The end of the back-up brands?

Marketing a patented chemical variation of a brand nearing expiry has become a new tool in the fight against generics. But getting prescribers to convert to back-up brands requires much more than clever marketing, say Jean-Michel Peny and Jean-Pierre Covilard

Generic competition is not a new phenomenon, but its detrimental impact on the performance of original brands has become highly important, including in newer generic markets such as France. Thus, last year, in the three months following their arrival, omeprazole generics captured on average 55% of the market for Mopral/Losec 20mg by units. Simvastatine generics, which started to compete against Zocor in May 2005, are following the same trend.

In this increasingly competitive environment, the most effective brand defence strategy remains legal and/or lobbying actions likely to postpone generics entry.[1] In addition, original brand companies have multiplied product line extensions to produce new dosages (eg Voltaren, TriCor/Lipanthyl), modified formulations (eg Procardia XL, Prozac dispersible) and fixed combinations (eg Hyzaar, Caduet) that can be patented. The efficacy of these initiatives is strongly dependent on their related medical benefits, expressed in terms of efficacy, tolerability and/or convenience for patients.

Recently, several pharma companies have opted for another strategic approach, the so-called 'back-up brand' strategy, which consists of developing a patented chemical variation of a product they already market but which is on the point of being genericised. These modified compounds are, in general, optical isomers such as Inexium/Nexium (esomeprazole magnesium) vis-à-vis Mopral/Losec (omeprazole), or Xyzall/Xyzal (levocetirizine) vis-à-vis Zyrtec (cetirizine). They can also be an active metabolite, a different ester, ether, salt and so on.

These modified molecules, marketed under a different brand name, cannot be considered as a brand defence strategy. In fact, the desired effect is the reverse. They are launched with the objective of converting physicians' prescriptions from an existing brand, threatened by generics, to a new one, that is slightly different and patent-protected. Thus, R&D-based companies can expect to maintain their presence in a given therapeutic area, as did AstraZeneca in the gastro-intestinal market, by launching Nexium to offset the impact of generics on Losec (see Figure 1).

However, in such a case, converting physicians and their patients from a well-known brand to a new one, even if the active substance is very similar, requires heavy clinical and marketing investment and takes, on average, three to four years. The rate of conversion achieved is also strongly dependent on the new brand's clinical benefits (efficacy, acceptability, and convenience), as perceived by physicians and, to a lesser extent, by patients.

Nexium, which four years after its first market introduction accounted for only 62% of Losec peak sales, illustrates the difficulties of capturing physicians' prescriptions from a sister brand. Although AstraZeneca has deployed an 'ambitious' clinical programme, involving more than 73,000 patients in over 60 countries, as of early 2005 Nexium had not yet offered all the indications registered by Losec (eg reduction in the occurrence of gastric ulcers, associated with continuous NSAID therapy in patients at risk).[2] It seems the superior efficacy demonstrated by Nexium over Losec and other proton pump inhibitors (PPIs) for the treatment of active peptic ulcer disease has not been sufficient to create a massive transfer of prescriptions. Besides, the average time between Nexium's launch and Losec's generics entry, as observed on major markets, was only one to two years for the tablet forms, which was definitely too short.

In an attempt to accelerate the conversion of physicians in favour of prescribing Xyzall, UCB Pharma (UCB) made the strategic decision to withdraw Zyrtec 10mg tablets from the French market. We evaluated the impact of this initiative within the overall strategy put in place by the drugmaker to maximise its antihistamine franchise in France.

