What is the value of authorised generic agreements? Assessments on the French market

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Abstract The worldwide generic market should keep on growing at the expense of brand-name companies and reach sales of US$97bn, in 2010. To resist this increasing competitive pressure and to maintain a slice of the market, brand-name companies may negotiate with generic companies to postpone the launch of their competitive products or they may license their own generic products to competitor generic companies. In the USA, these so-called 'authorised generics' have generated substantial profits for brand-name companies and to their generic partners, provided however that they are launched before patent expiry during an exclusivity period. In Europe, there are no legal exclusivity periods granted to generic companies that can challenge original brands, and the strategic and financial values relative to this strategy are not well established. This paper proposes a specific approach to assess the benefits of authorised generic deals for both the brand-name companies and their generic partners. The application of this approach on several authorised generic deals carried out in France shows that the duration of the exclusivity period, the number of generic partners involved, and their relative competitive position are the most important success factors. In addition, it appears that brand-name companies could have a financial interest to propose, for their 'easy-to-substitute' original brands, authorised generic licenses to all generic companies. In such a situation, generic partners will benefit from a guaranteed market access and a product identical to the original brand while avoiding risks of patent infringement.

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INTRODUCTION

Considering the population increase and ageing, the demand for more sophisticated diagnostic techniques and more specialised treatments, healthcare costs will keep on rising at a faster pace than national economies can

afford. To contain the resulting financing gaps, private and public payers support the development of generic products with measures that encourage:

- more cost-effective prescriptions by physicians;
- systematic substitution at the expense of brand-name products by pharmacists;
- higher level of patient acceptance for low cost drugs through more incentive co-payment schemes.

The worldwide generic market benefits from a favourable environment which should drive its size from US$55bn in 2005 to US$97bn in 2010, exhibiting a compound annual growth rate of 12 per cent. In 2010, the generic market should account for 12 per cent of the total pharmaceutical market in value, compared to 10 per cent in 2005. During the same period, the market share in volume should grow from 25 to 30 per cent.

Generic penetration should grow much faster in developing markets such as France, Italy and Spain where they currently account for less than 15 per cent of the pharmaceutical market, in volume, against more than 30 per cent in Germany or the UK. By 2010, however, their performance in value terms is likely to be affected by a series of price cuts imposed by health authorities to increase the price difference between generic and brand-name products from an average 50 to 70–80 per cent.

In addition to the flow of major brand-name products that will face patent expiry in the next three years, the generic market will start to benefit from the launch of 'biogenerics'. As they are not currently considered as bioequivalent, but rather 'biosimilar' their substitution by retail pharmacists is unlikely to be permitted in the short term. Besides, the offer will remain limited due to high technical entry barriers and defence strategies put in place by brand-name companies that are already preparing improved or second-generation products. At the horizon of 2010, 'biogenerics' should not contribute for more than 2 per cent in value of the worldwide generic market.

GENERIC DEFENCE STRATEGIES

In this context, the impact of generic competition on the performance of brand-name products intensifies and becomes less different between developed and developing markets.[1] Thus, certain brand-name products, for example Mopral/Losec 20 mg (omeprazole), have faced sales drops in the range of 50 per cent in France within three months of generic commercialisation (Figure 1).

Brand-name companies have developed a range of defence strategies to postpone generic market entry and/or to slowdown their speed of penetration as their products go off-patent. The most effective measures remain those that retard generic competition[2] and explains why brand-name companies do everything they can to prolong the duration of their patent protection especially in the period just before patent expiry. In the USA, brand-name companies are also systematically involved in legal actions to defend their intellectual property against the challenges initiated by generic companies. The 180-day marketing exclusivity period the latter can obtain if they win represents a strong financial incentive for them to challenge the patents involved.

