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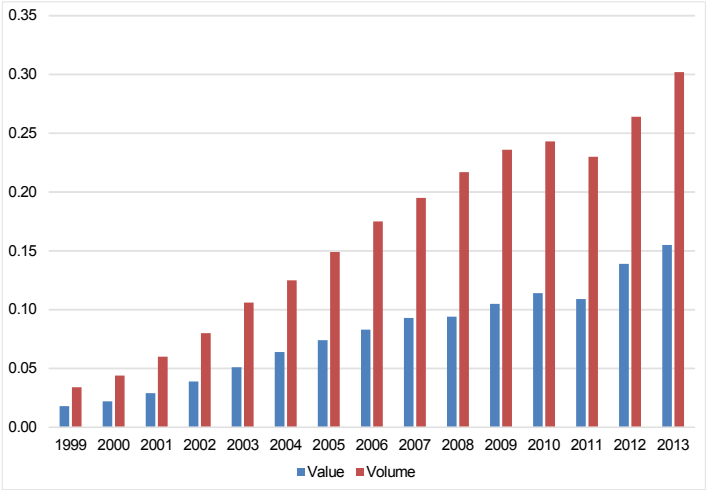
TRÉSOR-ECONOMICS

Strategies to expand the distribution of generic drugs

- When a pharmaceutical company wants to market a new molecule, it applies for a patent. The patented drug, known as the "originator" drug, is generally protected for between 10 and 15 years. After the patent expires, the pharmaceutical company no longer has the monopoly on manufacturing the drug, and can face competition from generic pharmaceutical firms. In France, whether they are made by generic companies or the company producing the originator, generic drugs must be manufactured from the same active ingredient, at the same dosage level and with the same route of administration as the originator.
- When a generic drug is introduced, it lowers prices in two ways: through the use of generic drugs that are less expensive than the originator (the regulated price for a generic is 60% lower than the initial price of the originator), and a drop in the price of the originator (an immediate regulated decrease of 20%).
- Because they offer a medical service equivalent to that provided by the originator while decreasing the cost to the national health insurance fund, generic drugs are an ideal way to curb healthcare spending.
- Certain measures encourage the substitution of generic drugs for originators (particularly the "third-party payer in exchange for generics" (*tiers-payant contre génériques*) system[1]). Substitution has become increasingly popular in recent years, and by 2014 represented 73% of the volume of drugs for which generics can be substituted, and 66% of the value. According to the Government Audit Office, these efforts brought down spending on drugs by the national health insurance fund by some €1.6bn in 2013, net of the potential savings passed on to pharmacies (€1.8bn).
- More could be done, however, to expand the use of generics. In France, generic drugs' share of total consumption of pharmaceuticals is nearly 1.6 times lower than the OECD average: the acceptable substitution rate of generics for originators (where such generics exist) is offset by the low number of prescriptions for drugs for which there are generic substitutes.
- To increase the penetration of generics and thereby generate savings, the current system could be adapted in various ways:
  - By lowering regulated prices even further, while ensuring that generic pharmaceutical companies remain viable. Various simulations result in savings of between €170m and €1bn.
  - By new incentives for physicians to prescribe more generic drugs
- Currently, two-thirds of the pharmaceutical products that are the most costly for the national health insurance fund are biologics rather than chemical drugs, and are not covered by the system that applies to generics. We therefore need to introduce a better governance framework for these drugs in order to generate the maximum possible savings when their patents expire.

Generics as a share of proprietary medicinal products eligible for reimbursement (hospital and non-hospital)



Source: Government Audit Office using ANSM data.
Note: The perimeter selected by the Government Audit Office differs from that of our study as it includes pharmaceuticals consumed in hospitals and those sold by hospitals to outpatients.

(1) Under this scheme, if patients do not accept the generic drug, they must advance the price of the originator and be reimbursed at a later date.

MINISTÈRE DE L'ÉCONOMIE
ET DES FINANCES

1. Generic drugs: definition and life cycle

1.1 Generic drugs In France: definition

When a pharmaceutical company wants to market a new molecule for a chemical drug, it may apply for a patent. The patented drug is then known as the reference medicinal product or originator. After the patent on the reference medicinal product expires, generic versions may be sold. These generics may be manufactured by the original pharmaceutical company or its competitors. A generic drug must have equivalent bioavailability (comparable absorption speed and intensity) in the human body as the originator drug, and therefore the same effectiveness.

In 1998, France created a list of groups of generic pharmaceuticals, the *Répertoire des Groupes Génériques*, which is maintained and updated by the National Agency for Medicines and Healthcare Product Safety (ANSM). It lists originators and the generic drugs that may be substituted for them by pharmacists. France's *Répertoire* is more restrictive than in other countries (where it is often based on pharmaceutical products having the same active ingredient), in that only those generics that have the same active ingredient, the same route of administration and are administered at the same dosage are listed as substitutes. Thus, substitution in France is only possible within relatively narrowly-defined generic groups.

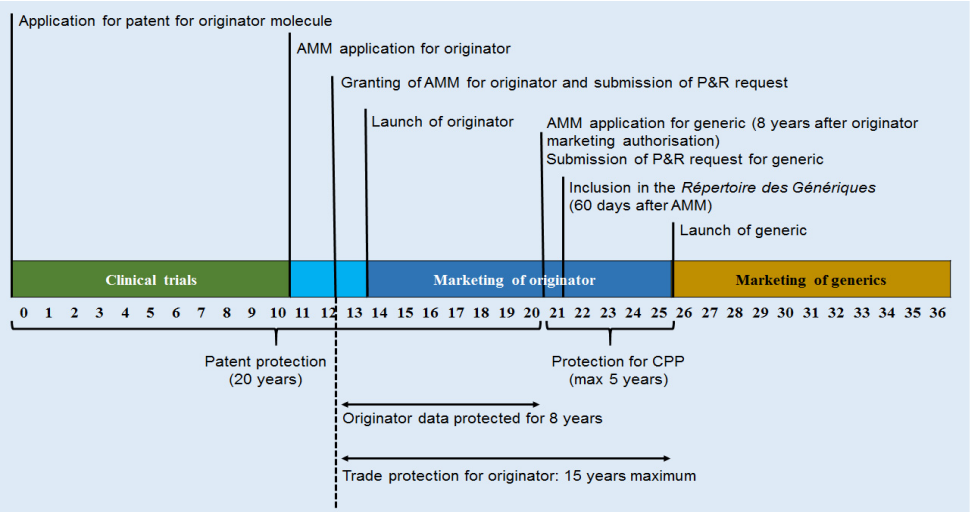
In 2014, the *Répertoire* consisted of 1,304 generic groups, of which 810 groups are eligible for reimbursement. Pharmaceutical products (both originators and generics) that are listed in one of these groups account for 29% of pharmacies' turnover[1] and 31% of social security reimbursements for drugs[2].