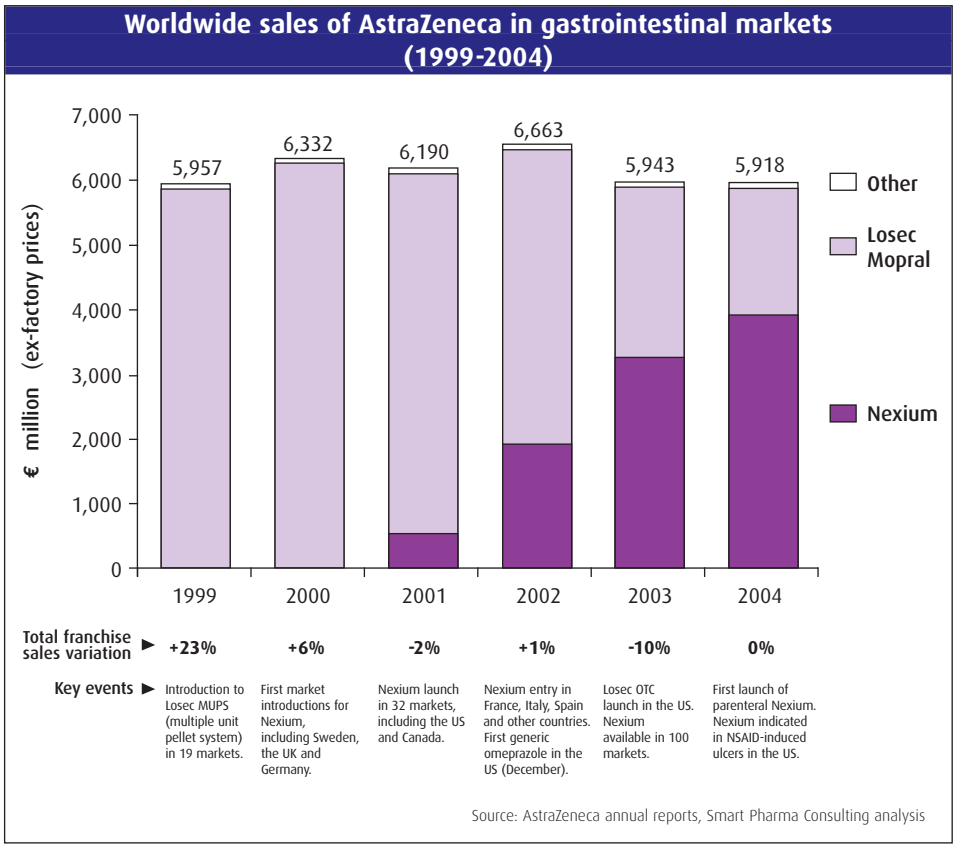

Figure 1: AstraZeneca maintained its presence in gastrointestinal markets by launching Nexium to offset the impact of generics on Losec/Mopral.

From Zyrtec to Xyzall

Since the late 1980s, UCB has generated revenues from its antihistamine cetirizine (10mg tablets and 10mg/ml solution forms) directly from its own brand Zyrtec and, indirectly, through a co-marketing agreement with Sanofi-Aventis which promotes the brand Virlix.

In early 2003, UCB introduced Xyzall 5mg tablets (corresponding to Zyrtec 10mg), two years before the entry of cetirizine generics. However, in December 2003, the conversion rate of Zyrtec 10mg to Xyzall 5mg, expressed in days of treatment, was less than 30%. At that time, the company started to inform physicians about its intention to withdraw Zyrtec 10mg from the market – which became effective in September 2004.

Since then, UCB has deployed extensive promotional efforts, including post-marketing surveys, to stimulate Xyzall to stimulate interest in prescribing Xyzall among physicians. As of August 2004, though it was successful in enhancing Xyzall prescriptions per prescriber, UCB was still lagging behind in converting Zyrtec prescribers.

A survey we carried out in early 2005 on 102 physicians showed that 69% of them maintained a neutral position vis-à-vis Zyrtec's withdrawal, while 6% reacted positively. Half of the remaining 25% who had negative reactions said they did/would transfer patients onto Xyzall in any case. The same study suggested that Xyzall could capture up to 49% of Zyrtec prescriptions, but competing brands, Aerius and Virlix, also appeared as major beneficiaries with respective gains of 23% and 10%. These results have been confirmed by the sales dynamics of those brands during the first half of 2005.

If Zyrtec's withdrawal from the market has been rather well accepted by physicians and patients, pro-generics pharmacists and generics manufacturers have been quite virulent in their reactions, even accusing UCB of anti-competitive practices. For the French generics market, which is mainly driven by pharmacists' substitution of original brands, the withdrawal of Zyrtec represents a loss of profits for both generics companies and pharmacists. In fact, for such a mass-market product, the most pro-active pharmacists can receive discounts of up to 75% from generics companies which may reach, overall, a market penetration of approximately 60% in total units, within one year. French physicians are not used to prescribing generically and they have confirmed in a recent survey that they planned to transfer only 5% of their prescriptions from Zyrtec to cetirizine generics and 10% to Virlix.

The position of health authorities regarding the market withdrawal of Zyrtec can only be favourable. In the absence of recognised medical benefits over existing antihistamines, health authorities have granted Xyzall an ex-factory price per tablet 6% lower than that of Zyrtec until June 2005, and 31% lower as of July 2005. With this new price, Xyzall has become the least expensive reimbursable antihistamine, on a daily treatment cost basis, along with cetirizine generics.

If this low price should, in theory, facilitate physicians' conversion, in practice it has no significant impact. French physicians' price sensitivity is low, especially for antihistamine drugs they do not perceive as expensive.

In fact, this low price constitutes a major issue for UCB cetirizine franchise sales and profit perspectives (see Figure 2).

