

Analysis of the Impact of Drug Delisting in France between 2002 and 2011

Sylvain Pichetti, Catherine Sermet (Irdes)

Between 2002 and 2011, the continuous increase in pharmaceutical expenditures prompted the public authorities to delist drugs with low therapeutic values. Of the 486 drugs considered inefficient in terms of medical services rendered (SMR, 'service médical rendu') still on the market in March 2011, 369 were delisted whereas 117 are still reimbursed, for the majority at the rate of 15%.

These successive waves of drug delisting have an immediate impact on drug prescription rates for the pharmaceuticals concerned, resulting in a significant drop in sales volumes. The subsequent increase in over-the-counter sales of delisted drugs for self-medication purposes does not compensate for sales volume loss. Patients who continue to take these drugs are faced with an average 43% price increase shortly after delisting.

An evaluation of delisting measures must equally take into account the tendency towards prescribing substitute classes of therapeutic drugs that are still reimbursed. If the substitute drugs are inappropriate from a medical point of view, the consequences both in terms of public health and National Health Insurance savings can be damaging; the greater the tendency toward prescribing reimbursable therapeutic alternatives, the lower the savings.

If drug delisting produces immediate savings, its long-term effectiveness can be put into question and would benefit from being accompanied by piloting tools enabling the impact of future exclusions from the reimbursable drugs basket to be anticipated and monitored.

In France, as in the majority of European countries, pharmaceutical expenditures are continuously increasing. Between 2005 and 2010, expenditures rose by 12.3%, increasing from 30.7 to 34.4 billion Euros¹. This regular increase in pharmaceutical spending prompted the public authorities to implement a series of measures aimed at either reducing the use of drugs or reducing its cost. Increasing patients' financial participation by delisting drugs with an insuffi-

cient or low therapeutic value is one of the methods commonly used.

The benefits of this type of measure for the public authorities is that it produces immediate, quantifiable savings on the therapeutic classes of drugs no longer reimbursed by public health insurance. The impact of these measures should, however, be analysed taking into account much broader consequences than simply measuring their impact on prescription

and consumption rates for the delisted drugs concerned. An analysis of international literature shows that an increase in patients' financial participation is effectively associated with a reduction in expenditures for the drug in question but can also lead to poorer observance, interruptions of treatment and an increase in the use of other medical services such as hos-

¹ <http://www.ecosante.fr>

Insert 1

Medical service rendered (SMR) and drug reimbursement rates

The drug reimbursement rate applied by National Health Insurance is directly dependent on a drug's medical service rendered (SMR) fixed by the French High Authority for Health (HAS) according to the severity of the disease in question on the one hand and on the other, data relating to the drug in question (effectiveness, adverse effects, its place in terms of therapeutic strategy, existence of therapeutic alternatives, its interest in terms of public health). Over the last few years, the weight of the criteria on which the definition of SMR is based has changed (Bouvenot, 2011). Initially, the disease severity criterion was almost always translated into a high SMR. The drug effectiveness criterion now has more and more weight to the detriment of the severity criterion that today has less importance. A pancreas cancer drug prolonging a patients' survival by 12 days was recently attributed an inefficient SMR illustrating the change in the hierarchy of criteria determining a drug's SMR.

SMR is measured at a given time but is not fixed for the drug's entire life-cycle. It can be re-evaluated, notably when new data becomes available or when more efficient alternatives appear on the market. Drugs can then be subject to modifications in their reimbursement rates.

If the attribution of SMR is under the responsibility of the Transparency Commission, deciding whether a drug should be included in the reimbursable drugs basket comes to the French Ministry of Health, in theory on the basis of advice from the Transparency Commission and its attributed SMR. The reimbursement rate is then decided on by the Director of the National Union of Health Insurance Funds (UNCAM).

For each of the four defined SMR levels (important or high, moderate, poor or insufficient) Health Insurance applies a different reimbursement rate: 100% for irreplaceable, costly drugs, 65% for drugs with important and high SMR, 30%¹ for a moderate SMR and, since 2010, a 15% reimbursement rate created for poor SMR drugs.

In certain cases, the strict equivalence between SMR and reimbursement rate is not respected, as emphasized by the Cour des comptes in its recent report on the Social Security: 'the ministerial decision to include drugs for reimbursement is not related to the Transparency Commission recommendations. The decision taken can thus be in contradiction with the advice given' (Cour des comptes, 2011).