1.2 The life cycle of pharmaceuticals and their generics

When an originator loses patent protection (after twenty years as a general rule), it can be copied. Data concerning the originator are only protected for about eight years starting from the marketing authorisation application, in order to allow other companies to develop generic drugs to compete with the originator. Nevertheless, the end of data protection does not mean that generic pharmaceutical companies are given a "how-to manual" for assembling the drug. It merely allows them to launch research in an attempt to copy the originator.

To be able to sell generic drugs, they must first be listed in the *Répertoire*. The amount of time that an originator may be sold without competition from generics ranges from 10 to 15 years after the marketing authorisation is granted (see Chart 1).

Chart 1: General timeline for marketing generic pharmaceuticals (with a Pharmaceutical Product Certificate - CPP)



Sources: DG Trésor, AANSM and Pharmaceutical Products Monitoring Centre.

Note 1: AMM = Marketing Authorisation, CPP = Pharmaceutical Product Certificate and P&R = price and reimbursement rate by the national health insurance fund.
Note 2: In the specific case of pharmaceuticals, although the length of the patent is the same as for other manufacturing innovations, it can take up to ten years for molecules to be granted marketing authorisation. In a bid to encourage innovation, pharmaceuticals are granted a Supplementary Protection Certificate (SPC), which prolongs the life of the patent for a maximum of five years, thus extending to fifteen years the average length of time that innovations are protected.

Nevertheless, pharmaceutical companies that produce originators have developed a range of strategies to prevent loss of turnover linked to the expiry of the patents on the molecules that they have developed. These include the development of "me-too" drugs (which differ only slightly from drugs whose patent protection is about to expire, but which have the same properties), and using court proceedings to delay the entry of generics onto the market.

(1) DREES, "Les dépenses de santé en 2014", 2015.
(2) Open Médic database, 2014.

Lastly, although the procedure for developing a generic is less risky than that for an innovative pharmaceutical, it is not entirely risk-free. As it turns out, only one of four generics are granted marketing authorisations, and for an average cost of between €500,000 and €2m[3]. This is to be compared with the average cost of developing an originator, which was €780m in 2012[4]. Against this background, it is important to encourage pharmaceutical companies to copy drugs whose patents are set to expire, and thereby expanding the *Répertoire Générique*.

2. Impact of the launch of generics on the market

2.1 Marketing generic drugs leads to decreased spending on pharmaceuticals

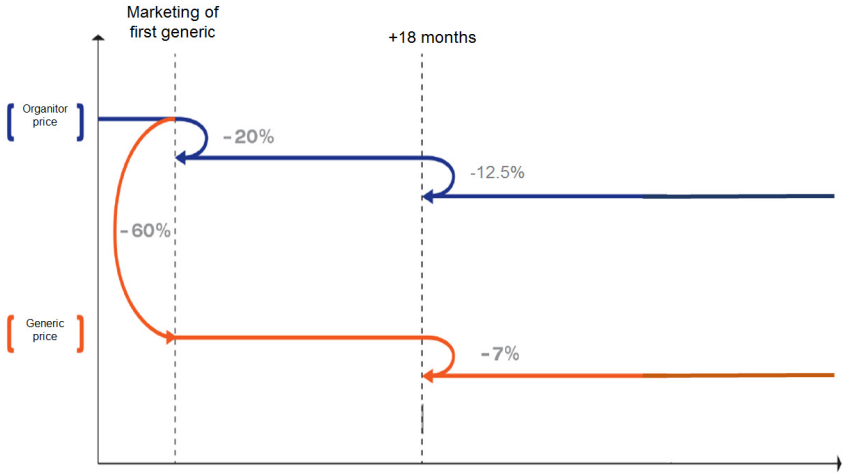
When generic drugs are brought to market, it results in savings for the national health insurance fund in two ways:

- Consumption of the originator is partly substituted by generics, whose price is generally lower (a volume effect)
- To remain competitive, the price of the originator is lowered (a price effect[5]).

2.1.1 The price effect: lower prices for originator and generics

When a generic drug is introduced, the regulated price of the originator is reduced. French regulations govern price reductions: a minimum 20% decrease when the first generic comes to market and at least another 12.5% decrease 18 months later. The maximum price for a generic pharmaceutical is also regulated (60% less than the originator price prior to the arrival of generics) and this price is also lowered after 18 months (–7%, see Chart 2).

Chart 2: Price regulation (manufacturer's price net of tax - PFHT) after the introduction of generic pharmaceuticals



Source: LEEM.

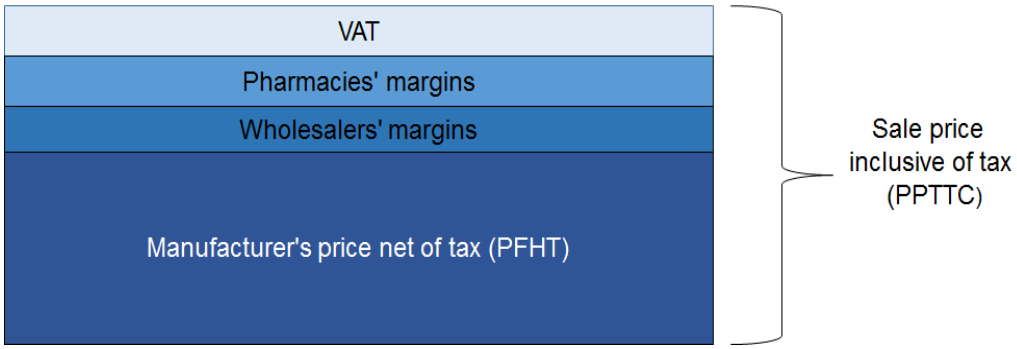
These adjustments do not apply to the sale price (either the retail price inclusive of tax (PPTTC), or the reimbursable portion of that price), but rather to the manufacturer's price net of tax (PFHT) prior to any discounts. The sale price is obtained by adding margins and VAT to the wholesalers' and pharmacies' (see Chart 3).

In practice, data for the generic groups show a drop in the PPTTC for originators, even after the wholesalers' and pharmacies' margins and VAT are taken into account[6].