UCB has recently registered a new labelling for Xyzall for persistent allergic rhinitis which could help differentiate it from other antihistamines and capture more patients. As per UCB Group's annual report, this indication is supported by a six-month trial (XPERT) that showed the product's efficacy and socio-economic benefits, including its ability to improve the quality of patients' lives, while reducing levels of absenteeism at work.[3] However, this new indication did not allow UCB France to obtain a better price from the

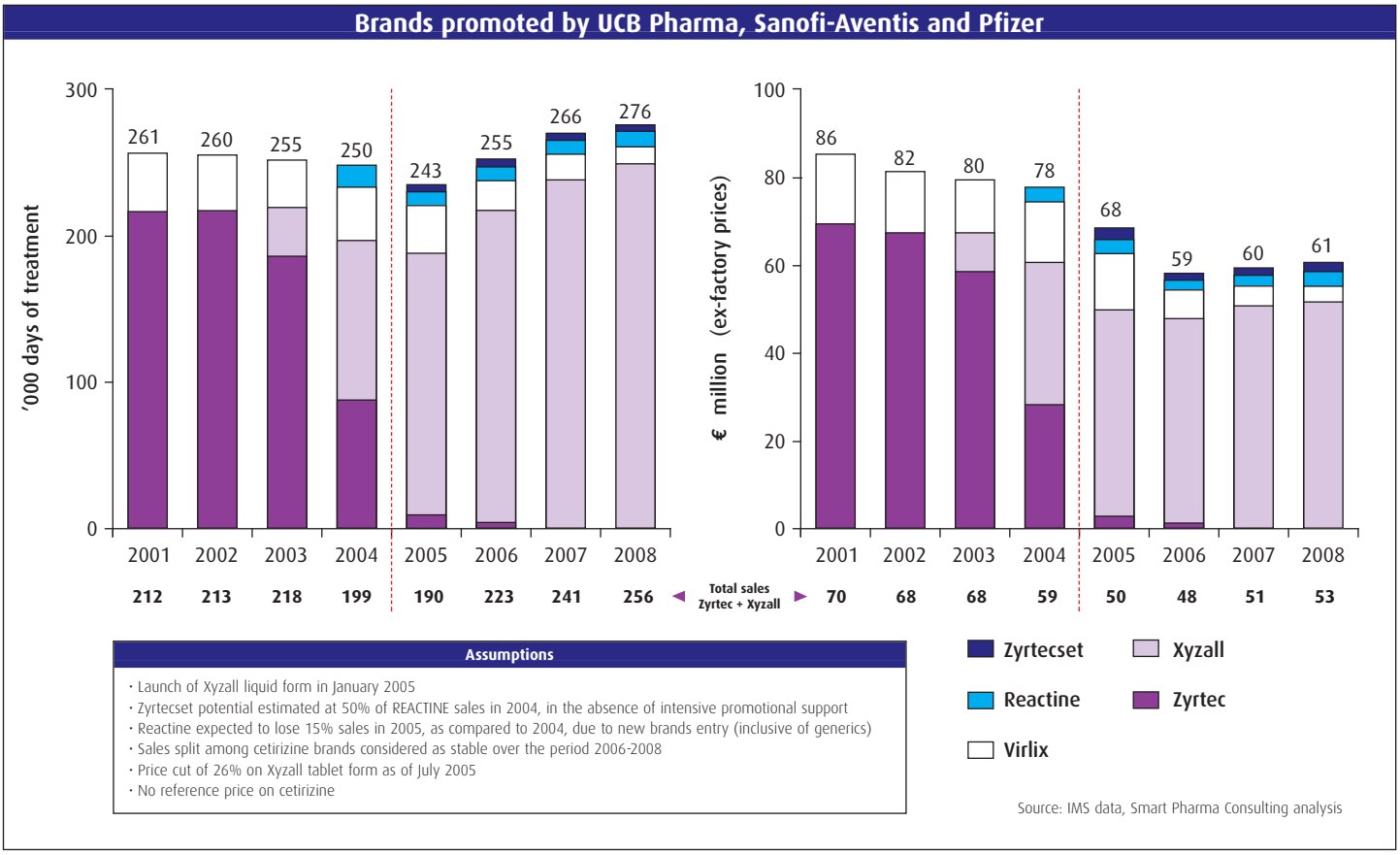

Figure 2: UCB cetirizine franchise sales trends in France are projected for 2005-2008. The brands shown are for tablets and liquid forms in the open care market.

drug pricing committee, CEPS, considering the repetitive heavy losses incurred by the Sickness Funds and the fact that allergy is not a public health priority.

Zyrtec switches to OTC

To maximise the revenues from its cetirizine franchise, UCB has also adopted a dual Rx-to-OTC strategy. The company first licensed out an OTC version of cetirizine 10mg to Pfizer and then marketed its own brand. Both products are sold in packs of seven tablets while the prescription-only versions are available in packs of 15 tablets.

