Barriers to substitution

The French government's goal of 50% generic penetration has not materialised. Jean-Michel Peny believes the target is neither realistic nor appropriate for each individual therapeutic class on both medical and economic grounds. He argues that product features, pathological conditions and patient profiles provide the key to settting generic penetration objectives

To reap real economic benefits from generic penetration, without jeopardising patient care, the French government needs to adjust its objectives on a product-by-product basis

Over the past decade, European governments have introduced an array of measures to boost the development of generic drugs. The two largest European generics markets, Germany and the UK for many years have been mainly driven by generic prescriptions written by physicians.

In France, the third largest European generics market, the government has tried, in vain, to get the support of physicians. Faced with their reluctance to prescribe generics, the government passed the responsibility for building a significant generics market to community pharmacists. Thus, in September 1999, French pharmacists obtained the right to substitute original brands with a corresponding generic. To render this measure sufficiently attractive to pharmacists, their mark-up was modified so that the dispensing of either an original brand or a lower-priced generic provides them with the same profit in euros. In addition, pharmacists were entitled to receive discounts of up to 10.74% of the ex-factory price for generics compared with only 2.5% of the wholesaler's price for original brands.

In practice, the discount ceilings are not adhered to. It is estimated that in 2004, total discounts granted to French pharmacists on generics averaged 45% against 6% for original brands. If one considers an original brand selling for €10 (ex-factory price), the profit made by the pharmacist will amount to €3.80 (margin + 6% discounts) compared with €6.12 for the corresponding generics (margin +45% discounts). Thus, by selling a generic, pharmacists generate, on average, a profit 60% higher than with an original brand. Generics account for 6% of total French community pharmacies' sales and 12% of their gross profits, so generic substitution represents an important economic incentive for pharmacists.

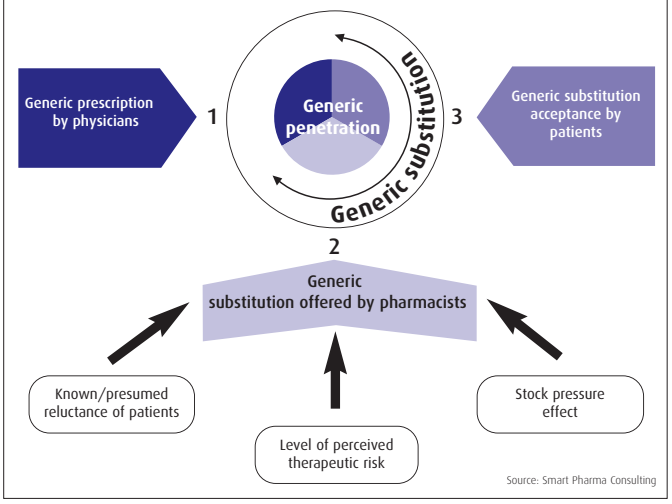
However, the French government, searching desperately for additional savings, introduced a reference price system in 2003. This measure, called TFR (Tarif Forfaitaire de Responsabilité), applies to each drug for which the generic penetration is not considered by health authorities to be high enough. In order to avoid inclusion in the reference price system, a substance would have to show a generic substitution rate of at least 45% in 2003. For the second wave of TFR, that should be applied in mid-2005, the French pricing committee, CEPS, has fixed a target of 50% to 60% for those drugs accounting for the greatest costs reimbursed by the Sickness Funds.

The TFR is viewed by pharmacists as an economic penalty. Once it is applied to a product, the pharmacist's margin on the generic concerned is no longer equal to the original brand in absolute terms and becomes proportionate to its price. In such a case, the discount is reduced from 10.74% to 2.5%, but actual discounts remain in the range of 45%. Another 'side-effect' induced by this measure is that brand companies reduce their prices to the reference level which is set at around the generic price levels. In fact, 65% of the original brands affected by the first wave of TFR have aligned their prices. The objective of such price cuts was to limit or even stop generic penetration growth, and this is what happened in fact. Many pharmacists and their staff do not like substituting the original brands with generics if they know both have the same price. In addition, most patients who know that their prescribed original brand is subject to a TFR do not accept the generic equivalent because there is no economic rationale for doing so. Conversely, brand companies which did not align their prices, preferring to preserve their profit margin per pack sold, have faced a sudden growth of generic penetration. For instance, Surgam (tiaprofenic acid), which was sold under this pricing strategy, has seen generic penetration grow from 24% before the introduction of TFR to 84% two months later. This sudden jump can be explained by the reluctance of French patients to pay the price difference from their pocket – the difference between the TFR and the price of the medicine. The great majority of the original brand companies affected by the second wave of TFR are expected to align the price of their products, which will impact the profit made by pharmacists on each pack dispensed.