Over and beyond regulated price reductions, there is a continuous decline in the price of the originator, even long after the introduction of generics, due to negotiations with the government[7]. Furthermore, the price of generics continues to fall: when the PPTTC of the originator decreases, pharmacies' margins on generics narrow as well, since the margin is based on the originator price (see below).

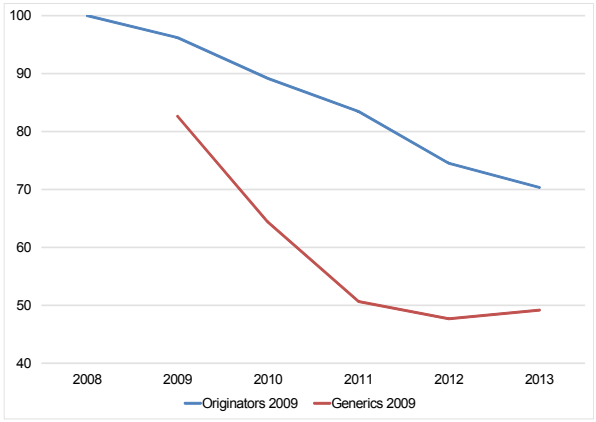
(3) Source: Medicines for Europe.
(4) LEEM, "Quel est le coût de développement d'un médicament?", 2014.
(5) Insee, "Pharmaceutical Prices, 2000-2010", 2012.
(6) This partly accounts for decreases that are less than those set out in legislation regarding the PFHT. VAT is proportional to prices (and thus has no effect on price changes) but it also applies to the wholesalers' and pharmacies' margins, which are not price-proportional.
(7) Some generics are even more expensive than the originator. In 2014, reimbursements by the national health insurance fund for generics that cost more than the originator came to €160m, which is €20m more than if the prices were equal.

Chart 3: Breakdown of the retail price of a pharmaceutical



Source: DG Trésor.

Chart 4: Average prices (reimbursable portion by quantity of substance, at constant volume) for originators and generics in generic groups that appeared in 2009

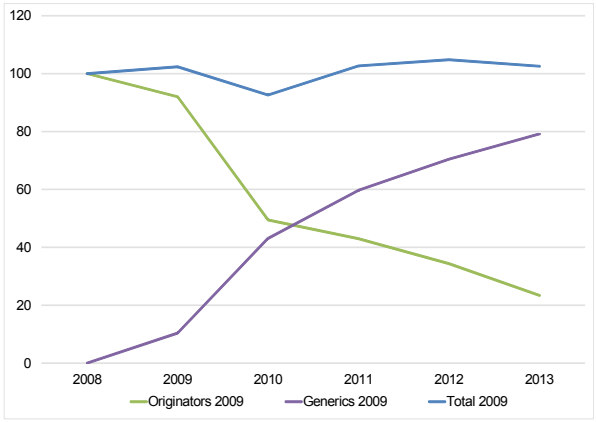


Source: Bases Medic'AM and Open Medic, DG Trésor calculations.
How to read this chart: the Y axis shows the prices of the various pharmaceuticals in base 100 = price of the originator in 2008. The effect of the arrival of generics on the market can be seen starting in 2009.

2.1.2 The volume effect

Due to measures introduced to encourage the use of generics (see below), average consumption grows quickly after generic drugs are introduced, even surpassing consumption of the originator. During the same period, consumption of the originator falls off sharply (see Chart 5).

Chart 5: Average consumption (quantity of substance sold by generic group, in base 100) of originators and generics in generic groups that appeared in 2009

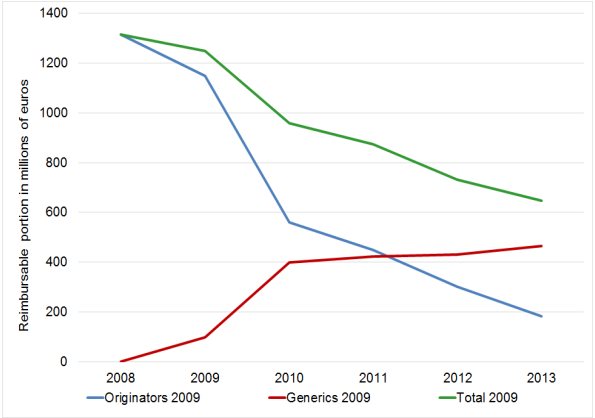


Source: Bases Medic'AM and Open Medic, DG Trésor calculations.

2.1.3 Decreased expenditure is the result of both price and volume effects

The reimbursable portion of the price of originators for which generics were marketed in 2009 decreased by 75% between 2008 and 2013, and the total reimbursable portion for the generic groups (originator plus generics) fell by half. The decrease cannot be attributed to obsolescence, as consumption volumes remained unchanged.

Chart 6: Value of consumption of originators and generics in generic groups that appeared in 2009



Source: Bases Medic'AM and Open Medic, DG Trésor calculations.

2.2 Nearly two decades' worth of measures to increase the penetration of generic drugs

In addition to establishing a list of generic drugs and giving pharmacists the right to substitute generics from that list in 1999, several measures have been introduced to encourage the use of generics.

2.2.1 Actions with respect to pharmacies

Three approaches were tried to encourage pharmacists to substitute generic drugs for originators:

- The fact that pharmacies' margins increased with the manufacturer's price net of tax (PFHT)[8] did not encourage them to substitute generics for the originator, since the latter was generally more expensive and therefore generated a higher margin. Since 1999[9], pharmacies' margins on a generic are generally the same as for the originator.
- *Rémunération sur objectifs de santé publique* (ROSP), a pay-for-performance scheme has successfully

encouraged more substitutions for originators. The scheme rewards pharmacists based on the rate of substitutions recorded in their pharmacies. For most compounds, the bonus is based on a rate of about 75%, and increases up to the target substitution rate of 85%[10]. In 2013, pharmacies earned an average of €6,000 under ROSP, for a total cost to the national health insurance fund of €135m.

- Discounts (also known as back margins) may be granted by pharmaceutical companies based on the PFHT for generics or originators. In a bid to encourage pharmacists to increase their margins by selling generics, the maximum allowable discounts for generic drugs are higher than those for originators. Since 2014, the gap between these two types of discounts has widened: discounts based on the PFHT for generics can reach as high as 40% (against 17% previously) compared with 2.5% for originators.