¹ The drug reimbursement rate for moderate SMR drugs dropped from 35% to 30% on May 2nd 2011.



This study fits within the framework of IRDES research on drugs regulation. It provides an overview of French studies focusing on the impact of drug delisting measures. The first elements of the evaluation presented here provide an understanding of the application of rules defined by the Social Security Code and enables the impact of drug delisting on prescriptions and its consequences in public health and financial terms to be measured.

Drug reimbursement rates not always in line with its SMR

The attribution of a drug's actual benefit, or medical service rendered (SMR), is carried out by the French High Authority for Health² through its Commission for Transparency whereas the positive listing of reimbursable drugs is decided by the Ministry of Health and Social Security and the reimbursement rate by the Director of UNCAM³ (insert 1). Although the Commission for Transparency solely provides consultative advice, 99% of Ministry decisions are based on the Commission's evaluations. Insufficient SMR is not an indication of a drug's therapeutic inefficiency but simply signifies that, in relation to medical advances and progress in scientific knowledge, it no longer has sufficient priority in terms of therapeutic interest to warrant its reimbursement by national solidarity. Theoretically, according to article R-163-3 of the Social Security Code⁴ a drug with an insufficient SMR classification should no longer be reimbursed by public health insurance. As soon as the Commission for Transparency attributes an insufficient SMR, the Ministry of Health should remove the drug from the reimbursable drugs basket. However, not all drugs announced as having an insufficient SMR have been delisted. In March 2011, of the 486 pharmaceutical

² Haute Autorité de santé.

³ Union nationale des caisses d'assurance maladie

⁴ Article R322-1 of the Social Security Code, paragraph 14°: 'The insured's participation is fixed at 85% for drugs whose medical service rendered (SMR), as defined by article R.163-3 is classified as poor for all therapeutic indications, in application of paragraph 6° of article R.163-18'.

pitalisation or emergency services (Anis *et al.*, 2005; Gibson *et al.*, 2005). A study carried out in Italy after the delisting of phlebotonic drugs appears to indicate an increase in the number of hospitalisations for venous insufficiency (Allegra, 2003). Numerous studies highlight the risk of prescription transfers towards drugs that are still reimbursed, or better reimbursed, with the risk of reducing or cancelling the savings generated by the drug delisting measures (Gür and Topaler, 2010; Meissner *et al.*, 2006). Moreover, beyond the economic considerations, these substitutions do not always result in therapeutic improvement, even in the case of older drugs with a debateable therapeutic efficiency (Soumerai *et al.*, 1990). Finally, these changes in reimbursement rates have a considerable impact on pharmaceutical laboratories' marketing strategies. Certain drugs are effectively taken off the market whereas others are transferred onto the self-medication market. Price rises frequently accompany the

transfer to the self-medication market and unavoidably has a negative impact on patients' out-of-pocket payments if they continue to consume the drug in question.

In France, a re-assessment of drugs' medical services rendered (SMR, 'service medical rendu') led to the delisting or reduced reimbursement of a number of drugs (inserts 1 and 2) between 2002 and 2011. This study aims at gathering existing information, (namely provided by grey literature (National Health Insurance and Mutualité Française reports...) and recent research articles), on the impact of drug delisting so as to provide the first elements in the evaluation of these measures. The evaluation is based on two dimensions: prior to the delisting decision, the process and application of rules defined by the Social Security Code are discussed; subsequent to the decision, the impact of measures in public health, treatment practice and financial terms.

products⁵ with insufficient SMR still on the market, a little under 76% had effectively been delisted whereas 24% were still reimbursed, in the majority at the rate of 15%. Created in 2006 this 15% reimbursement rate was initially limited to the phlebotonic class of drugs that was subsequently completely delisted on January 1st 2008. The 15% rate was then applied to other therapeutic classes and since 2010 has been written in the Social Security Code. It should henceforth be exclusively reserved for drugs with poor SMR on all therapeutic indications. In practice, it essentially concerns the class of vasodilatory drugs attributed an insufficient SMR. The introduction of this 15% reimbursement rate is globally contested, especially by complementary health insurance companies that had to rule on the reimbursement of beneficiaries 85% participation rate. In its 2011 Social Security Report, the Cour des comptes considered that this rate generates an additional cost of 35 million Euros per year (Cour des comptes, 2011).