Factors driving generic penetration

In the light of these economic facts, it is surprising to note that generic penetration rates still vary significantly from one drug to

Figure 1 – Generic penetration model in France



another, even when they belong to the same therapeutic area. To better understand the mechanism that drives generic penetration, a survey was carried out in October 2004 by Smart Pharma Consulting of 162 community pharmacists to specifically analyse four central nervous system (CNS) therapeutic classes (anxiolytics, antipsychotics, antiepileptics and antiparkinsonians) whose generic penetration is particularly low.

The results of this study show that generic penetration is driven by three key factors (see Figure 1):

1. Generic prescribing by physicians.
2. Generic substitution by pharmacists.
3. Generic substitution acceptance by patients.

Generic prescription by physicians

Unlike the UK, where 74% of prescriptions are written generically, in France, the overall generics prescription rate is as low as 9%. However, for products that are substitutable, 30% of prescriptions written by physicians are by international non-proprietary name (INN). In this case, the dispensing of generics by pharmacists becomes mandatory. No substitution in favour of the original is permitted unless there is no price difference with the generic equivalent. When a physician's prescription mentions a specific generic manufacturer (eg, sulpiride Sandoz) or a branded generic name (eg, Synedil), pharmacists are allowed to deliver an alternative generic brand which they have in stock, provided the price difference remains within the limit of €0.08 per pack.

Thus, it appears that the higher the generic prescription rate, the higher the dispensing of generics and therefore the generic penetration rate. For example, in 2004, within the CNS therapeutic classes, the three molecules with the highest generic penetration rate (ie, the two anxiolytics, alprazolam and bromazepam, and the antidepressant, fluoxetine) were the most genericised. Thus, together they achieved an average penetration rate of 57%, while their average generic prescription rate was 29%. In the specific case of the antipsychotic drug, sulpiride, generic penetration is estimated at 45%, but as much as 90% of the corresponding packs dispensed by pharmacists originate from generic prescriptions. This exceptional weight of generic prescriptions is explained by the presence of the branded generic Synedil, which accounts for two thirds of the generics sold. In fact, Synedil has been marketed in France for the past 22 years and is not viewed by the great majority of physicians as a generic, but as a branded product, like the original brand Dogmatil.

The study of the 162 pharmacists showed no evidence that generic penetration of CNS drugs is significantly influenced by the weight of specialists' prescriptions. Pharmacists admit that generic substitution may be less frequent when prescriptions originate from specialists, but it remains marginal.

Unless coercive measures are put in place by health authorities, there are few reasons to expect a rapid and drastic increase in generic prescriptions by physicians. Indeed, at the present time they have no formal obligation to prescribe generically, nor any incentives for doing so.

It could be assumed that computer-aided prescription programmes that are routinely used by 35% of physicians would help them modify their prescription habits in favour of generics. However, for the time being, the most widely used software packages are not designed to facilitate the prescription of generics. When physicians enter an original brand name they are used to prescribing, the corresponding INN does not appear on their computer screens, nor do they get the list of branded and unbranded generic equivalents being marketed.

Another important limiting factor is the absence of medical visits. Unlike in Germany or Spain, generics companies do not pay visits to physicians. They prefer to focus their promotional efforts on pharmacists who have the power to alter physicians' prescriptions in favour of the generic brand of their choice.

Generic substitution by pharmacists

Analysis of the interviews with the 162 pharmacists shows an average generic substitution rate of 59% within the French drug agency list (répertoire des groupes génériques) of substitutable products. These results were confirmed by a larger survey of 800 pharmacists carried out in 2004 by the market research organisation IPSOS, which showed that 56% claimed to regularly substitute original brands with generic equivalents.

However, theses figures do not reflect the strong heterogeneity among pharmacies, which depends on the interplay of pharmacists' offer of generics and patients' acceptance of them.