If brand-name companies do not come to an agreement with the first-to-file generic company, they may decide to compete directly with them during the 180-day exclusivity period. Following this strategy, in 2003, GlaxoSmithKline (GSK) granted Par Pharmaceutical a license to market a so-called 'authorised generic' version of its brand Paxil during the 180-day exclusivity period won by the generic company Apotex. It is estimated that this specific deal generated US$200–300m for GSK.[3] The number of authorised

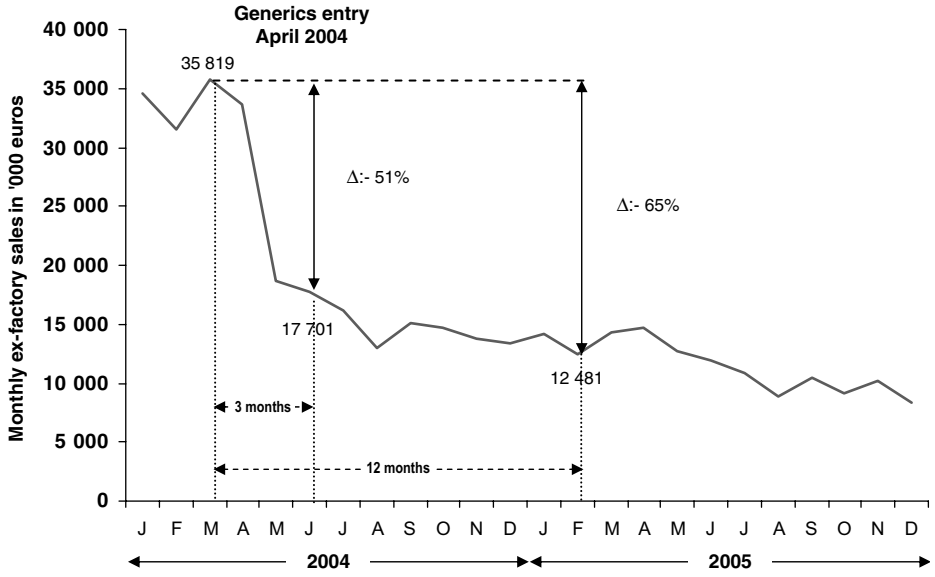

Figure 1: Impact of generics on Mopral/Losec 20 mg (omeprazole) sales on the French open care market (2004–2005)
Source: Smart Pharma Consulting analyses after GERS market data

generics that have been launched in the USA has increased significantly recently and these authorised generics are either marketed by a generic partner or by the brand-name companies own generic subsidiary, such as Schering-Plough's Warrick or Pfizer's Greenstone.

Authorised generics provide additional revenues to brand-name companies and early access for their generic partners, which can generate significant profits during the 180-day exclusivity period. Once the exclusivity period is over, the fierce competition among generic companies drives prices and therefore profits down.

In Europe there is no such legal exclusivity period granted by health authorities and the financial benefits of authorised generic deals remain unclear. To estimate the potential value of this strategy, for both the brand-name and generic companies in the European markets, the authors have developed a specific approach that has been applied to several deals signed in France.

The French generic environment

In 2005, the French generic market was still limited to a market share of 7 per cent by value and 14 per cent by volume and French physicians wrote less than 10 per cent of their prescriptions under generic names. The current healthcare system does not incite/oblige physicians to prescribe, and patients to ask for or accept generic products. The introduction of a reference pricing system (RPS) in 2003 has not significantly modified patients' behaviour as most brand-name products have had their price aligned at the reference price level.[4] Only retail pharmacists, who receive attractive discounts from generic companies, have a strong financial interest to develop the generic market through substitution.

Generic companies do not compete on drug prices, which are capped by health authorities, but on discounts offered to retail pharmacists. Officially, these discounts should not go beyond 10.74 per cent of the ex-factory price for generic products and

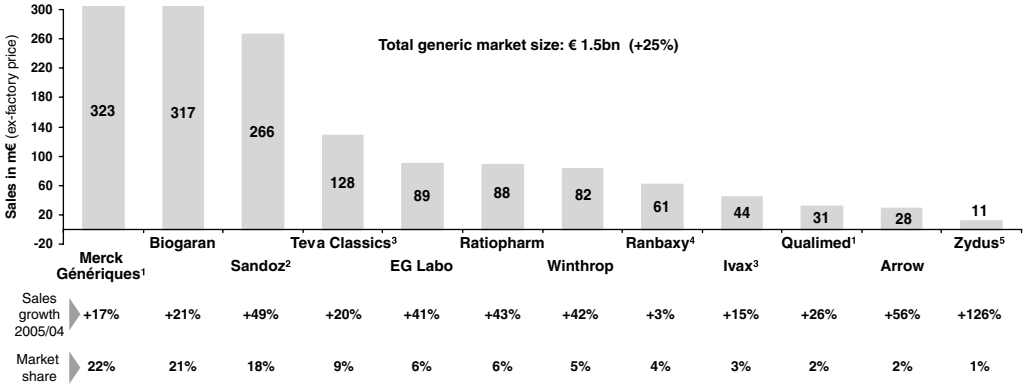

Figure 2: Generic companies on the French open care market (2005). [1]Both companies belong to Merck KGaA, [2]Acquisition of G. Gam (Hexal) in 2005, [3]Acquisition of Ivax in 2006, [4]Acquisition of RPG from Aventis in 2004, [5]Acquisition of Alpharma in 2003
Source: Smart Pharma Consulting analyses after GERS market data