Pfizer launched its own brand, Reactine, in April 2004, eight months before patent expiry of cetirizine, at the beginning of the peak season for allergy. In spite of ambitious investment in DTC advertising and direct sales to pharmacists, Reactine only reached €3.6 million (US$4.40 million) sales (at ex-factory prices) after nine months of commercialisation. In the case of France, 78% of physicians say they are not in favour of self-medication for allergy and 80% of them do not prescribe OTC drugs. A study of 103 patients indicated that physicians are their preferred pathway to get a specific anti-allergy drug and that they prefer to self-medicate with prescription-only drugs – patients will ask the pharmacist to give them a repeat of a previous prescription without actually having a prescription note from a physician.

Of those patients interviewed who purchased Reactine in 2004, 22% declared that they would not buy it again in 2005, preferring to get reimbursed drugs. With an average public price of €6 per pack, Reactine was also viewed as being too expensive, compared to other antihistamines purchased by patients without physician prescriptions.

UCB launched its own OTC version under the trademark Zyrtecset in January 2005. Almost 90% of physicians interviewed said they would not prescribe Zyrtecset as it is not reimbursable and, therefore, physicians will not push sales. If pharmacists consider the brand heritage of Zyrtec as a key factor for Zyrtecset's success on the self-medication market, then the proportion of patients who declared they were prepared to buy Zyrtecset is rather limited (26%).

As of June 2005, the branded generic Humex Rhinite Allergique (Urgo) and two unbranded generics – Merck Génériques (Merck KGaA) and Hexal (Novartis) – were also competing against Reactine and Zyrtecset.

Generics companies admit this market segment is neither strategic nor attractive for them. It is just an opportunistic move to build up their generic OTC portfolio. Overall, OTC cetirizine products reached sales of only €5.6 million during the period January-June 2005. Reactine amounted €2.4 million, Humex Rhinite Allergique €1.7 million, Zyrtecset €1.2 million, while Merck Génériques and Hexal totalled less than €0.3 million together.

Generics companies agree that to be attractive for patients, pharmacists should price them at least 20% below Reactine or Zyrtecset. In doing so, they will need to propose discounts in the range of 60% on their price lists, so that pharmacists both stockpile their generics and maintain the required price difference with OTC brands.

Humex Rhinite Allergique, like Reactine, follows a consumer-driven strategy, including press ads and TV commercials backed up by a well-established OTC sales force of 80 pharmaceutical representatives and ten merchandisers, who help promote their company's products in pharmacies.

Unbranded OTC generics and Zyrtecset appear to be positioned as 'pharmacist-driven' drugs. Pharmacists' preference for recommending Zyrtecset and Reactine to patients, will primarily depend on discount levels, expected to be in the range of 40%, and on the timing of commercial offers, considering the seasonality of this market.

Strategic implications

The results of UCB's strategy on the French antihistamine market highlight the increasing difficulties faced by R&D-based companies to protect the equity of their molecules. In spite of a market withdrawal, Zyrtec prescriptions were not massively converted to Xyzall. It is estimated that in 2004, Xyzall missed the additional required sales to compensate for Zyrtec's withdrawal. On such a promotion-sensitive market as allergy, UCB would need to maintain a share of voice on Xyzall higher than the competition to expect to offset Zyrtec's withdrawal by the end of 2006.

The relevance of the back-up brand strategy, with or without withdrawal of the initial brand, is directly dependent on the medical added-value brought by the new brand. In the absence of tangible medical benefit, the new brand will be priced as generics, and the impact on sales and profits could be particularly deleterious, especially in countries where physicians are not price conscious.

In addition, the national implementation of the recent European directive 2004/27/CE, which stipulates that "…different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same substance, unless they differ significantly in properties with regard to safety and/or efficacy", allows substitution by pharmacists from an initial brand to its chemical variation, irrespective of the patent status. Thus, in countries where this directive is applied and substitution permitted, in principle, pharmacists could dispense a generic of cetirizine when physicians prescribe its isomer, Xyzall.

The majority of the European health authorities seem to be in agreement with the French government, supporting generics as long as they represent a means to reduce drug expenditure. When there is no saving at stake, they have no preference between original brands and generic equivalents.

In general, Rx-to-OTC switches do not represent an attractive option to leverage the equity of an established molecule. Possibilities of switches are rarely appropriate for medical reasons, and a review of historical cases shows that opportunities of additional sales and profits are very limited, with the probable exception of the US market. The point is clearly illustrated by sales projections of Reactine and Zyrtecset in France.

Thus, any back-up brand introduction should be supported by strong clinical studies, showing tangible medical benefits in terms of efficacy, new indications, acceptability and convenience compared to all existing players. This has become a prerequisite if the expectation is a massive transfer of prescription from physicians, the avoidance of generics substitutability and to obtain a fair price from health authorities.

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