# Are generic defence strategies worth the effort?

by Jean-Michel Peny and Robin Young

After its long period of double-digit growth in the 1980s, the pharmaceutical industry now faces the challenge of maximising product life in a price-sensitive market where increasing R&D costs, fierce competition, accelerating generic penetration and declining prescriber loyalty are slowly eroding its performance.

Pharmaceutical companies have focused on two ways of increasing a drug's contribution: compressing development time at the beginning of the product life cycle, and adopting a range of generic defence strategies at its end.

R&D productivity has been improved by focusing on fewer therapeutic areas, re-engineering core processes and developing strategic alliances. While R&D costs are still climbing, time to market is falling dramatically and, given that a 20% reduction in time to market can add two or three years of marketing exclusivity, these strategies can successfully extend the productive life of a drug.

At the other end of the life cycle, companies have implemented a variety of generic defence strategies, but with rather mixed results. It is therefore worth considering whether they are worth the effort.

The impact of generics on original drugs coming off-patent is influenced by a range of factors including regulation, price, prescribing patterns, dispensing practices and the sales level of the original drug.

The case of SmithKline Beecham's Tagamet (cimetidine) shows how market development can vary. Generic competitors to Tagamet were launched at a discount of 50% in Germany, 40% in the US, 25% in the Netherlands and 14% in the UK. One year after the Tagamet patent expired, generics accounted for 35% of cimetidine sales by value in Germany, 65% in the US, 15% in the Netherlands and 45% in the UK. Despite the low discount in the UK, penetration was high because generic prescribing is common (accounting for 52% of UK scripts in 1994) and pharmacists benefit from dispensing generics.

Price discount is very dependent on the number of generic competitors. In the US for example, the price discount on Warner-Lambert's Lopid (gemfibrozil) went from 21% when the first competitor was introduced to 55% with eight competitors on the market. When Bristol-Myers Squibb's Capoten patent expired in February 1996, more than ten generic captoprils entered the market at discounts of up to 90%. This last example shows that given free generic availability, it can be very difficult for an original drug company to influence competition.

The key question for such companies is: what factors reduce generic competition and can any of them form the basis of a strategy to limit brand erosion?

Four important factors can be identified:

- Absence of bioequivalence guidelines, preventing generic companies from submitting abbreviated new drug applications (ANDAs), applicable, for example, to inhaled drugs such as Ventolin (Glaxo Wellcome).
- Limited availability of raw material – for one year, the Slovenian company Lek was the only generic manufacturer with US Food and Drug Administration (FDA) approval for bulk cimetidine.
- Technical barriers due to manufacturing complexity, for example in the case of biopharmaceutical products such as recombinant human insulins.
- Niche drugs for which the market potential is too small to be attractive or too specialised to enter easily, as in the case of anti-epileptic drugs, for instance.

## Defence strategies

While these factors have proved effective, they do not constitute a lever that research companies can activate. However, there are other strategies that can be used to delay, or limit the impact of, generic entry (see Figure 1).

Three basic approaches have been used by original drug companies to delay generic entry:

- Lobbying for the introduction or extension of patent protection (eg, TRIPS, Supplementary Protection Certificates).
- Taking proactive and systematic legal action for patent infringement of active ingredients, manufacturing processes or 'trade dress'.
- Changing bioavailability standards (as American Home Products did with its oestrogen preparation Premarin).

| Strategic objective | Strategic options | Global efficacy index* | Key issues |
|---|---|---|---|
| Delay generic entry | • Lobby for introducing/extending patent protection | ◕ | • Industry-wide initiative |
| | • Take legal action for patent infringement | ◕ | |
| | – active ingredients | ◔ | • Requires a systematic and aggressive approach |
| | – manufacturing process | ◑ | • Does not necessarily block all production routes |
| | – 'trade dress' | ◔ | • Short-term impact (few weeks) |
| | • Change bioavailability standards | ◑ | • Relevant for very few drugs |
| Limit generic impact | • Improve brand value | ◑ | • Decreasing number of opportunities |
| | – product value: – new formulation/indication | ◑ | • Does not prevent sales erosion for basic indication |
| | – new dosage/packaging | ◔ | • Increases manufacturing costs and complexity |
| | – service value: – for patients | ◔ | • Difficult to implement outside US for regulatory reasons |
| | – for payers (MCO) | ◔ | • Payers reluctant to pay a premium for service |
| | – for prescribers | ◑ | • Prescribers urged by payers to prescribe generic drugs |
| | • Expand market (Rx-to-OTC) | ◔ | • Few drugs eligible for Rx-to-OTC switches |
| | • Compete in the generic market | ◔ | • Negative or limited positive impact over the short term |
| | – own subsidiary: – start-up | ◔ | • Lack of expertise – risk of cannibalisation |
| | – acquisition | ◔ | • Limited number of attractive candidates – risk of cannibalisation |
| | – strategic alliances | ◔ | • Risk of conflicts of interest and cannibalisation |