Although these measures directed at pharmacies have boosted the consumption of generics, they are costly for the government, since they reroute a portion of the potential savings from generic substitution to private-sector professionals. According to The Government Audit Office, measures aimed at pharmacists to promote the consumption of generics cost a total of €1.75bn for the year 2013 alone, which represents roughly half of the potential savings.

Table 1: Financial benefits to pharmacists following the introduction of measures to promote generics (2007-2013)

Measure	2007	2008	2009	2010	2011	2012	2013
Equalising margins	203	248	271	339	351	368	451
Pay-for-Performance scheme (ROSP)	–	–	–	–	–	73	135
Back margins (discounts)	Unknown	291	314	351	361	410	467
Commercial services	Unknown	Unknown	Unknown	Unknown	Unknown	600	700
Total	203	539	585	690	712	1,451	1,753

Source: Government Audit Office, "La diffusion des médicaments génériques : des résultats trop modestes, des coûts élevés", 2014.

Note: Commercial services = To gain access to the non-hospital pharmacy market, pharmaceutical manufacturers have developed "commercial cooperation" or "compensation for services" schemes, which consist of hidden back margins (investigation by the offices of the Directorate General for Competition Policy, Consumer Affairs and Fraud Control (DGCCRF) in 2013). The DGCCRF has qualified this as an anti-competitive practice.

2.2.2 The Tarif Forfaitaire de Responsabilité (TFR)

Medicinal drugs with a low generic penetration rate may be assigned a single reimbursement rate, known as the *Tarif Forfaitaire de Responsabilité* (TFR). This rate is calculated based on the price of the least expensive generics. In return for implementing the TFR, pharmaceutical companies are free to set their own prices. If patients refuse a generic drug because they prefer a brand-name product or a higher-priced generic[11], they will be reimbursed on the basis of the TFR.

This measure has generally brought the prices for originator and generics into line with the TFR, but without radically altering their respective market shares[12]. As it turns out, when a TFR is introduced, the prices for originators and generics tend to fall into line with the TFR. Lower prices for originators generally do not increase their market share: patients who are accustomed to take a generic drug rarely change their behaviour due to prices becoming more equal.

This measure also changes the maximum back margins given to pharmacies by the manufacturers of originators (capped at 2.5% of the PFHT). The law states that if the sale price is identical, the allowable discount should be identical[13]. In this way, originators can also generate back margins of up to 40% of the PFHT, and generic drugs thus lose their main competitive advantage.

Since 2003, (when the first round of TFRs was rolled out), the number of generic groups assigned a TFR increased by 17% per year, such that by 2014 there were 400 such generic groups. These accounted for 31% of total generic groups, or 5% of the total turnover generated by pharmacies on pharmaceuticals[14].

2.2.3 The "tiers-payant contre génériques" system

The "third-party payer in exchange for generics" (*tiers-payant contre génériques*) system has been in widespread use since July 2012. Under this scheme, third-party payment is granted only if a patient agrees to accept a generic instead of the originator (with the exception of those listed as non-substitutable on the prescription form).

This initiative appears to have been particularly effective in increasing the market share of generic drugs. The substitution rate (in numbers of boxes) amongst the generic groups already on the market in 2011[15] rose from 65% to 79% between 2011 and 2014.

(8) With a degressive rate: the pharmacist's margin increases with the PFHT, but not proportionally.
(9) "Order of 28 April 1999 relative to margins on pharmaceutical drugs reimbursed by the national health insurance fund"
(10) More specifically, a substitution rate was set for 26 compounds listed in an amendment, with goals ranging from 45% to 90%. Most were in the 80-85% range.
(11) CNRS, "Tarif forfaitaire de responsabilité : quels impacts sur le pharmacien", 2013.
(12) Source: Discussion between DG Trésor and GEMME in July 2016.
(13) Article L138-9 of the Social Security Code, amended by the 2014 Social Security Budget Act.
(14) DREES, "En 2014, la décroissance du marché de ville des médicaments remboursables hors rétrocession se poursuit mais faiblit", 2015.
(15) We should differentiate between the full set of generic groups and those already present on the market in 2011, since the appearance of new generic groups automatically lowers the penetration rate in the first year.

2.2.4 Actions with respect to physicians

When it comes to physicians, measures have primarily focused on getting them to change their prescribing habits:

- Physicians may, for reasons strictly having to do with the patient (such as an intolerance to certain excipients), prevent pharmacies from substituting a generic for a prescribed originator. To do so, they can write "may not be substituted" on the prescription. Physicians who overuse this option can be summoned by the local national health insurance office, or even penalised. The effect is primarily dissuasive, since penalties are rare.
- The goal of the International Nonproprietary Name (INN) is to clear up confusion about pharmaceuticals with similar active ingredients but whose trade name varies. In France, the use of the INN has been mandatory since 2015, forcing physicians to no longer prescribe the originator and theoretically encouraging the prescription of generics. However, there is a great deal of non-compliance: in 2015, 73% of prescriptions had only the brand name[16].

2.3 The impact of adopted measures on the consumption of generic drugs

Partly due to measures put in place from the late 1990s, generic drugs now account for a growing share of reimbursable pharmaceutical drugs sold in pharmacies.

Generics' share of total consumption of pharmaceutical drugs increased continuously between 2008 and 2014 (the market share of generic groups in the reimbursable drugs market outside of hospitals and excluding drugs sold by hospitals to outpatients) rose from 22% to 33% in value and from 31% to 46% in volume due to the arrival of new generics on the market and the higher rates at which generics were substituted for originators.

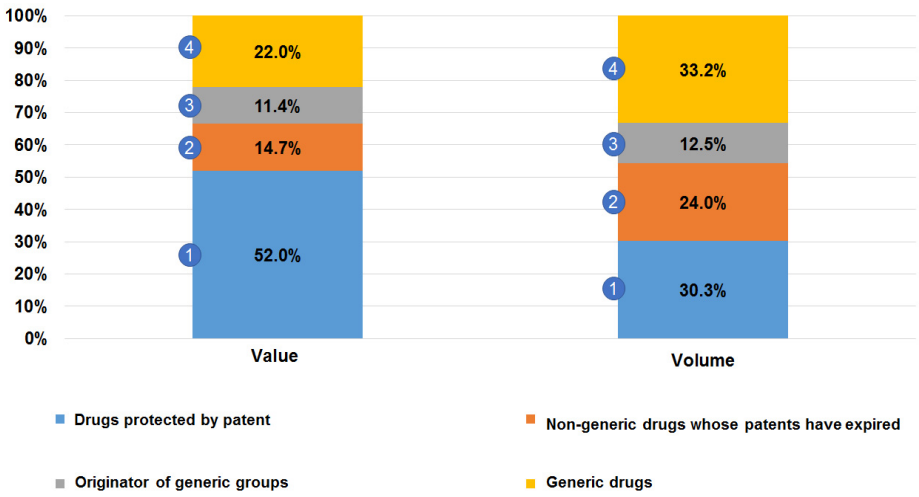
Thus, within the generic groups, the share of generics in relation to originators increased:

- For 2014, the substitution rate for generics (the ratio between zone (4) in Chart 7 and the sum of zones (3) and (4) was 73% in volume and 66% in value
- On a like-for-like basis[17] (generic groups in existence in 2008), the substitution rate for generics rose sharply between 2008 and 2013, increasing from 69% to 84.5% (in numbers of boxes).