2.5 per cent for those subject to the RPS, but in practice the situation is different. These discounts were estimated on average at 50 per cent in 2005 and up to 75–80 per cent for generic versions of 'blockbusters' such as omeprazole or simvastatin. A new law has recently been introduced to limit discounts granted to retail pharmacists at 20 per cent in 2006 and 15 per cent in 2007. If in 2006, the levels of discounts actually offered have decreased they are still in the range of 30–35 per cent. With an average gross margin estimated at 60 per cent of their ex-factory sales price, only the two or three largest generic companies are likely to generate operational profits in France.

Between them, the two leaders Merck Génériques and Biogaran hold more than 40 per cent of the total generic market (Figure 2). The relative position of generic players on the market has been stable since 2000, with few changes in their market share and sales rankings. Their products and services are less and less differentiated and their commercial conditions relatively similar. From the mid 1990s until it was taken over by Ranbaxy in 2004, RPG, the generic arm of Aventis, has pursued an active strategy to obtain authorised generics from brand-name companies, including those from its parent company. Some of these deals included an early-entry clause allowing RPG exclusivity or semi-exclusivity periods. The main intention of RPG management was to build a competitive advantage by offering generic products strictly identical to the original brands. If retail pharmacists acknowledge that 'strictly identical' generics make the substitution easier, they also recognise that the size of the products portfolio and the commercial terms are the two most important criteria while selecting a generic supplier.

Following the same strategy, Biogaran has also signed several authorised generic agreements with third-party companies and its parent company, the pharmaceutical group Servier. Recently, Sanofi Aventis announced that as a part of its corporate strategy, it will market generic versions of its original brands through its generic division Winthrop once they are off-patent.

Case study No. 1: Authorised generic of Prozac

In 2001, Prozac (fluoxetine) was the leading brand of Lilly France with annual sales of €102m in the open care market that represented 36 per cent of its total sales. Lilly France signed an agreement with RPG, which was at that time the fourth largest

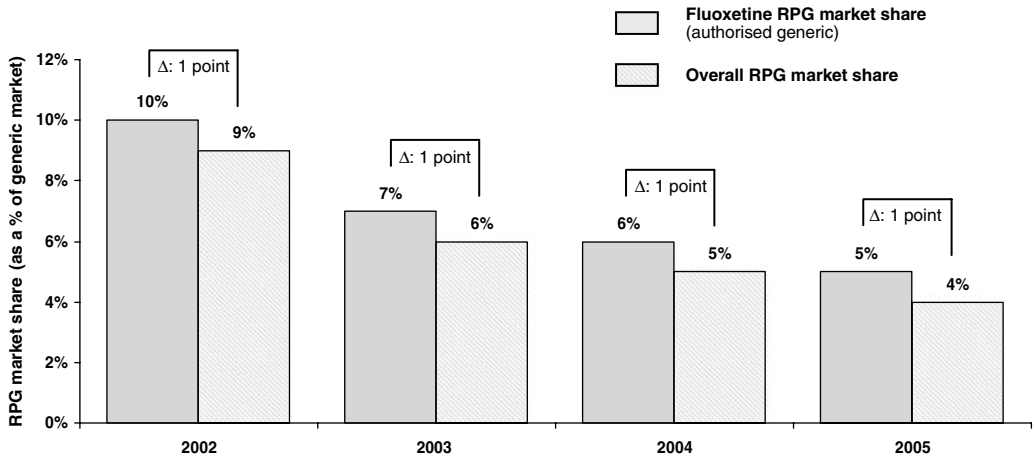

Figure 3: Differential of market share between fluoxetine RPG and Overall RPG (2002–2005)
Source: Smart Pharma Consulting analyses after GERS market data

generic company with €38m sales and a market share of 7 per cent. Through this agreement RPG was allowed to enter the market in October 2001 with a generic version of Prozac three months before the patent expired in January 2002. Thus, RPG benefited from a three-month exclusivity period before six other generic companies entered the market with their own generic versions of fluoxetine. To evaluate the benefit of such a partnership, it is proposed to compare the overall generic company market share to the specific market share of its authorised generic. We can assume: the higher the differential of market share in favour of the authorised generic, the higher the competitive advantage. When applied to fluoxetine RPG, this method showed that over the period running from 2002 to 2005, the differential of market share was of 1 point, for each considered year (Figure 3).