Drugs with an insufficient SMR that have been delisted can be divided into 32 different therapeutic classes but essen-

⁵ Here, this term refers to a box of drugs defined by a name, dosage and a number of units per box (tablets, ml, etc.).

T1 Reimbursement rates for the 486 drugs with insufficient medical service rendered (March 2011)

Reimbursement rate	Drugs concerned	
	Number	Percentage
0%	369	75.93
100% ^a	3	0.62
15%	112	23.05
35%	2	0.41

^a Three presentations of a drug whose main indication is the treatment of lung cancer benefit from a 100% reimbursement rate.

Source: Thésorimed 2011, calculations IRDES.

tially concern ATC⁶ classes A07 (anti-diarrhetics, anti-inflammatory drugs and anti-intestinal infection drugs), C05 (vasculoprotection drugs), N05 (psycholeptic drugs) and R05 (cold and cough medicines).

An immediate drop in the delisted drug prescription rates...

The immediate impact of drug delisting concerns the delisted drug itself: all the studies reveal an immediate drop in the prescription rate for the drug removed from the reimbursable drugs basket.

⁶ Anatomic Therapeutic and Chemical class. It is an international classification of drugs by the World Health Organization (WHO).

An analysis of the overall market concerned by drug delisting conducted by the Mutualité Française shows that the drug delisting wave of March 2006 resulted in a significant drop (-50%) in the number of packages of drugs sold; from 213 million in 2005 to 106 million in 2006 (Mutualité Française, 2007). The turnover generated by the drugs delisted on March 1st dropped from 657 million Euros to 384 million Euros, but the loss in turnover (-41 %) was nevertheless lower than sales volume loss (-50%). This can be explained by the pharmaceutical laboratories' general tendency to raise the price of a drug immediately following its delisting. This drop in the number of packages sold is related to the -61% drop in prescriptions on the one hand and a parallel increase in self-medication (+33%) on the other.

Insert 2

The different drug delisting waves

The major delisting waves implemented over the last few years are the result of a Transparency Commission re-evaluation of the Medical Service Rendered (SMR) for 4,490 reimbursable pharmaceutical products¹ between 1999 and 2001 (decree of October 27th 1999). Following this re-evaluation, 2,815 specialities were attributed an important or high SMR, 840 a moderate or poor SMR and 835 an insufficient SMR. This new classification was strongly contested by the pharmaceutical laboratories leading the government to decide on a new evaluation of the 835 drugs with insufficient SMR which was completed in 2002.

This SMR evaluation should theoretically lead to the systematic delisting of drugs with insufficient SMR, and reductions in the reimbursement rate of drugs with poor SMR. This rule is not always applied, certain delisted drugs having been replaced by a drop in the price or reimbursement rate.

In July 2000, the Aubry plan first organised a reduction in the reimbursement rate of certain drugs with an insufficient SMR still reimbursed at 65% at the time as well as price reductions following a three year plan. Certain laboratories voluntarily decided to remove their drugs from the reimbursement list during this period. A second wave of price reductions occurred in 2001 (Guigou plan), and a third in 2002.

¹ Here, products refers to 'a drug prepared in advance, presented in specific packaging and characterised by a special denomination' (art L 5111-2 of the Public Health Code).

The delisting of drugs with an insufficient SMR began in 2003 and was announced in three phases:

- **August 2003:** delisting of 84 drugs that did not have their place in therapeutic strategy (multiple or outdated active principles).
- **March 2006:** the second delisting wave concerned 282 drugs available in pharmacies without prescription: expectorants, bronchodilators, homeopathic products, oligo-elements and digestive tract disorder drugs.
- **January 2007:** the third delisting wave concerning prescription drugs was differed. Contrary to advice from the High Authority for Health (HAS) the government does not delist 89 drugs whose SMR is judged inefficient. Peripheral vasodilators are maintained at the 65% reimbursement rate whereas a new 15% reimbursement rate is created and applied to phlebotonic. These were completely delisted in January 2008.