* compounded index taking into account technical, legal and financial feasibility, appropriateness and protection of original drug profits

○ Low ● High

**Figure 1: An assessment of the various defence strategies that companies can use to delay generic entry or limit its impact.**

These strategies are generally short-term but they are very effective in protecting profits. In the US or Germany, for instance, where sales of a 'blockbuster' can fall by 80% within a year of generic entry, each additional three months of marketing exclusivity represents a substantial cash saving. Figure 2 shows the potential benefit of delaying generic competition to Tagamet in the US.

There are also three main strategies that original drug companies have deployed to limit generic impact – improving brand value, expanding the market, and competing in the generic market.

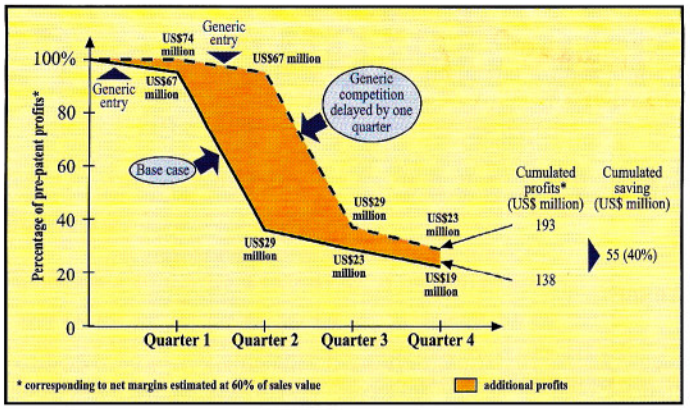


**Figure 2: The potential financial benefit of delaying generic competition to Tagamet in the US by a period of three months.**

## Improving value

There are several ways of building on brand value. New patented formulations can be developed. Marion Merrell Dow (now Hoechst Marion Roussel) collaborated with the drug delivery company, Elan, to develop Cardizem CD, a patented once-daily formulation of diltiazem. The immediate-release tablets and twice-daily capsules went off-patent in the US in November 1992 but two years after generic entry, Cardizem sales had decreased by only 12%, and generic drugs had captured only 15% of market share in value terms. The improved patient convenience combined with a reasonable price enabled Cardizem CD to capture 80% of total brand sales in 1994 and during the period 1992-1994, cumulative Cardizem CD sales reached US$1.5 billion.

New indications are a useful brand-building strategy. Based on the results of the Helsinki Heart Trial, the FDA granted a new indication for the prevention of coronary heart disease to Warner-Lambert's lipid lowering drug, Lopid. The company also gained a three-year patent extension because of the extensive additional clinical work represented by this trial.

Brand value is also promoted by new dosage forms or packaging, an approach Ciba adopted with Voltaren. Moreover, the development of multiple packaging and dosage forms designed for specific customer groups (the elderly, children, diabetics, etc) increases economic and technical entry barriers that help to reduce the likelihood of generic substitution.

Each of these tactics can be very effective, provided they are introduced long enough before patent expiry, the benefits over basic formulation are significant, and pricing is carefully determined. However such opportunities to prolong patent protection will be fewer in the future. The great majority of drugs facing the loss of patent protection have already been introduced in once-daily formulations and marketed in multiple dosage forms and presentations, whenever relevant or feasible.

The above examples illustrate efforts to improve product utility. However, brand value can also be increased by improving services to patients, payers and prescribers.

Patient programmes can build up loyalty and increase compliance, with a resulting increase in drug consumption. A good example of this is the Wellspring programme implemented in the US by Zeneca for Tenormin one year before the product patent expired. However, introduction of such programmes requires careful preparation, an organisation capable of dealing with thousands of patients, significant investment and, given the unproven benefits, a steady nerve. Restrictions on direct-to-patient communication also make patient compliance programmes difficult, if not impossible, to launch outside the US.

