offers a more rapid onset of action, allows smaller doses to be used and has a better efficacy-to-safety ratio compared with systemic therapy. Furthermore, aerosol delivery of drugs is painless and often more convenient, especially compared with parenteral administration. However, inhaled drug therapy also has its disadvantages. One of the most significant drawbacks is related to the inhaler devices through which the drugs are delivered (see Table 1), since each available device requires a specific inhalation technique.

There are two main types of portable inhaler devices used in the treatment of respiratory diseases: metered dose inhalers (MDIs), including pressurised MDIs (pMDIs) and breath-activated MDIs (BAIs), and dry powder inhalers (DPIs), including single-unit dose DPIs, multi-dose reservoir DPIs and multi-unit dose DPIs. There is a wide variation in inhaler design, especially among the DPIs, making it impossible to learn only one technique to use them correctly.

The standard pMDI is the oldest and most often used inhaler since it is cheap and widely available for many different molecules. Nonetheless, a large proportion of patients cannot use pMDIs correctly, with one of the most common problems being the inability to coordinate actuation with inhalation of the device (pressing the canister to release the drug and inhaling at the same time). Because of the problems associated with pMDIs, attention has focused on the improvement of inhaler devices to optimise the delivery of medication. Breath-activated MDIs (BAIs) help to overcome the problem of coordinating actuation with inhalation, thus providing the opportunity to improve drug delivery and overall disease control. However, the BAI’s major drawbacks are the high cost involved in its development and the limited availability of drugs in this type of device. Since BAIs do not cover the full spectrum of
drugs required by the average patient, physicians are forced to switch back to pMDIs or combine different devices in one treatment regimen.

Dry powder inhalers offer a different solution to the difficulties associated with pMDIs. These devices release the drug by passing air from the patient’s inhalation effort through medication formulated as a dry powder. The active ingredient is in the form of micronised drug particles that can be mixed with larger glucose or lactose particles, or bound into loose aggregates. Although this partially resolves the coordination problem since the drug is only released when the patient inhales, there are disadvantages to DPIs. The wide variety of DPI devices available is reflected in an equally wide variety of inhalation instructions, whereas the inhalation technique for pMDIs is generally the same. Furthermore, it is necessary for the patient to inhale deeply and quickly enough to ensure that most of the active molecules emitted from a DPI reach the lungs. Several patient groups are often unable to do so – especially the elderly, children and those with severe airflow limitation.

Nevertheless, DPIs were the best-selling group of devices in the six major markets, reaching more than $9.2 billion in revenues in 2007 (1) (see Figure 1). This was mainly driven by their high price, reflecting the fact that they mostly contained branded molecules (as opposed to generic molecules). Although the pMDIs were the bestselling group in terms of volume in the same year, they only reached value sales of $4.6 billion (1). This illustrates the fact that most molecules delivered in a pMDI are generic and therefore much cheaper. Finally, while the BAIs are meant to overcome many of the disadvantages associated with DPIs and pMDIs, they represent only a small share of the market ($152 million) (1) due to their relatively high price and limited availability across molecules.

### IMPORTANCE OF THE INHALER DEVICE

Although a direct link between device type and level of disease control has never been shown, it is possible that

![Table 1: Overview of key portable inhaler device types](image)