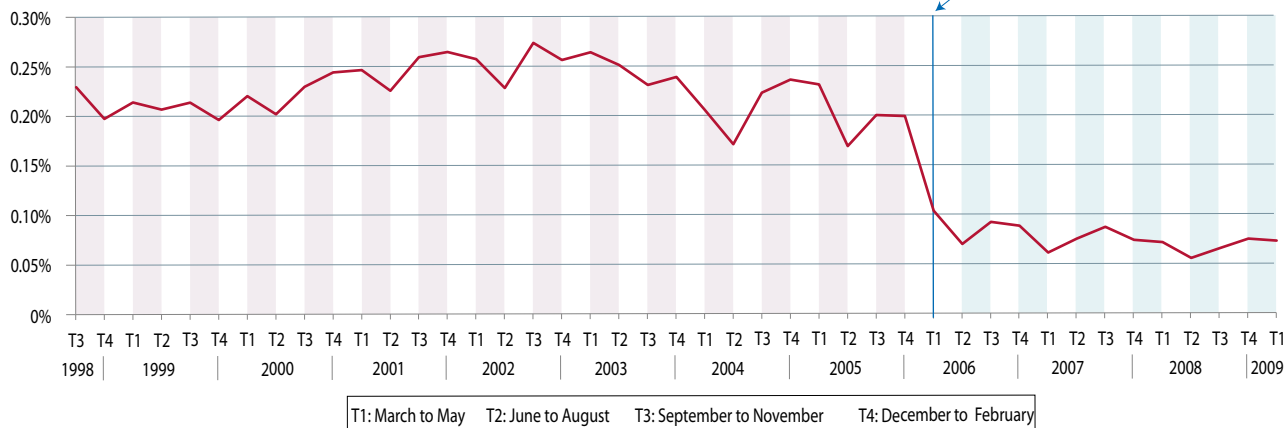
In April 2010, 150 drugs, including peripheral vasodilators, are subject to a reduction in their reimbursement rates from 35% to 15%.

On October 6th 2011, a new delisting wave concerning 26 drugs was implemented. This delisting included 17 drugs at the 15% reimbursement rate.

G1

Prescription rate for mucolytics and expectorants before and after being delisted in March 2006

Prescription rate for mucolytics and expectorants



Source: IRDES.

Data: Permanent Survey on Medical Prescriptions (EPPM) IMS-Health.

IRDES carried out a more specific analysis on the impact of the March 2006 delisting wave on the prescription rate of mucolytics and expectorants in consultations motivated by acute diagnoses (acute upper respiratory tract infections, acute bronchitis, coughs...). This study carried out on the basis of prescription data taken from the IMS Health⁷ EPPM⁸ data base (Pichetti *et al.*, 2011) is a continuation of research on the same class of drugs⁹ using another data base (IMS Health Disease Analyzer) (Devaux *et al.*, 2007). This new study confirms a 50% drop in prescription rates for this class of drugs after its delisting in March 2006 (Pichetti *et al.*, 2011). It equally shows that it applies to all patients independent of age or gender (Devaux *et al.*, 2007) and that the drop in prescription rates has remained stable through time. 56% of general practitioners reduced the number of consultations resulting in prescriptions for expectorants by at least 50%, 36% by 5% to

50%, whereas 4% did not modify their prescription behaviour and 4% increased the number of prescriptions. If the drop in prescriptions does not appear to be related to physicians age or gender, it is on the other hand influenced by their volume of activity or region of practice. The higher a physician's volume of activity, the greater the reduction in the number of prescriptions for expectorants delivered. Furthermore, 77% of physicians in the Northern France reduced the number of prescriptions for expectorants by at least half against only 40% in the Paris region. These regional disparities could be explained by differences in patients' income levels together with differences in medical density and therefore volume of activity. Households in Northern France, for example, have low available income levels and a low density of medical healthcare services that as a result have a high volume of activity. On the contrary, it is in the Paris region that the density of medical services and households' gross available income are the highest.

In addition, a reduction in drug reimbursement rates equally has a considerable impact on prescription rates for the drugs concerned. A third of patients who regularly consumed phlebotonic were thus no longer prescribed these drugs

after the reimbursement rate dropped from 35% to 15% in March 2006. For patients who continued to consume phlebotonic, the average prescription rate dropped slightly (around -6%) [Dumontaux and Pichetti, 2009].

... but sales volume loss only partially compensated by self-medication

The majority of drugs targeted by delisting are currently still on the market. In an attempt to limit the loss of market share, pharmaceutical laboratories introduced new presentations packaged for over-the-counter sales purchasable in pharmacies with or without prescription at freely set prices. The significant drop in prescription rates incited certain patients to continue purchasing the drugs delisted between 2005 and 2006 generating a +33% increase in self-medication. This increase, representing an additional 8 million packages of medication sold in 2006, nevertheless fails to compensate for the considerable drop in sales volume (115 million less packages prescribed and delivered in 2006 compared to 2005 [Mutualité Française, 2007]).