According to The Government Audit Office, generics generated savings of €3.3bn in 2013. These savings, which have resulted in lower earnings for pharmaceutical companies, were primarily shared out between the national health insurance fund and pharmacies (roughly 50%), resulting in net savings of €1.6bn for the national health insurance fund in 2013, and €12.1bn since 2002[18].

Nevertheless, due to France's restrictive guidelines governing the constitution of generic groups, two-thirds of the pharmaceutical market (in value, see zones (1) and (2) in Chart 7) consist of drugs that do not belong to any generic group. At the same time, nearly 15 % of the refundable portion of drugs concerns products whose patents have expired but which were not, as of 2014, part of any generic group (see zone (2) of Chart 4 – total amount refunded: €2.5bn)[19].

Chart 7: Percentage of the refundable portion and the number of boxes of generic drugs in pharmacy sales of reimbursable drugs in 2014 (excluding drugs sold by hospitals to outpatients)



Source: DG Trésor calculations based on the Open Médic Database.

Note: The number of non-generic drugs whose patents have expired is probably underestimated due to the methodology used to determine patent expiration dates (see below). Their share fluctuates depending on the expiry of patents and the arrival of new generics on the market.

(16) UFC Que Choisir, "Enquête sur la prescription en DCI", 2016.
(17) As mentioned above, it is important to separate out specific and set groups of generics to be able to assess the penetration rate, since the arrival of new generic groups brings down the overall penetration rate.
(18) Government Audit Office, "La diffusion des médicaments génériques : des résultats trop modestes, des coûts élevés", 2014.
(19) DG Trésor calculations. Less than the actual figure, since it was based on a conservative hypothesis concerning the length of patent protection.

Box 1: **Savings in the area of drugs also have an impact on the generic pharmaceutical industry**

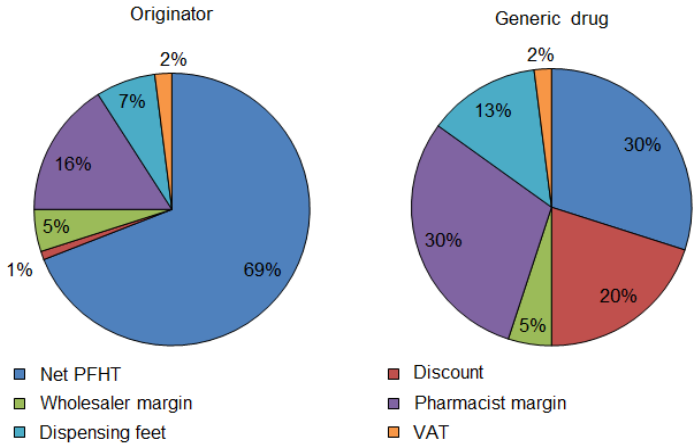
For the period 2013-2015, price decreases for all drugs sold in pharmacies (regardless of origin) brought down reimbursement expenditure by nearly €2bn[a]. Price decreases for generic drugs accounted for 28% of this amount, even though they represented only 22% of the reimbursable expense.

Savings measures relating to pharmaceuticals achieved as part of the national healthcare expenditure growth target (ONDAM) have thus had a significant impact on the margins of generic pharmaceutical companies. In 2013, their margin was 1.4%, compared with 3.1% in 2010[b]. By comparison, the margins of the ten main producers of originators varied little during the same time-frame (20.3% in 2013, against 20.0% in 2010).

A breakdown of the PPTTC of originators and generics gives a better idea of the economic models of these two types of pharmaceuticals. Although the PFHT net of discounts accounts for nearly 70% of the PPTTC for an originator, this figure is only 30% for a generic drug, an important share of the price of which goes to pharmacies.

Thus, even though the price of generics may seem high in France[c], this appears to be the result of mechanisms that bring about a sharp gap between the PPTTC and the PFHT net of discounts (particularly due to payment to pharmacists). If we compare the PFHT net of discounts for generic drugs in France, the UK and Germany[d], (based on the PHFT net of discounts per standard unit on a like-for-like basis – same molecule, same route of administration and same dosage) we can see that the PFHT net of discounts in France is 43.4% lower than in Germany and 2.8% lower than in the UK.

Chart 8: Breakdown of the PPTTC (sale price inclusive of tax) for a generic drug and an originator



Source: GEMME calculations.

Note: calculation based on a generic speciality whose PFHT is equal to the average PFHT (about €3.90), this PFHT was calculated with a 60% discount over the PFHT of the reference medicinal product (orginator PFHT = €9.75), by applying margin rates and maximum discounts as defined by various pieces of legislation.

a. CEPS, "Rapport d'activité 2015", 2016.
b. Source: Infogreffe (online commercial court registries).
c. CNAMTS, "Coût des génériques en Europe et mécanismes de régulation des prix en Allemagne, en Allemagne, en Angleterre et aux Pays-Bas", 2012.
d. IMS Health, "Le marché pharmaceutique en France et dans le monde : bilan 2011 et perspectives", 2013.

3. Possible reforms to build generic drugs' potential

Despite a series of initiatives designed to increase consumption of generics, it appears that the model in which the pharmacist plays a key role has nearly reached its limits. The French market now enjoys a very healthy substitution rate, even though other OECD countries have a higher share of generics in total consumption of pharmaceuticals.

France is in 20th place in terms of the market share of generics in numbers of boxes sold (29% of total consumption, against an average of 48% in the 26 OECD countries for which we have data). In value terms, the situation is the same: France ranks 19th (16% of total consumption, compared with a 26-country average of 24%). Nevertheless, care should be taken with these figures, since they conceal certain disparities.