Disease management programmes, such as the Lilly/Mylan ulcer programme, offer some potential for protecting market share by tying-in managed care organisations (MCOs). So far, however, these programmes seem to offer just one-stop shop, bundling deals and, although they are good in theory, in practice large buyers are increasingly reluctant to enter bundling deals for high price brands despite quid pro quos on other drugs.

Specific service programmes for prescribers offer another opportunity for improving brand value. Programmes can be designed to strengthen and sustain loyalty from die-hard original brand enthusiasts. For whatever reason, there are high prescribers with low price sensitivity. The more drug companies understand their motivations and propose services accordingly, the lower will be the impact of generic drugs. However, this approach requires a customer-oriented culture and expertise that few original drug companies have.

## Expanding market

Efforts to expand the market by moving into the over-the-counter (OTC) sector can help to limit generic impact. While OTC switches move ethical companies into a different market, it is still one in which brand strength determines success. Prescription (Rx)-to-OTC switches can be either partial (as with Merck's lower-dose OTC Pepcid AC in the UK) or complete (Schering-Plough's OTC Gyne-Lotrimin replaced the Rx version). Some companies prefer to launch their OTC versions with a different brand (Johnson & Johnson's loperamide is marketed in the UK as Imodium for the Rx market and as Arret for the OTC market).

But Rx-to-OTC switches have severe limitations as strategies to extend brand value and successful examples are extremely rare. For example, in its first year in the UK market, Tagamet 100 generated sales of only US$1.4 million, (5% of global Tagamet sales) despite a promotional campaign estimated at US$10 million.

The first barrier is technical: only 5% of drugs coming off-patent before the year 2000 are likely to be therapeutically eligible for switches. The second barrier is the commercial risk of cannibalisation of high-profit Rx by lower-profit OTC business. This was observed in the UK and the US after low-dose OTC versions of $H_2$-antagonists were introduced. The OTC products were expected to replace antacids but instead were bought mainly by patients switching from an Rx brand to the corresponding OTC version.

A third drawback is slow uptake. OTC consumers are conservative and slow to experiment with unfamiliar new treatments. And, lastly, the OTC market is comparatively small (US$43 billion worldwide, or 17% of the total pharmaceutical market), slow growing (3% per annum), and low profit (margins of OTC companies are generally around a third of Rx companies). In the most attractive market, the US, payback might be achieved in around three years but in most other markets, it is likely to be nearer ten years. So, except in very rare cases, the initial enthusiasm generated amongst executives involved in OTC switches is likely to be short-lived.

### Competing directly

The third strategy, competing directly in the generic market, has been adopted by several major companies. This participation in the generic business has followed three routes:

•Setting up a generic subsidiary. In 1992 Merck set up West Point Pharma to market a generic form of Dolobid but, disappointed by the results, it moved away from direct involvement in generics two years later. Now Merck subcontracts its generic business to Endo Labs, a DuPont Merck subsidiary.

•Acquiring or taking a stake in a generic company. Marion Merrell Dow took over Rugby-Darby in 1993 for US$280 million, while Hoechst-Celanese paid US$546 million for a 51% stake in Copley. In the US and the UK, more than 80% of generic sales are now controlled by original drug companies.

•Forming strategic alliances with generic manufacturers or distributors. Upjohn signed up Geneva in 1993 to market generic versions of Xanax and Halcion, while Syntex supplied bulk naproxen to generic manufacturers with approved ANDAs.

The first option is slow and difficult, since the subsidiary's product range will be limited and management styles can conflict. The second option is very expensive: Hoechst-Celanese paid 70 times earnings for Copley, a ratio out of all proportion to its growth. In addition, generic companies that are publicly available and performing well (like Mylan for example) are becoming rare. A marketing alliance with a generic partner may be the best, most flexible choice, provided potential conflicts of interest are addressed.

If a decision to participate in the generic market has been made, when is it best to enter and what price strategy should be followed?

It has generally been assumed that the first entrant would secure long-term market share at reasonable prices by loading distribution channels and developing relationships.

## The generic market

Generic growth is being driven by new healthcare cost-containment policies, simplified registration procedures, the improved image of generic drugs and the patent expiry of leading products (products worth US$25 billion in 1994 will come off-patent by 2000).

In 1994, worldwide sales of generic drugs were around US$23 billion, or 11% of the total prescription market. The global generic market is forecast to grow at 14% per annum (compared with 6% for the innovative drug market), and should reach US$50 billion by the year 2000.