Based on this performance indicator, it can be assumed that RPG did not manage to transform its exclusivity period into a competitive advantage. The comparison of RPG rankings on the fluoxetine generic market and on the national generic market were identical during the period 2002–2005, which confirms the absence of a measurable strategic benefit. The cumulated additional sales generated by this agreement were estimated at €1.8m and represented a 28 per cent increase *v* the base case up to the end of 2005. The base case option was defined as the entry into the market with a 'conventional' generic product the day Prozac came off-patent (Figure 4).

With regards to the estimated profits associated with the authorised generic agreements, it is necessary to consider the potential difference between the cost of goods sold (COGS) invoiced by the brand-name company and an alternative source available on the market. In general, the supply agreement signed with the brand-name company is less favourable and it is common to observe a difference of gross profitability in the range of 10–20 percentage points for the generic partner. Assuming that the COGS of the authorised generic marketed by RPG was 30 per cent of its ex-factory price and that it would have been 20 per cent in the base case, the additional cumulative gross profit at the end of 2005 would have reached €625,000. Combined with the savings made by RPG through not having to develop and register the fluoxetine generic file would increase the marginal gain up to €925,000.

From the RPG perspective, this early entry agreement has failed to prove that it significantly reinforced the company's competitive position within the generic

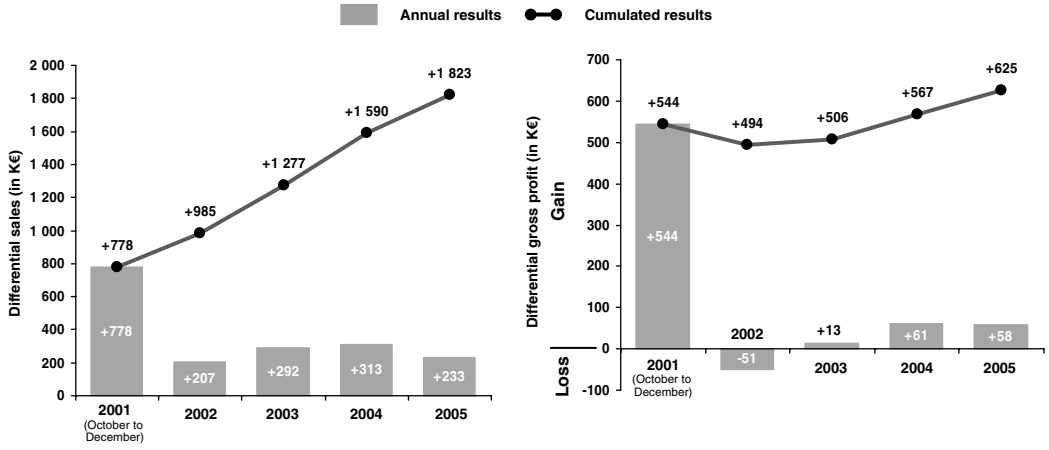

Figure 4: Relative performance of RPG fluoxetine authorised generic (2001–2005). The differential sales and gross profit correspond to actual *v* base case performance. The base case is defined as a conventional/non-authorised generic

Source: Smart Pharma Consulting analyses and estimates after GERS market data

market. Considering that the 'authorised fluoxetine' accounted for less than 4 per cent of RPG total sales during the period 2001–2005, however, a significant improvement was unexpected.

For the brand-name company, the duration of the early-entry period is a key element of the authorised generic agreement as the longer the exclusivity period, the higher will be the cannibalisation of its original brand and the associated loss of profit. While the gross margins of original brands are in the range of 90 per cent, brand-name companies would only see profits of 10 to 20 per cent through the supply of authorised generics. In the case of Prozac, it is estimated that the three-month exclusivity period granted to RPG induced for Lilly France a profit loss of €863,000 (Figure 5), that has been compensated through profits related to the supply agreement signed between both companies.