⁷ A study using the same methodology, this time focusing on the phlebotonic class of drugs is part of the IRDES research programme.

⁸ Enquête permanente sur la prescription médicale.

⁹ The new IRDES study uses the segmented regression method that permits an analysis over the long-term (ten years). It detects tendency shifts and prescription rates on time series. The previous study was exclusively based on data relative to one year before and after March 2006.

Drug substitutions increase the prescription rates for other classes of drugs

One of the common consequences of this type of measure is to prescribe substitute drugs still included in the reimbursable drugs basket. Substitution is extremely frequent when delisting concerns either an isolated drug or part of a therapeutic class. It is recommended when the drug concerned has become obsolete and has been replaced on the market by a more effective treatment. It limits potential savings for public Health Insurance if the substitute drug is more expensive. It can be ineffective or even dangerous in terms of public health if the therapeutic effect of the substitute drug is different from that of the delisted drug. Although drug substitution is foreseeable prior to delisting, for example by anticipating the classes of drugs that can act as substitutes, it is more difficult to anticipate the scale of substitution. Substitution is not limited to pharmaceuticals but can also involve other medical goods (such as elastic compression stockings to replace phlebotonic), and other types of care or medical

specialities such as physiotherapists etc. (Dervaux *et al.*, 2004).

The CRESGE (Catholic University of Lille) conducted an experimental evaluation of the changes in therapeutic practices among general practitioners hypothetically confronted with the delisting of phlebotonic drugs. This study suggests a considerable change in care management for patients treated primarily by phlebotonic but unwilling to assume the cost. The prescription of phlebotonic is maintained in around two out of five cases (37%). In 42% of cases, the abandonment of phlebotonic results in a substitute drug prescription, essentially towards non-steroidal anti-inflammatory drugs or antalgic drugs (52% of substitutions), referral to a specialist (35% of substitutions) and elastic compression stockings (22% of substitutions). The authors of this study equally reveal a significant increase in sickness absences from work (Dervaux *et al.*, 2004).

In the case of mucolytics and expectorants, the IRDES study suggests that the prescription of substitute drugs essentially concerns cough suppressants (+12.9 points) and the 'other bronchodilator' class of drugs (+4,4 points) [Pichetti

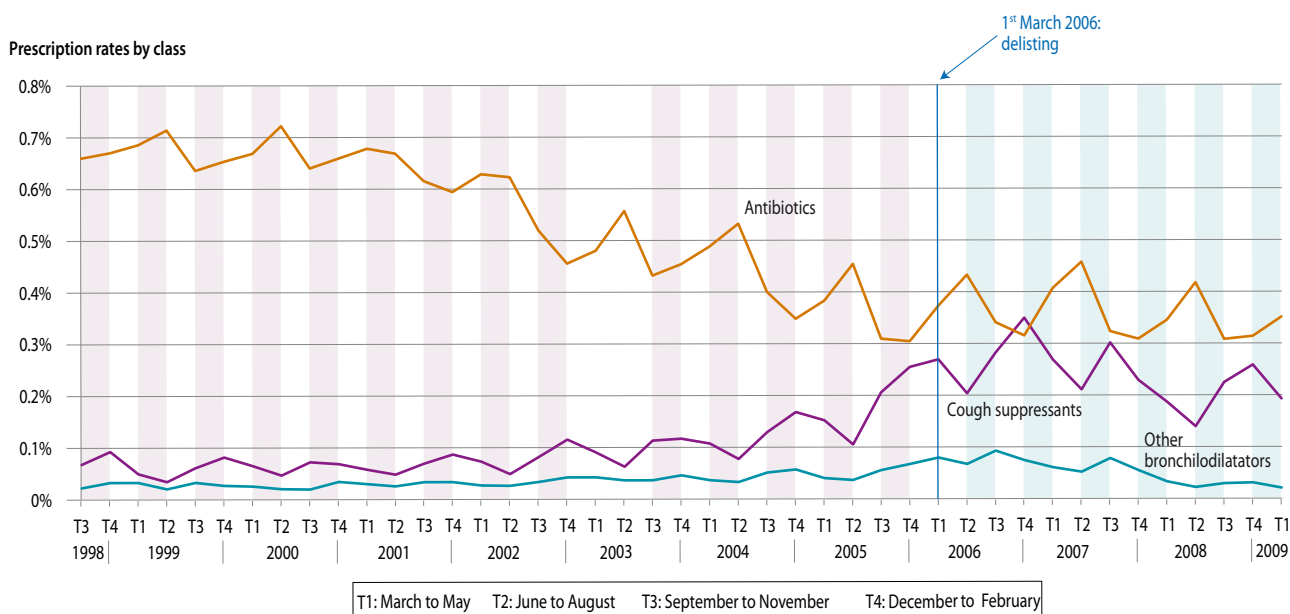
et al., 2011]. These substitutions are observed on consultation data involving a prescription, which does not permit monitoring individually changes in prescription rates for a same patient. This being the case, the results obtained on macroeconomic data indicate a concomitant increase in the prescription rate of cough suppressants and other bronchodilators that, after reviewing all the possible explanatory factors, can only be interpreted as a substitution effect aimed at compensating for the delisting of mucolytics and expectorants. The results obtained by the IRDES study are furthermore corroborated by a study conducted by URCAM¹⁰ Rhône-Alpes revealing an increase in the reimbursements and prescriptions for bronchodilators that the authors of the study explain as a substitution effect resulting from the delisting of mucolytics (Urcam Rhône-Alpes, 2007).