Generic penetration varies widely from one country to another (see Figure 3). The US, Japan and Germany account for 60% of total world generic sales whereas France, Italy and Spain have minimal generic competition. The favourable regulatory and market environments in the US, Germany and the UK should guarantee average annual growth in the range of 12-14%, leading to a respective market share for generics of 16%, 24% and 40% by value by the turn of the century. In Japan also, conditions are evolving in favour of generic drugs, which could account for 10-12% of the market by 2000.

In countries such as France, Italy and Spain, where pharmaceutical prices are low, generic market share will reach only 4-5% unless governments introduce drastic measures like budgetary control of prescribing or compulsory generic substitution by pharmacists.

It is interesting to note the approach recently adopted by the French government to stimulate the development of the generic market. Through the drug pricing committee (the CEM), major pharmaceutical companies have been strongly encouraged to launch generic drugs. The recent acquisitions of generic companies – Biogalénique by Rhône-Poulenc Rorer, Irex by Synthélabo, for example – as well as the introduction of generic drugs by Sanofi and Merck & Co probably result from a strategic decision aimed more at pleasing the government than seizing an attractive opportunity.

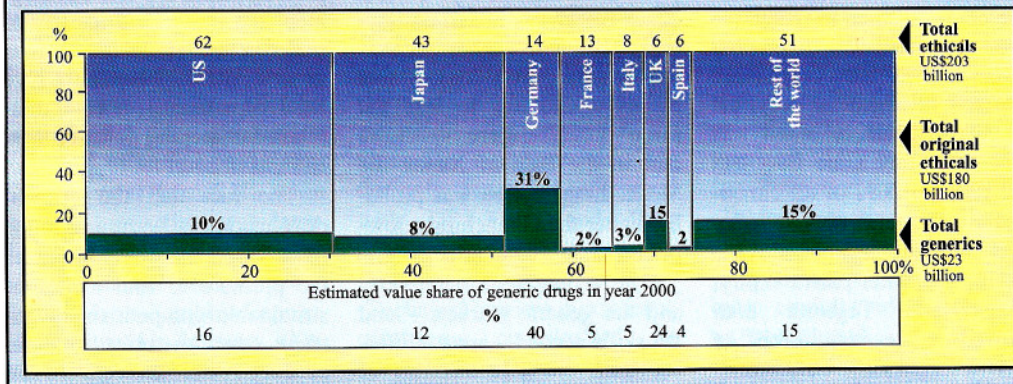


**Figure 3: The share by value of generic drugs in the leading pharmaceutical markets in 1994, with estimates for 2000.**

Based on this belief, Syntex launched its own generic naproxen in the US, at a 20% discount, eight weeks before the Naprosyn patent expired. In Germany Bristol-Myers Squibb and its co-marketer Schwarz Pharma introduced generic captopril ten months before patent expiry, at a 25% discount to the original brand.

However, it is now common to see as many as ten generic competitors on the market in the week following patent expiry. In these circumstances, price goes into free-fall. To maintain market share, the 'pre-emptive' generic drug could follow the price down, but then profit margins would be slim. If the 'pre-emptive' generic drug were to maintain its initial price, market share will then be trivial. Either way, contribution is small. There is also the impact of pre-expiry cannibalisation to consider. Any pre-expiry sales are made at the expense of the brand unless the presence of the generic drug expands the market significantly, and this is unusual.

Early entry is therefore almost certain to have a negative impact on profitability. 'Defence generic' drug launch should be left to the last possible moment.

Pricing strategy needs careful consideration. Upjohn chose to lead the price of alprazolam down to secure the largest market share in volume. A year after patent expiry, Upjohn retained around 75% of alprazolam volume, of which 50% was through its generic division, Greenstone, and its generic partner, Geneva. However, prices were only 10% of the previous brand price. Although Upjohn achieved its objective of maintaining high capacity utilisation of its manufacturing plants, the opportunity cost was a catastrophic loss of Xanax contribution.