Thus, it is in the interest of the brand-name company to negotiate the shortest possible exclusivity period and, if at all possible, to avoid it. Signing an authorised generic agreement without exclusivity period may be of particular interest for generic players who are behind schedule to obtain their marketing authorisation by the day the original brand comes off patent. They could also envisage such a deal for products like antiepileptics, antipsychotics or antiparkinsonians which can occasionally induce a loss of seizure control or side effects following generic substitution.[4] In this specific case, some generic companies may be ready to pay a premium to possess in their portfolio an authorised generic strictly identical to the original brand. Before entering into such an agreement, however, the brand-name company must be sure that the sales generated by their potential generic partner will mainly be at the expense of the other generic competitors.

The study of the authorised generic deal signed between Lilly France and RPG for the fluoxetine shows that they have not drawn a substantial benefit from their partnership. Lilly France had to face a payback period of almost three years that was mainly due to difficulties encountered by its generic partner to defend its leading position on the fluoxetine generic market. Actually RPG has been severely penalised by the commercial aggressiveness of its generic competitors that the company decided not to match.

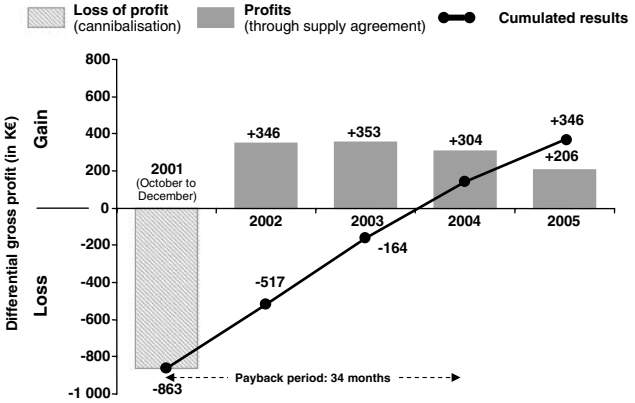

Figure 5: Profit gain/loss of Lilly France related to fluoxetine authorised generic agreement (2001–2005). The differential gross profit corresponds to the actual *v* the base case performance. The base case is defined as the absence of authorised generic licence granted to a generic partner
Source: Smart Pharma Consulting analyses and estimates after GERS market data

Case study No. 2: Authorised generics of Augmentin

GSK adopted the same early-entry strategy as Lilly France, but signed deals with three generic companies for its antibiotic Augmentin, which is a fixed combination of amoxicillin and clavulanic acid (amoxiclav). RPG and Biogaran entered the market in November 2001 while GNR (renamed Sandoz since 2004) launched its generic amoxiclav in April 2002. This time difference is explained by the fact that GNR obtained its authorised generic from GSK in the scope of an out of the court settlement regarding patent infringement litigation for GSK's Zovirax (acyclovir). While the patent of Augmentin expired in France in January 2002, other non-authorised generic companies did not market their product before March 2003. This delay is mainly explained by problems of manufacturing capacities for the generic version of clavulanic acid. Note that the modification of the amoxicillin:clavulanic acid ratio from 7:1 to 8:1 made by GSK in the formulation of its original brand, in 1999, had little impact on this delay and in fact the non-authorised generic companies had enough time to take into account these late modifications and to adapt their registration file. In this particular situation, GSK had to face a longer period of pre-entry than initially anticipated as RPG and Biogaran benefited from a semi-exclusive period of 16 months and GNR of 11 months.

The performance analysis of the three generic partners shows that during the 12 months preceding the arrival of the conventional generic competitors, Biogaran took the lion's share with 55 per cent of the units sold, against 26 per cent for GNR and 19 per cent for RPG. The calculation of the additional gross profit related to the agreements signed with GSK showed 57 per cent for Biogaran while for RPG and GNR the proportion was, respectively, 22 and 21 per cent (Figure 6). The better results achieved by Biogaran can be explained by its larger client base and a competitive commercial strategy allowing a faster market penetration than its two early-entry competitors.