Finally, the widely mediated fear of an increase in the prescription of antibiotics in response to the delisting of mucolytics and expectorants appears to be unfounded. An analysis of the time series before

¹⁰ Union régionale des caisses d'Assurance maladie.

G2

Prescription rate for antibiotics, cough suppressants and other bronchodilators before and after the delisting wave of March 1st 2006



Source: IRDES.

Data: Permanent Survey on Medical Prescriptions (EPPM) IMS-Health.

and after March 2006 shows no variations in antibiotic prescriptions that could be attributed to the delisting of mucolytics.

Inappropriate substitutions in terms of public health ...

No French study to date permits a full evaluation of the impact of prescribing substitute drugs on the health of the population. The IRDES study on mucolytics however outlines the existence of inappropriate substitutions towards a class of drugs with different therapeutic indications. In effect, if the increase in prescriptions for 'other bronchodilators' is medically justified in that these drugs have the same therapeutic indications as mucolytics in the treatment of productive coughs (producing phlegm), an increase in prescriptions for cough suppressants, however, appears arbitrary. These medicines, indicated for non-productive coughs (dry coughs), should not be prescribed for patients treated for productive coughs. Several explanations can be put forward to account for what is in appearance an inadequate substitution. The hypothesis according to which physicians lack information concerning both the indications and therapeutic effects of the drugs they prescribe seems highly improbable. Having full knowledge of the therapeutic indications of mucolytics in the treatment of productive coughs, physicians are probably equally aware of the doubts concerning their effectiveness after the SMR re-evaluation in 2001. These doubts may explain that, confronted with patients' high demand for treatments, physicians may have been tempted to prescribe mucolytics in that they considered them more as a placebo. It ensues that prescribing a cough suppressant as a substitute drug for a mucolytic, considered as being another placebo by certain authors, cannot be considered totally inappropriate in such circumstances (Eccles, 2010; Schroeder et Fahey, 2004). A possible solution would consist in informing patients and physicians of suitable alternatives as an accompaniment to the delisting measure.

... and a reduction in savings for National Health Insurance

In its June 2006 report, the Social Security Audit Commission¹¹ insisted on the difficulty of precisely anticipating the financial consequences of delisting measures for National Health Insurance in that the financial return could be diminished if medical prescriptions turned towards substitution drugs with a higher SMR that are still reimbursed (Commission des comptes de la Sécurité sociale, 2006). In its 2011 report, the Cour des comptes equally stressed that following the delisting of a therapeutic class of drugs, the effect of prescribing substitute reimbursable products or classes risked limiting or cancelling the effects of the measure (Cour des comptes, 2011).

The substitution of mucolytics and expectorants by other therapeutic classes (bronchodilators and cough suppressants) reduces the savings made by National Health Insurance through delisting. The IRDES study estimates that the savings from the delisting of mucolytics and expectorants, based purely on the treatment of acute diagnoses

¹¹ Commission des comptes de la Sécurité sociale.