Lower consumption of generics in France compared with other countries can be attributed to two main factors[20]:

- Sometimes, certain patients do not trust generic drugs.
- In France, the way drugs are prescribed encourages the use of new medicines. On average, only 40% of prescriptions concern pharmaceuticals listed in the *Répertoire des Médicaments Génériques* (both originator and generics), whereas new drugs account for 60% of prescriptions. In other European countries, these proportions are inverted, and in Germany, generics account for nearly 80% of prescriptions[21]. This is the primary roadblock to increasing the market share of generics in France.

These international comparisons indicate that there is still work to be done in France to derive greater savings from generic drugs. A model in which physicians are encouraged to prescribe generic drugs appears to be more effective, as we can see in Germany. However, since the necessary infrastructure that gives pharmacists a central role in the distribution of generics has been put in place, our goal here is not to fundamentally overhaul the model, as this would encounter strong resistance from both physicians and pharmacists.

(20) GEMME, "Mention Non-Substituable : La CNAM va lancer une campagne ciblée", 2014.
(21) GEMME, "Les opportunités de développement du marché des médicaments génériques et biosimilaires", 2016.

Box 2: **Methodology used for measuring the effects of various measures related to pharmaceutical prices**

Using the health insurance databases (Open Médic and Medic'AM) and administrative data derived from the French National Agency for Medicines and Healthcare Product Safety's database of medicinal products, we simulated the effects of changing various parameters in the rules governing reimbursements by the national health insurance fund. The model used to calculate the first three measures is based on an analysis of consumption of pharmaceuticals in 2014 and their prices. It can be used to accurately simulate the impact on the budget of a change in regulated prices. On the other hand, however, it does not address the behavioural effects that such changes could bring about. Such effects appear to be limited, since they lead to only very small variations in the non-reimbursable amounts that patients must pay.

The first three measures described below involve determining which drug is the least expensive (within a generic group or group of pharmaceutical products with the same molecule). The value of this method of calculation is that it allows us to define the price per ml or mg of active ingredient in order to factor in the existence of various forms[a], rather than using the standard indicator of numbers of boxes. The price used is thus the lowest price per mg/ml of the active ingredient per generic group or group of pharmaceutical products with the same molecule (ATC5[b] code).

To simulate an expansion of the *Répertoire*, one needs to know the drugs that are no longer patent-protected. Given the lack of readily-available patent data[c], we need to make assumptions about drugs that are still under patent. To avoid overestimating the savings resulting from redefined prices for originators and generics, we conservatively estimated that a drug is protected for 17 years after being granted marketing authorisation[d].

Definitions:

The TFR sets a maximum rate that the national health insurance fund will reimburse patients for. This rate applies to all pharmaceutical drugs in the same generic group (originator and generics). This price equalisation supposes that the back margins (discounts) that pharmaceutical companies producing originators and generics may provide to pharmacies are equal (40%).

Rate convergence is equivalent to bringing prices for originators and generics closer together, without necessarily making them equal, and thus allowing for different discount rates (2.5% for originators and 40% for generics).

a. This involves, for each drug, determining the dosage of the active ingredient for each unit (tablet, tube, millilitre, etc.) to obtain the total quantity of the active ingredient. The price is then divided by this total quantity.
b. The WHO's Anatomical Therapeutic Chemical (ATC) Classification System uses five levels of classification, starting with the anatomical main group (with 14 categories, such as the digestive system or central nervous system) and ending with the chemical substance, which is classification level ATC5.
c. The French Patent Office (Institut national de la propriété industrielle) has a nationwide patent database, but it entails entering drug names one by one, which renders it impractical for the purposes of this study.
d. LEEM, "Le brevet et la marque, deux précieux sésames", 2006. This studyindicates an average of 15 years after the marketing authorisation is granted.

3.1 Taking action concerning the price of generics

As France is lagging behind other advanced countries, there is great scope for improving the penetration of generics. Nevertheless, it is important to ensure that these new measures do not threaten generic pharmaceutical companies – which provide positive pressure on prices – by, for example, putting too much strain on their modest margins (see Box 1).

Without generic pharmaceutical companies, negotiations to lower the price of originators would be much more complex for the public authorities.

Four measures are considered below. The first three involve greater price decreases after patent expiry, using three different mechanisms. The fourth consists of adjusting regulated price decreases for generics that are currently too expensive to produce to be profitable.

*3.1.1 **Measure 1:** Converging prices for originator and generics as soon as the patent expires*

As seen above, when the first generic comes onto the market, its price is set at a maximum of 40% of the originator price prior to the arrival of the generic, while the price of the originator is set at 80% of its original price. In a bid to bring about faster price decreases while giving generic pharmaceutical companies a competitive advantage[22], one could cut the price of the originator further and thus converge its price with those of the generics as soon as the first generic is marketed, while maintaining a 10% surcharge for the originator. Given this difference and due to regulations, these drugs would not be sold with the same discount (back margin) as for generic drugs, which means that generic pharmaceutical companies would be able to enter new markets.

This reform would primarily have an impact on:

- All pharmaceuticals listed for at least eighteen months in the *Répertoire* as of 2014 to which TFRs have not already been applied
- All pharmaceuticals listed for less than eighteen months in the *Répertoire* as of 2014

Introducing such a reform would – assuming the consumption of the various pharmaceuticals remains unchanged – cut reimbursements by the national health insurance fund by some €635m. To keep the price convergence from encouraging patients to refuse generics because they think they are of lower quality[23], thereby weakening generic pharmaceutical companies, a test phase should be carried out prior to implementation.

*3.1.2 **Measure 2:** Systematically assigning a TFR to all generic groups after three years*

Another way to generate savings would be to systematically assign TFRs. In contrast to the previous hypothesis, this measure would eliminate the 10% surcharge for originators and thus reduce healthcare spending a little further. Nevertheless, if this was done immediately after patent expiry, there would be a risk that some generic pharmaceutical companies would not survive, as there would be no incentive for pharmacists to substitute generics for originators.

To avoid this, TFRs could only be assigned across the board three years after generic drugs in the group enter the market.

(22) When prices are equal, consumers tend to prefer the brand name drug.
(23) Caucheteux L., "Les moteurs et les freins au développement des médicaments génériques", 2011.