For GSK, the loss of profit that occurred during the semi-exclusivity period has been absorbed in the middle of 2004, that is almost three years after first authorised generics were launched (Figure 7). This payback period has been longer than expected by GSK's management due to the late entry of

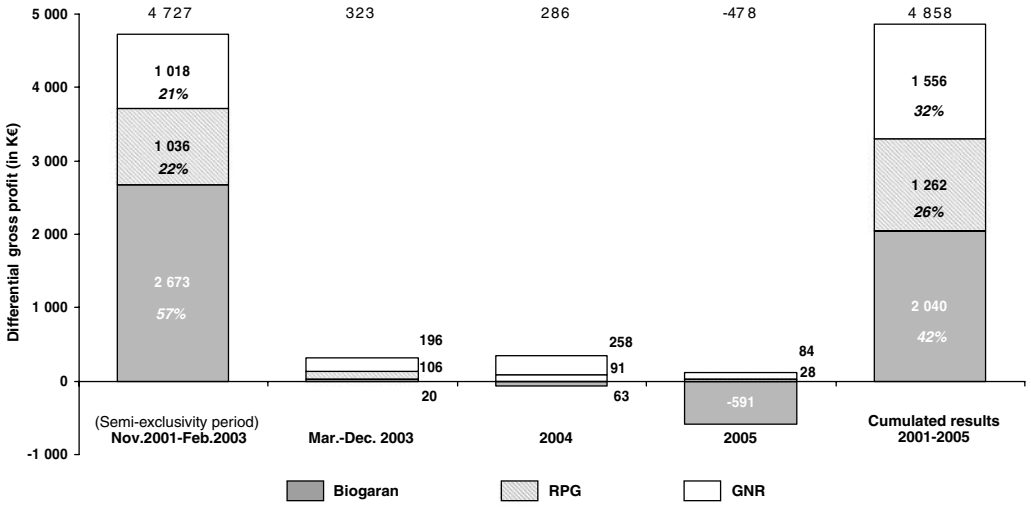

Figure 6: Profit gain/loss of generic companies involved in an authorised generic agreement for amoxiclav (2001–2005). The differential gross profit corresponds to actual *v* base case performance. The base case is defined as the absence of authorised generic licence granted to a generic partner
Source: Smart Pharma Consulting analyses and estimates after GERS market data

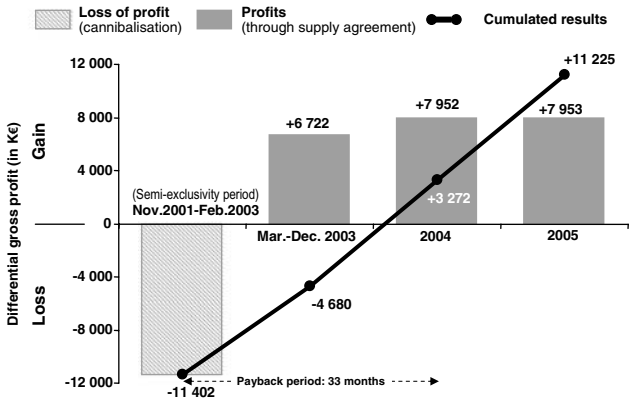

Figure 7: Profit gain/loss of GSK France related to the amoxiclav authorised generic agreements (2001–2005). The differential gross profit corresponds to actual *v* base case performance. The base case is defined as the absence of authorised generic licence granted to a generic partner
Source: Smart Pharma Consulting analyses and estimates after GERS market data

conventional generic competitors that was difficult to anticipate and to the multiple authorised generics that have been licensed. During this excessively long period of semi-exclusivity, the three authorised generic products have cannibalised 31 per cent of Augmentin sales in units and induced a gross profit loss of €11.4m.

Case study No. 3: Authorised generics of Stilnox

In January 2004, five months before the patent expiry of its original brand Stilnox/Ambien (zolpidem), Sanofi Aventis launched on the French market its own generic version through its own generic subsidiary Winthrop (formerly named Irex). This strategic decision