<table>
<thead>
<tr>
<th>Inhaler type</th>
<th>Overview</th>
<th>Examples</th>
<th>Average price*</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressurised metered dose inhaler (pMDI)</td>
<td>A pMDI consists of a pressurised aerosol canister that contains the medication and a metering system that controls the volume of drug mixture that is released when the actuator is pressed</td>
<td>Standard pMDIs like the salbutamol inhalers</td>
<td>Delivering a branded molecule: $0.20</td>
<td>Portable and durable</td>
<td>Time-dependent dose variation</td>
</tr>
<tr>
<td>Dry powder inhaler (DPI)</td>
<td>DPIs create the aerosol by passing air from the patient’s inspiratory effort through medication formulated as a dry powder. The active ingredient is in the form of micronised drug particles that can be mixed with larger glucose or lactose particles, or bound into loose aggregates</td>
<td>Turbuhaler, Diskhaler, Novolizer, Clickhaler</td>
<td>Delivering a branded molecule: $1.28</td>
<td>Stability of dry powder</td>
<td>Reservoir systems prone to be affected by environmental factors</td>
</tr>
<tr>
<td>Breath-activated metered dose inhaler (BAI)</td>
<td>BAIs provide a metered dose of drug in response to the inspiratory effort of the patient, and therefore overcome the difficulties that some patients have in coordinating actuation with inhalation</td>
<td>Easi-Breathe, Autohaler</td>
<td>Delivering a branded molecule: $0.12</td>
<td>Easy coordination</td>
<td>Lack of drugs available</td>
</tr>
</tbody>
</table>

* Price per inhalation (‘puff’); CFC = Chlorofluorocarbons; HFA = Hydrofluoroalkanes

Source: Datamonitor, 2008

![Figure 1: The respiratory market by method of drug delivery and the portable inhaler device market by type, in the six major markets (2007)](image)

Source: Datamonitor, 2008 (based on MIDAS Sales Data, IMS Health, April 2008)
the inhaler – through its effect on the patient’s inhalation technique and compliance – influences disease control. In turn, these factors are influenced by a device’s ease of use, its airflow resistance and patient preference. Unfortunately, none of the devices currently on the market combine all the characteristics of an ideal device, meaning that physicians need to find the best match for individual patients by prioritising their respective needs and circumstances. The cost of a device will play an increasingly important role in this decision, since many governments encourage physicians to start their patients on a cheap pMDI, and to only prescribe a more expensive inhaler when necessary.

Nevertheless, the concept of matching an inhaler to a patient becomes redundant if inhaler availability is a problem, as there can be quite a difference in the availability of inhaler devices across molecules. An example is AstraZeneca’s popular Symbicort (budesonide/formoterol), which in Europe is only available in the DPI Turbuhaler. If a physician wants to prescribe Symbicort as a patient’s main treatment, choosing any additional drugs would require their availability in the same device. Since there are only very few molecules available in the Turbuhaler, this may significantly impact a patient’s treatment regimen. On the other hand, if a patient has problems handling the Turbuhaler, a drug like Symbicort would be completely unavailable to them, and an alternative drug in a different type of inhaler would have to be found.

PRODUCT DIFFERENTIATION VIA INHALER DEVICES

With an increasing number of similar molecules being launched and considerable unmet needs with regard to devices, there are several opportunities to gain market share by differentiating with an improved inhaler device.

One would be to develop a completely novel type of inhaler in order to protect the franchise in the face of newly launched competitors or generics. A prominent example is Boehringer Ingelheim’s development of the Soft Mist Inhaler (SMI) Respimat. This device delivers medication in a soft and slow-moving mist with a high fine-particle fraction, allowing the active compound to penetrate deep into the lungs. Although this may not necessarily improve the efficacy of a drug, it makes it easier for the patient to inhale the drug coming out of the device and to coordinate actuation with inhalation. The Respimat was recently launched in several European countries containing the drug Spiriva (tiotropium bromide), the only long-acting anticholinergic (LAMA) available for the treatment of COPD. Patients with COPD may particularly benefit from this new type of device since they are often older and have more severe disease, making coordination and deep inhalation more difficult.

Spiriva has been a very successful product in its original DPI HandiHaler, reaching sales of $1.8 billion in the six major markets in 2007 (1); however, Spiriva’s revenues are under threat from at least three other LAMAs in development (Novartis’s glycopyrrolate, Almirall/Forest’s aclidinium bromide and GlaxoSmithKline’s darotropium), which are estimated to enter the market from 2010 onwards. Additionally, the first generic tiotropium products are expected to be launched in 2015, and will have a rapid uptake due to significant price discounts. By launching Spiriva in the Respimat device, Boehringer Ingelheim is attempting to differentiate its product well in advance in order to minimise the rate of patients switching to competitor or generic products. However, while there will certainly be a group of patients that will stay loyal to Spiriva formulated in the Respimat, a novel device is not likely to protect this product’s revenues completely.