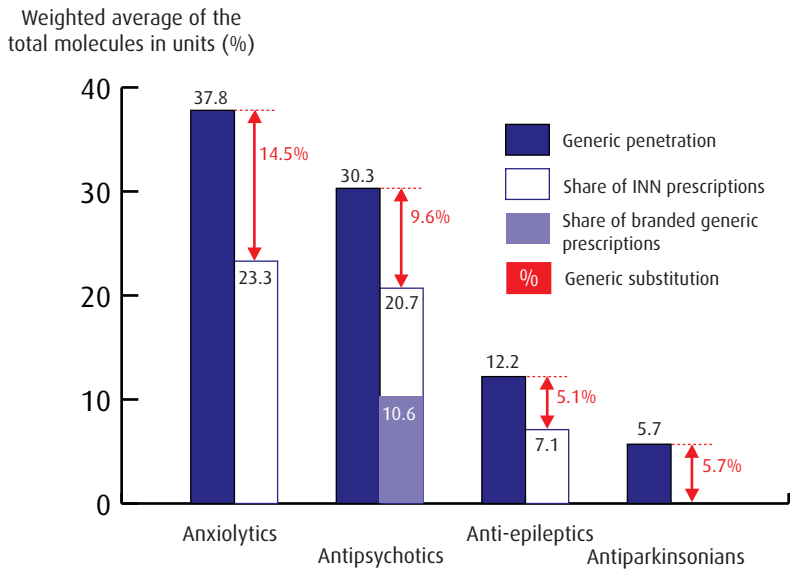
Even if the economic benefit of generic substitution is unanimously recognised by pharmacists, not all of them show the same enthusiasm to push generics sales. Certain pharmacists said that they focus their efforts on high-volume brands and especially on drugs for acute conditions, like antibiotics, that are easier to substitute than psychiatry and cardiology treatments. Of the pharmacists interviewed, 93% said they give orders to their staff with regard to the substitution policy they wish to be applied in their pharmacy. The general message conveyed by 84% of them could be summarised as "substitute as much as possible but do not be too insistent with patients". Pharmacists admit that among their staff members, substitution behaviour is not homogeneous. They are strongly dependent on the personality of the employees and on the nature of the relationships they maintain with the patients they serve. Employees who are sensitive to the economic benefits of generics for the Sickness Funds and/or for their employer are likely to be more pro-active. It is the same for those that are self-confident – they will tend to offer generics more systematically to patients.

The least genericised products are occasionally or rarely offered to patients by pharmacy staff. The antiepileptic sodium valproate, whose generic penetration is 11%, is never offered for substitution by 91% of the pharmacists interviewed. With the anxiolytic lorazepam, for which 86% of pharmacists said they never offered generics, the penetration rate is lower than 7%.

There are three main reasons why pharmacists do not regularly offer generics:

1. Approximately 78% of pharmacists said that they do not offer generics when they know or presume that a patient is reluctant to take a different drug from what is prescribed. One third of the pharmacists register the name of those who do not accept generic substitution in their patients' database, so that staff members do not continue to suggest a generic product each time they come into the pharmacy. The proportion of patients resisting substitution that is recorded is estimated at 8%, with variations from 1% to 30%, depending on the pharmacies. By being too insistent, pharmacists risk losing some of their clients or, at least, jeopardising the quality of the relationships they have so far maintained with them.
2. Under certain circumstances, generic substitution may be perceived as risky by pharmacy staff. About 35% of pharmacists said they do not offer generics to elderly patients, especially when they are poly-medicated, for fear of creating confusion. Substitution is also considered by some pharmacists as not appropriate for other subsets of the population, like infants or pregnant women. Besides, the perceived risks associated with generic substitution may depend on the therapeutic area. For instance, 12% of pharmacists indicated that they do not feel comfortable substituting products like antipsychotics or antiepileptics, which can occasionally induce a loss of seizure control or side-effects. This is especially relevant with products having a narrow therapeutic index like phenytoin, carbamazepine or sodium valproate.
3. The third factor playing a significant role in substitution behaviour is the so-called 'stock pressure effect'. When a sizeable number of packs are stocked on a pharmacy's shelves, staff are used to dispensing them first to avoid stockpiling. Direct sales by generics' suppliers to pharmacists capitalise on the stock pressure effect. Generics companies will offer attractive discounts to pharmacists provided they order the equivalent of at least two months' sales. Sometimes, when they consider that the stock turnover of certain drugs is low, pharmacists may not purchase the corresponding generics directly. Instead, they prefer small quantities of supplies from the wholesalers that can guarantee two to three deliveries per day.

Figure 2 – Generic penetration in France



Substitution rates and generic penetration for a selected number of CNS therapeutic classes. (Moving annual total – September 2004)

Source: GERS and IMS Health data, Smart Pharma Consulting

Direct purchasing and the resulting stock pressure effect will also depend on the availability of products within the portfolio of a pharmacist's regular generics suppliers. Unless the missing generic products represent an important opportunity in terms of sales and profits (ie, high stock turnover and high price) most of the pharmacists will place orders with the wholesalers. At the national level, it has been observed that the lower the number of generics marketed for a given drug, the slower and the lower is the generic penetration. Thus, while with one generic on the market, lorazepam, showing a penetration rate of 3%, bromazepam, with 14 different generics available, displays a penetration rate of 52%. When there is only one generic product marketed, the risk of being out of stock is also higher. In fact, this problem is quite frequent in the case of lorazepam.