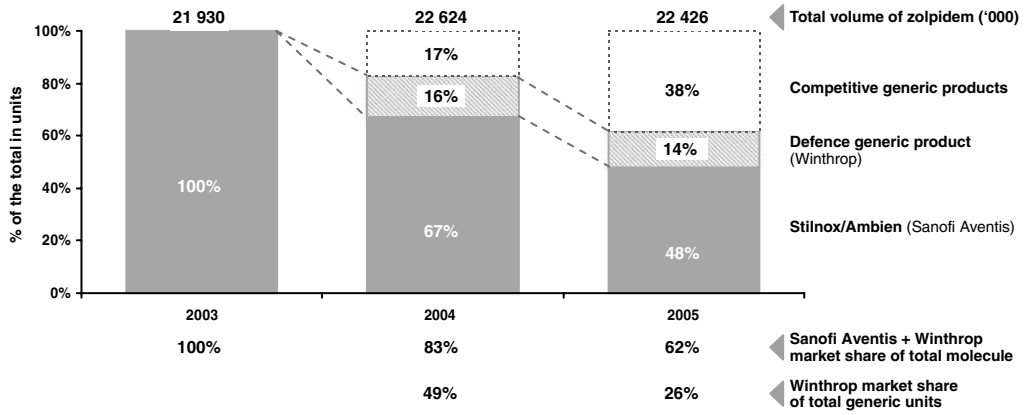

Figure 8: Impact of zolpidem authorised generic agreement on Sanofi Aventis and Winthrop-related sales (2003–2005). Pre-entry period from January to May 2004
Source: Smart Pharma Consulting analyses after GERS market data

enabled the brand-name company to retain 83 per cent of the total volume of the molecule in 2004 and 62 per cent in 2005 (Figure 8). Moreover, with a share of 26 per cent in the zolpidem generic market in 2005, which is five times higher than its national market share, Winthrop appears to have been the main beneficiary of this in-house 'authorised generic' agreement and it capitalised on the five-month period of exclusivity to try to open new client accounts. In addition to attractive discounts offered for its generic version of zolpidem, retail pharmacists were also proposed commercial conditions on Stilnox. By encouraging the maintenance of a high level of stock for its brand-name and its authorised generic products, Sanofi Aventis intended to slow-down the normal penetration rate of competitive generics once they went on the market. In general, this stockpiling strategy shows effects during the two or three months following the entry of conventional generic competitors. Once their stock of authorised generics is exhausted, retail pharmacists stock up again with the generic product by placing an order to the preferred generic companies they used to collaborate with. When compared to other major brand-name products having signed an authorised generic deal, the payback period is shorter, but still longer than two years. The analysis of the overall gross profits directly related to this operation, however, showed positive results for Sanofi Aventis as soon as 2004 (Figure 9).

CONCLUSIONS

The success of an authorised generic agreement is strongly dependant on the duration of the exclusivity period, the number and the competitive strengths of the early-entrants. The leading generic players who benefit from a larger client base will cannibalise more severely the brand-name product during the period of exclusivity. But, once the conventional generics competitors have entered the market, they will be able to retain a larger share and will therefore generate more sales for the brand-name company.

To attract generic players, the COGS proposed by the brand-name company should not differ by more than 10 to 20 percentage points from that available on the free market. To get the supply agreement renewed, after three to four years, the brand-name company must consider reducing the price gap, or even filling it in.

In the French market, over the past ten years, only a handful of brand-name companies have licensed a dozen authorised generics. The good results observed with the

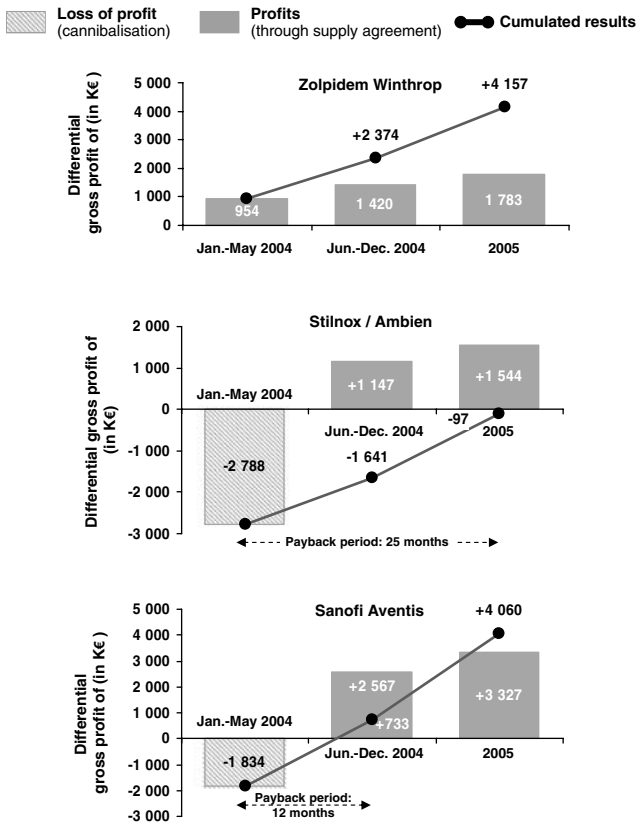

Figure 9: Profit gain/loss of Winthrop and Sanofi Aventis related to zolpidem authorised generic agreement (2004–2005). The differential gross profit corresponds to actual *v* base case performance. The base case is defined as the absence of authorised generic licence granted to a generic partner. Pre-entry period from January to May 2004
Source: Smart Pharma Consulting analyses and estimates after GERS market data