SAME DEVICE FOR PRODUCT RANGES

Another strategy to differentiate through device is to introduce a product line of different molecules in the same device model in order to make it easier for patients to learn one inhalation technique, which can then be applied to all their inhaled medications. McDonald & Gibson (2) studied whether the increase in the number of different devices would lead to ‘inhaler device polypharmacy’ – a situation in which an
individual uses multiple types of inhaler devices to deliver their medications. They concluded that inhaler device polypharmacy is a common problem among adults with respiratory diseases like asthma, especially among patients using three or more different delivery devices, and could lead to poor disease control through inadequate delivery of medication.

For this reason, having a range of molecules available in the same device may be an interesting strategy in drug classes with lower unmet needs. Here, devices could play an important role in determining the choice of drug or brand. Meda Pharma, for example, markets the Novolizer containing salbutamol, formoterol or budesonide, while Orion Pharma markets the Easyhaler containing salbutamol, formoterol, beclometasone or budesonide. Both types of inhalers cover all the needs of a standard asthma patient and allow for consistent delivery through the same device. However, physicians cannot afford to be too demanding with regard to the particular molecule they want to prescribe; they may be limited to, for example, budesonide when using Meda Pharma’s range, since this is the only inhaled corticosteroid available in the Novolizer.

THE US SABA MARKET

Finally, an interesting opportunity has arisen in the US. In this market, the highly genericised salbutamol class has started to convert back to a branded market due to the phase-out of pMDIs powered by chlorofluorocarbons (CFCs) (see Figure 2). Salbutamol products are short-acting beta2-agonists (SABAs) that are widely used as rescue medication during asthma exacerbations. CFCs have been clearly shown to deplete ozone once they reach the stratosphere and this issue has caused governments to enter into treaties to reduce CFC emissions.

The pharmaceutical industry developed an alternative in the form of hydrofluoroalkanes (HFAs) for use in pMDIs and BAIs; however in the US, only one company (3M) owns the patents covering the use of HFA propellants and it has been difficult for manufacturers to develop HFA-pMDIs that do not infringe these. While there were previously many generic CFC-propelled SABAs available – driving the price of individual products down to about $0.07 per inhalation (1), after 31st December, 2008, only four HFA-propelled SABAs will be available. This means that all patients currently taking generic products will need to switch to one of these four products. The HFA-propelled brands are more expensive than the current generics, ranging between $0.11 and $0.14 per inhalation (1). This means that the overall market will almost double in size and the companies producing the four remaining products will benefit greatly. Sales of these four products have already grown significantly, with a CAGR varying between 140 and 400 per cent (2006-07) (1), and will continue to do so until all patients are switched in early 2009.

CONCLUSION

Unfortunately, a one-size-fits-all strategy to optimise commercial opportunity does not exist. Each drug class and molecule needs to be looked at separately in order to develop a successful strategy. Possibly the most attractive markets at the moment are those that are medium-mature, with high sales in combination with large volumes sold; these still provide a profitable space in which to launch a new product (see Figure 3). However, a market needs to consist of several equivalent molecules with similar efficacy and safety in order for the device to become an important factor in prescription choice. The most mature markets will be less attractive for differentiation through device, since competition is fierce with a large number of companies offering similar and cheap products, reducing the potential return on investment. Going forward, under-developed market segments with few products available and relatively high unmet needs look most promising, because – even here – it is only a matter of time before inhaler devices start to have a significant influence on drug choice.

The author can be contacted at loversteegen@datamonitor.com

References
1. MIDAS Sales Data, IMS Health, April 2008

Figure 3: Opportunities for successful differentiation by inhaler device in different types of markets