SmithKline Beecham adopted a different strategy for Tagamet. It launched a generic version through Penn Labs to supply hospitals and MCOs and signed an agreement with Lederle to

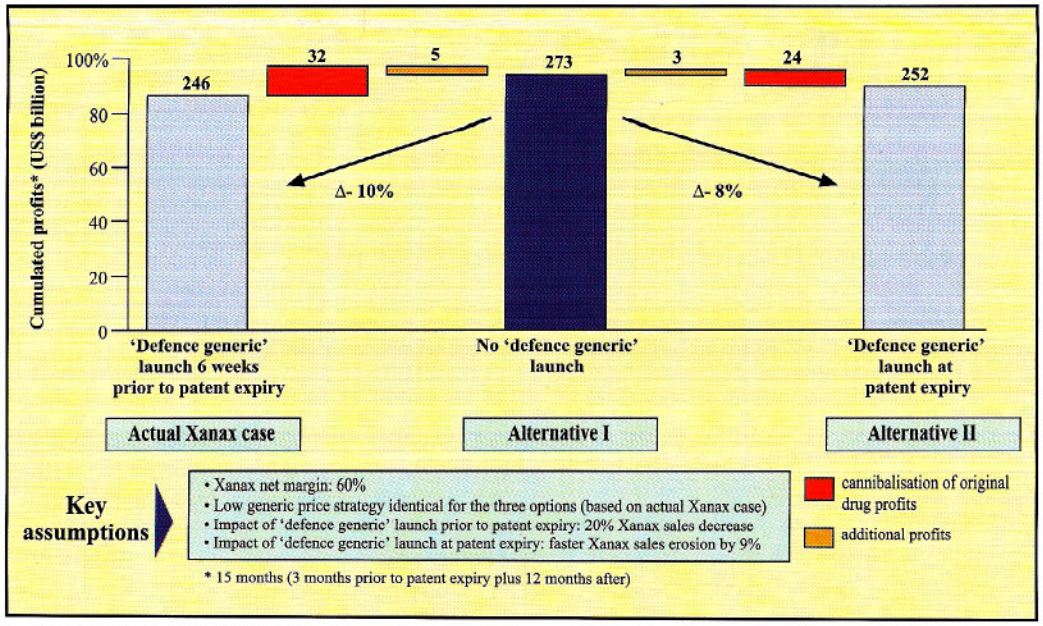


**Figure 4: The impact of a 'defence generic' launch on original drug profits, based on the example of Xanax in the US.**

cover wholesalers and pharmacies, but it did not attempt to dominate the cimetidine market. The company tried to match the price of generic competitors, but never to lead the competition. One year after generic entry, the average discount to brand was 50% and SmithKline Beecham had retained 20% of all cimetidine volume sales, almost exclusively through Tagamet sales.

One year after patent expiry, Xanax and Tagamet both showed a revenue drop of around 70%. Thus both strategies failed to protect original brand profits and neither company made money in the generic market, Upjohn because margins were insignificant, SmithKline Beecham because its share was low.

Generic entry, like OTC switching, is less attractive in practice than in theory. On that basis, the key is not to do anything that will further accelerate original drug loss – that means do nothing to lead the price down. Figure 4 shows that in the case of Xanax the 'do nothing' option was probably better than launching a low-priced 'defence generic' drug.

The economics of the OTC and the generic markets – and the skills needed – are so different from the core business of original drug companies that, for most of them, generic defence strategies based on competing in these sectors are unlikely to be worthwhile. Truly successful strategies for maintaining value from original drugs start long before patent expiry. Therapeutically valuable line extensions prolong patent life and can fragment the market sufficiently to make it less prone to vigorous generic attack. They also give legal departments more ammunition for keeping potential new entrants in court for longer.

The fact that the original drug market is becoming much more price sensitive increases the pressure to find niches or sustainable competitive advantages over low-priced me-too products, and this should be tackled in the early stages of the product life cycle. This places a continuing burden on R&D. Each time a new chemical entity comes to market, the aim of research companies must be to create a dynasty of follow-on products. Entering the OTC and generic markets will at best generate some pocket money – it will not fill the gap in profits. There are no hard and fast rules for success and, for individual products and countries, there may be scope for some profitable interventions. But these defensive strategies should not distract companies from their main business – bringing a constant flow of innovative drugs to market as quickly as possible, and maximising their value after launch.

Those rare companies such as Astra, that retain the focus on their original drug business and do not compete in the generic and OTC markets, seem to perform better than the others. In 1994 Astra achieved one of the best profitability ratios (operating profits of 32.5%) and the fastest growth (+24%) in the industry. It is difficult to predict whether this strategic option will prove to be the best over time but experience suggests that companies focusing on their core business have a better competitive position and show enviable results. SM

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***This article is based on a paper presented at a seminar organised in October 1995 by IIR.***