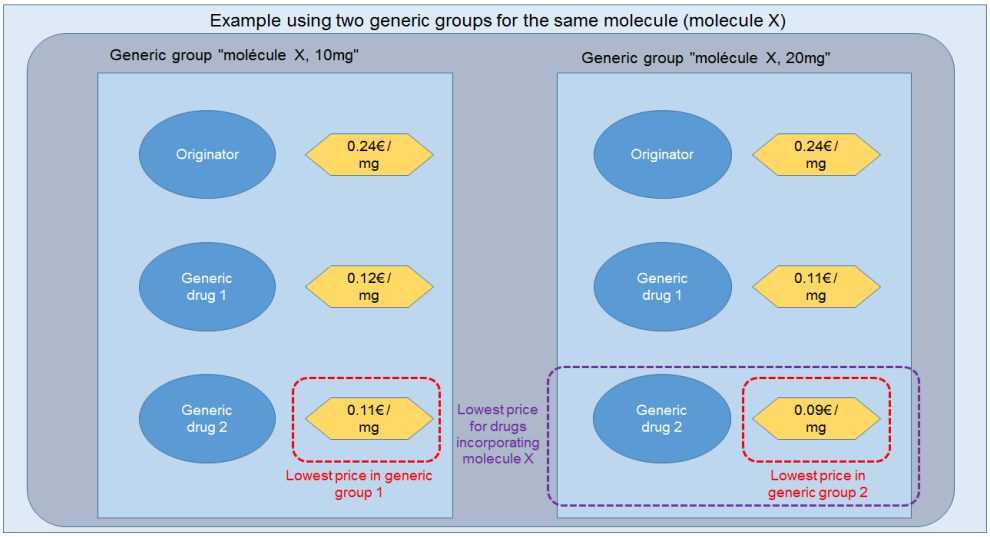
This would allow generic pharmaceutical companies to enter the market, since the assignment of a TFR in an existing market does not erode the market share of those companies (see above). This time lag would thus neutralise the harmful impact of the TFR. Currently, only 49% of generic groups that contain reimbursable pharmaceuticals are the subject of TFRs, which means that these measures could be continued.

This reform would then affect all pharmaceuticals listed for more than three years in the *Répertoire* as of 2014 to which TFRs have not already been applied. Such a measure would result in some **€170m** in savings, calculated on a 2014 basis. This lower figure is due to the lower number of drugs affected by the reform (27% of dosage forms belonging to a generic group, compared with 70% in the first option), since a large portion of patents expired between 2011 and 2014. Some of the savings associated with this measure would also occur in subsequent years due to the three-year time lag.

*3.1.3 **Measure 3:** Three years after a patent expires, set drug prices on the basis of the lowest TFR within an expanded perimeter (ATC5)*

Since there are a large number of pharmaceutical products whose patents have expired, but for which there are no generics available, one could set the price of drugs whose patents are about to expire using a larger basis than that of the current generic groups. Thus, drug prices could be determined on the basis of lowest-priced drug amongst drugs made from the same molecule, rather than merely those in the same generic group (see Chart 9). Even if this were done, the criteria would remain stricter than those applied in other European countries such as the UK and Germany[24].

Chart 9: Example of setting a price based on the least expensive pharmaceutical in the same generic group vs. the least expensive drug made from the same molecule



Source: DG Trésor.

To prevent too great a shock to the pharmaceutical market, this measure could be applied only to the drugs whose patent had expired more than three years earlier. It could take the form of a price convergence while maintaining a difference between originator and generics, in the same way as in the first measure. This would lead to the creation of a "List of Reference-Rated Molecules", which would contain details of drugs whose active ingredient is no longer patent-protected, and for which prices (per mg of active ingredient) are similar.

For health safety reasons of, substitution can be carried out only on the basis of the speciality (same molecule / same route of administration / same dosage), this principle would not be called into question. This would result in a two-level scheme: on the one hand a reference price for drugs whose patents have expired more than three years earlier and, on the other hand, a substitution reference list for drugs in the same generic group.

The resulting savings from such a measure would be significant: some **€1.015bn**, or nearly 5% of pharmacy purchases of reimbursable drugs (excluding drugs sold by hospitals to outpatients) and would break down as follows:

- The alignment of prices for non-generic drugs: €725m. This would only concern drugs whose patents have expired more than three years earlier.
- The alignment of prices between different generic groups: **€290m**. This amount is comparable with the second measure, but would have a much greater impact due to the fact that it would take into account the lowest price amongst all generic groups with the same molecule, rather than the lowest price within individual groups (see Chart 9).

(24) Government Audit Office, "La diffusion des médicaments génériques : des résultats trop modestes, des coûts élevés", 2014.

3.1.4 ***Measure 4:*** *Expand the* Répertoire *by more modest price decreases for generic drugs that are the most expensive to produce*

Some drugs for which patent protection has expired have not been copied. For some of these, manufacturing generics is not profitable after regulated price adjustments are applied. In this case the originator remains the only drug of its kind on the market.

Some dosage forms (such as effervescent tablets) are too expensive to produce when the price is 60% lower than that of the originator. The same is true of some active ingredients for which development costs are too high and the number of patients is limited. The GEMME estimates that these drugs accounted for **€1bn** in health insurance expenditure in 2014.

If legally-required price decreases are found to be not viable, one could imagine a second price decreases process could be used. This would involve a 20% price decrease, for example, for groups in which no generic appears within a certain period of time, say three years. This would generate savings of some €200m over time, thanks to the inclusion of these drugs in the *Répertoire*.

3.2 Encouraging prescribers

3.2.1 ***Measure 5:*** *Boost incentives to get physicians to prescribe generics*

a) Through the use of the International Nonproprietary Name (INN) on prescriptions

There is little compliance with the current obligation to use the INN (see above) in prescriptions. Since this measure brings about an important change in physicians' prescribing habits, support should be provided.

There are several ways to do this, including:

- During the initial training for new doctors, a special training course solely on using the INN for prescriptions, and not the brand name
- A change in regulations governing prescribing softwares which would prevent users from deactivating the function that automatically changes the brand name to the INN (thus displaying both names)
- Increased controls by national health insurance offices of the use of INNs on prescriptions

b) Through the ROSP for primary care physicians

The Pay-for-Performance scheme (ROSP), which also exists for physicians, represents a non-negligible share of income earned by generalists (7.5% in 2014, or an annual average of some €6,000). Currently, only 22%[25] of objectives have to do with the prescription of generic drugs, and are only concerned with certain classes, with a maximum annual compensation of €2,030. To encourage the prescription of generic drugs, it would be useful to introduce a single indicator for the share of prescriptions by physicians within the Répertoire.

c) Via financing arrangements for Maisons de Santé Pluriprofessionnelles

Maisons de Santé Pluriprofessionnelles (MSP) are multidisciplinary health centres that serve rural areas. Public funding is available for their regional expansion. In return for this financing, however, MSPs have no corresponding obligation with respect to their medical activities.