authorised generic of zolpidem and the more rapid generics penetration observed for a couple of years on high awareness brands should, however, incite brand-name companies to pay more attention to the potential benefits of such agreements.

For original brands like Mopral/Losec, Stilnox/Ambien or Zocor that are extensively prescribed and rather easy-to-substitute, brand-name companies could evaluate the impact of a more proactive approach which would consist in offering a short exclusivity period, of one or two months maximum, and in proposing all the generic companies, or at least the leading players, a duplicate of their marketing authorisation along with a compulsory supply agreement. Assuming that AstraZeneca would have managed to license authorised generics to all generics players, with a two-month exclusivity period, then €74m of gross profit could have potentially been generated by the end of 2007. The payback period would have been five months after the date of patent expiry. In the case 80 per cent of the generic volume sold were manufactured by AstraZeneca, which is more realistic, the additional gross profit would have amounted to €59m (Figure 10). To these figures should be added the positive impact on manufacturing facilities running at a higher capacity.

Provided the COGS are aligned on the prices proposed on the market, generic companies would have good reasons to accept

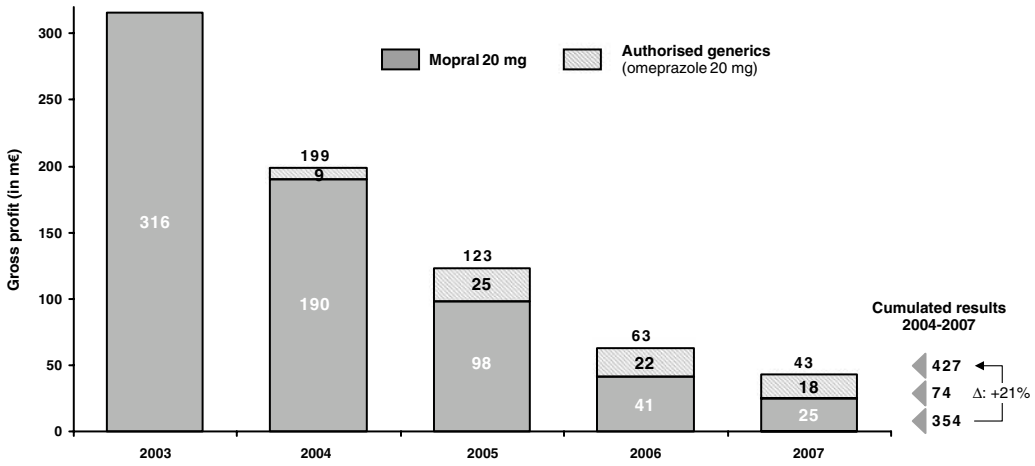

Figure 10: Potential impact of authorised generic agreements on AstraZeneca gross profits (2003–2007). Estimates based on 100 per cent of generic volumes supplied by AstraZeneca and on a two-month early-entry period granted to generic partners, achieving an average penetration rate of 50 per cent. Assuming that 80 per cent of generic volume are provided by AstraZeneca, the 2004–2007 additional gross profit would have amounted: 66m€ (Δ: + 16 per cent)
Source: Smart Pharma Consulting analyses and estimates after GERS market data

these types of authorised generic agreements. In this case they would not take advantage of pre-patent expiry periods, since they would be open to all the players, but they would have the guarantee to reach the market on time, to save on development and registration costs, to have a secure source of active pharmaceutical ingredients (API) and to avoid the risks of patent litigation. This generalised approach of authorised generic agreements could be particularly relevant for products whose sales erode drastically once they are genericised. Once more the pharmaceutical companies would demonstrate their ability to collaborate with their 'foes' for their mutual interest and in this particular case, not at the expense of the patients and/or the buyers of these products.

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