Considering that as many as 39% of pharmacists said that they forget to offer generic equivalents to original brands, the way storage is organised within the pharmacy is also important. There are two basic approaches. The first one consists of placing the original brands and their generic equivalents side by side on the shelves, so that the employees do not forget to suggest a substitute. In general, pharmacists who actively support generics keep only minimal stocks of original brands. In the second option, certain shelves are dedicated to the storage of generics and are usually located in a convenient place, close to the counter, for easy access.

Acceptance of substitution by patients

The third key lever influencing the generic penetration rate is patient acceptance of substitution. The acceptance rate averages 65% for the least substituted CNS products, including sodium valproate, lorazepam, carbamazepine and sulpiride. The reason most often cited by pharmacists for patients' refusal to take substitutes is the fear of lower product effectiveness (55%).

According to 31% of the pharmacists interviewed, patient resistance to substitution may be triggered by differences in product and packaging design between the branded drugs and the generic equivalents. These differences may cause anxiety and confusion in patients, especially in the elderly, and occasionally result in a patient inadvertently taking two formulations simultaneously[1].

Some pharmacists have noticed that refusal to accept a substitute is slightly higher when prescriptions are issued by a specialist. From a psychological standpoint, a specialist's prescription conveys a feeling of authority which leads patients to demand exactly what is written on the prescription.

It has also been observed that patients are less reluctant to accept a generic when the original brand is prescribed to them for the first time. In such a case, they are not yet used to the brand and, moreover, cannot make comparisons.

Implications for health authorities

Under the current French healthcare system, physicians do not get any medical or economic benefits from prescribing generics, which explains their lack of involvement. The government signed an agreement with physicians in 2002 under which they agreed to write 25% of their prescriptions generically. They are far from having reached this target and the government has no intention of implementing penalties. It seems the government has abandoned, for the time being, the idea of leveraging physicians' prescriptions to boost generic penetration.

Like physicians, patients have few incentives to take generics. In fact, 92% of the French public are fully covered for the reimbursable drugs prescribed by physicians, either generics or branded equivalents. Of course, if they want to purchase an original brand whose price has not been aligned with the TFR level, they would have to pay for the difference. But this situation is still quite rare. Indeed, the government does not seem to want to act on patients to stimulate generics usage either. At the most, they may sponsor, as in the past, public campaigns to convince them to accept generic substitution by pharmacists. However, this type of initiative has not proven to be very effective so far.

To boost the market share of generics, the health authorities are concentrating all their efforts on stimulating generic substitution by pharmacists, by using the carrot and the stick approach of extra discounts and the TFR threat, respectively. However, the study of 162 community pharmacists has highlighted the difficulties pharmacists have in reaching a high substitution rate in certain therapeutic classes. As shown in Figure 2 for anxiolytics and antipsychotics, the average generic penetration is 38% and 30% respectively in volume terms, but only one third is driven by substitution. The remainder originate from generic prescriptions by physicians. In the antiepileptic class, generic penetration averages 12%, of which 42% is driven by substitution. Generics of antiparkinsonian products account for only 6% of the total and they are almost exclusively driven by physicians' prescriptions.

Thus, the objective set by the French government to reach at least 50% generic penetration, irrespective of the therapeutic class, may not be realistic, nor appropriate on medical and economic grounds. A large study carried out in the UK[2], showed that 10.8% of patients with epilepsy, who were switched, reported verified problems (ie, increased seizure frequency or side-effects). These results suggest that economic savings generated by generics could be outweighed for the person with epilepsy, because of a rise in the number of consultations and higher social costs through increased sick leave. These findings were also confirmed in a recent Canadian study[3] which estimated that switching patients from the brand name clozapine to generic equivalents would be more expensive in terms of direct costs (drug purchase and treatment of relapse) if the absolute difference in relapse incidence were greater than 11.2%.

If in the great majority of cases, generics contribute to limiting healthcare costs without creating medical complications, there are specific circumstances where substituting original brands may require particular care. Substitution could potentially alter the risk-benefit ratio of a treatment when:

- The original drug has a narrow therapeutic index (eg, phenytoin), non-linear kinetics (eg, sodium valproate), or poor water solubility (eg, carbamazepine).
- The pathological condition is severe or debilitating (eg, schizophrenia, epilepsy, Parkinson's disease, stroke, arrhythmia, etc.)
- The patient is old (eg, confused), very young (eg, is sensitive to small variations in bioavailability) or psychologically fragile (eg, anxiety).

For these at-risk situations, the French government could envisage an individualised approach. Depending on the drug, the generic penetration target could either be removed or lowered and the TFR measure excluded. In addition, to facilitate substitution by pharmacy staff and guarantee optimal safety conditions, specific substitution guidelines could be developed. Generic substitution should not be an end in itself, but remain a means to better manage drug expenditure without jeopardising individual patient care.

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