(70.5 million Euros four years after delisting) were reduced to 32.1 million Euros due to the concomitant increase of the prescription of cough suppressants. In order to determine the additional costs incurred by the increase in prescriptions for cough suppressants, the authors of the study calculated the difference between the actual prescription rate and the one that would have prevailed if mucolytics and expectorants had not been delisted, supposing that the pre-delisting growth rate for cough suppressant prescriptions had remained the same.

For patients taking delisted drugs, prices increased by an average 43%

The introduction of delisted drugs on the market, as self-medicating drugs purchased over-the-counter, is generally accompanied by a price rise. Based on recent measures (March 2006, January 2008...), the average price increase is around 43%. This average rate however conceals significant disparities: the highest price decrease is established at 25% whereas the highest price increase reaches 249%.

Based solely on the 2006 delisting wave, the Mutualité Française reveals an average 36% increase in the price of delisted drugs. This overall average again conceals signi-

T2 Cumulated savings over four years related to the delisting of mucolytics and expectorants and additional costs related to prescriptions for substitute drugs in other therapeutic classes

	In millions of Euros			
	Mucolytics and expectorants	Other bronchodilators	Cough suppressants	All classes
	Gross savings	Additional costs	Additional costs	Cumulated net savings
2006	18.7	-0.7	-5.6	-12.4
2007	36.2	-0.69	-13.1	-22.41
2008	53.7		-25.7	-28.0
2009	70.5		-38.4	-32.1

Reading note: In 2006, the delisting of mucolytics and expectorants generated savings amounting to 18.7 Euros on this class of drugs. The increase in prescriptions of other bronchodilators and cough suppressants, however, reduced these savings to 12.4 million Euros. Three years after the reform was implemented, the gross cumulated savings amount to 70.5 million Euros for the mucolytics and expectorants class. An increase in prescriptions for cough suppressants (38.4 million Euros cumulated over the period) considerably reduces net savings that do not exceed 32.1 million Euros.

Source: IRDES, data EPPM-IMS Health 1998-2010.

ificant disparities: up to August 2006, the highest price increase concerned drugs for digestive tract disorders (+59% between February and August) whereas the lowest price increase during the same period concerned cardiovascular disorder drugs (10% between February and December 2006) (Mutualité française, 2007).

Laboratories try to limit the impact on turnover

Raising the price of a delisted drug constitutes a means of limiting laboratories' loss of turnover following its removal from the reimbursable goods basket. This price increase does not, however, totally benefit the laboratories in question.

Drug delisting in fact results in an increase in VAT from 2% to 5.5% and their removal from the regulated price system permits each of the actors in the distribution chain (pharmaceutical laboratories, distributing wholesalers, pharmacists) to choose their profit margins.

The study conducted by Mutualité Française shows that the manufacturers price, (excluding the average tax on these drugs), increased by 16% between February and December 2006 whereas the distribution margins (wholesalers and pharmacists) increased by 55%, the combination of the two explaining the overall price rise of 36% over this period.

Furthermore, an increase in prescriptions for over-the-counter drugs, even modest, allows laboratories to limit the impact of delisting.

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In a context of mounting tensions concerning health expenditures, delisting drugs with low therapeutic effectiveness has the

7 FURTHER INFORMATION

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advantage of producing immediate, quantifiable savings on the therapeutic classes no longer reimbursed by public health insurance. Nevertheless, these delisting measures should equally take into account the eventual prescription of drug substitutes still included in the reimbursable drugs basket. These substitution effects are susceptible of having an impact both on public health, if the substitute drug is medically inappropriate, and on National Health Insurance savings if the prescription rate for alternative, reimbursable drugs is high. It would thus be recommended that the regulatory authority acquires piloting tools in order to both anticipate and monitor the impact of future delisting policies. Prior to imple-

mentation, the identification of drugs susceptible of being candidates for future delisting together with monitoring and analysing the results of foreign experiences could allow for anticipating the impacts of delisting policies. Measures designed to accompany and inform physicians and patients would favour a greater acceptance of delisting measures and prevent unsuitable drug substitution. Following implementation, a reporting schedule should be set up to monitor the delisted class and classes of drugs potentially suitable as substitutes. This would permit carrying out impact analyses and implement corrective actions should a massive substitution effect towards a reimbursable drug occur. ♦