A portion of their public funding could be granted in return for compliance with a target prescription rate for drugs listed in the *Répertoire*. This measure, if carefully implemented, could generate savings: spending on pharmaceuticals would decrease if MSPs meet their objectives (if not, funding for the establishment where the prescribing physician practices would be rolled back).

Such an arrangement would be all the more incentivising as a failure to meet the objective by a single physician would penalise all of his or her colleagues in the same MSP. Nevertheless, it is important to ensure that such a measure does not hamper the development of MSPs, which address specific needs (such as the rural exodus of physicians).

3.3 Other measures

3.3.1 ***Measure 6:*** *Stepped-up marketing authorisation processes*

Although pharmaceutical companies are generally primed to launch their products as soon as the patent on the originator expires, they are often hampered by the National Agency for Medicines and Healthcare Product Safety's failure to issue marketing authorisations in a timely manner. The French Pharmacists' Association[26] confirms this observation, noting that the average time-frame for obtaining marketing authorisation in France was 300 days in 2014, whereas European regulations stipulate a 180-day maximum.

This lengthy time-frame delays the marketing of generics (and prevents prices from coming down), thus diminishing the savings that they produce.

The GEMME[27] estimates that some €125m in savings was lost in both 2014 and 2015 due to these holdups (largely dependent on the patent expiration dates).

(25) CNAMTS, "ROSP médecins traitants", 2015. Five objectives out of 29 in all.

(26) French Pharmacists' Association, "Médicaments, dispositifs médicaux, compléments alimentaires : quelles sont les règles applicables ?", 2014. This figure includes both generic drugs and originators. There does not appear to be statistics for generic drugs alone.

(27) Source: Discussion between DG Trésor and GEMME in July 2016.

4. A framework for developing biosimilars must be quickly put in place

In 2015, 13 of the 20 top-selling drugs (pharmacies and hospitals combined)[28] were biologic medicines. By 2019, the patents on 13 of these drugs will expire, thus opening up a €2.5bn market in "biosimilars". This could represent a significant source of savings for the national health insurance fund.

Even though their situations are fairly similar, the rules governing chemical drugs do not apply to biological ones[29]. Biologics are drugs that are produced or derived from living organisms; vaccines are the best-known examples of biologics. Much like generic drugs, biosimilars are copies of biologics whose patents have expired. Biosimilars must have similar physicochemical and biological properties, as well as the same active ingredient and dosage form, as biologic originators. Moreover, they must have the same safety and effectiveness.

Current legislation allows biosimilars to be substituted for biologics only at the start of treatment, and not after treatment has begun[30]. Nevertheless, it is possible that this perimeter could be expanded without added risk for patients[31], provided that certain precautions are taken (clinical monitoring during treatment, product traceability, etc.).

It is more expensive to develop biosimilars than generics, since the process requires a wider pool of volunteers, which nearly doubles the development time (7 to 8 years, compared with 3 to 4 for generics). A stable and fair legal framework is needed for companies producing biosimilars (maximising savings, to be shared equally between the national health insurance fund, manufacturers and healthcare professionals). It appears that the price of biosimilars can only be lowered by an average of 25%, as opposed to the 70% decrease for generics[32].

To generate these savings, a model for distribution of biosimilars needs to be set. Whereas pharmacists, more so than physicians, play a central (and sometimes debatable) role in the development of generics[33], a different approach would probably be needed for biosimilars – one that is more focused on physicians, who would prescribe only molecules and not brand names. Prescription targets concerning the list of biosimilars would complete this scheme.

Daniel CABY, Jean-Denis ZAFAR

(28) Among the 10 pharmaceuticals generating the highest turnover in pharmacies and the 10 generating the highest turnover in hospitals. Source: GEMME, "Les opportunités de développement du marché des médicaments génériques et biosimilaires", 2016. The figure of €2.5bn comes from the same source.
(29) ANSM, "Médicaments biosimilaires - Point d'information", 2011.
(30) Article L5125-23-2 of the Public Health Code.
(31) ANSM, "État des lieux sur les médicaments biosimilaires", 2016.
(32) Académie de médecine, "Observations et propositions sur le coût des nouveaux traitements et solidarité nationale", 2016.
(33) Government Audit Office, "La diffusion des médicaments génériques : des résultats trop modestes, des coûts élevés", 2014.

Counterpoint by... Brigitte Dormont

The national health insurance fund's accounts reveal that the growth in healthcare spending has been slowing since 2003, and especially after 2012. The policy pursued since the end of 2012 seeks to maintain social security coverage while achieving efficiency gains. The data from recent years are interesting, since they show that the national health insurance fund was able to "absorb" costly medical innovations – such as Sofosbuvir, which has a 90% success rate in treating hepatitis C – without ballooning total expenditure. This was made possible through efforts to rein in the price of pharmaceuticals and develop generics.

Expenditure efficiency is critical, because it can generate resources to finance widespread access to major healthcare innovations. And yet, much more progress could be made in France to increase the consumption of generics. Data from the OECD show that the share of generics in reimbursable drugs was 83% in the UK, 80% in Germany and only 30% in France in 2015.

This article focuses on measures that could boost the distribution of generics in France, but also result in savings thanks to price reductions. There are four main stakeholders: on the supply side there are the manufacturers, along with the issue of the length of patent protection for originators, the problem of pseudo-innovations – the so-called "me-too" drugs that extend patents without offering any real new therapeutic benefit – and the prices that need to be high enough to encourage generic pharmaceutical companies to enter the market. On the demand side there is the prescribing physician, the pharmacist and the patient. In France, government actions focused on pharmacists, with incentives to replace originators with generics from a pre-defined list. This policy has run its course, due to the cost of the incentives and the limited perimeter of the list of generics, which accounts for France's lagging behind.

To prevent me-toos from hindering the development of generics, physicians must comply with the obligation to prescribe using the International Nonproprietary Name (INN). Action should also be taken to make patients more responsible, by making the single reimbursement rate, or Tarif Forfaitaire de Responsabilité (TFR), systematic and expanding its perimeter beyond the confines of the Répertoire. The alignment ofprices through the TFRs provides information on the effects of a market for products of identical quality. Patients would thus have access with complete coverage to the molecule that meets their needs, but would have to pay the difference if they wanted a me-too instead, or if their physician refuses to prescribe using the INN. Hopefully, the interest of patients would affect physicians' behaviour.

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