Questions d'économie de la Santé

n° 128 - December 2007

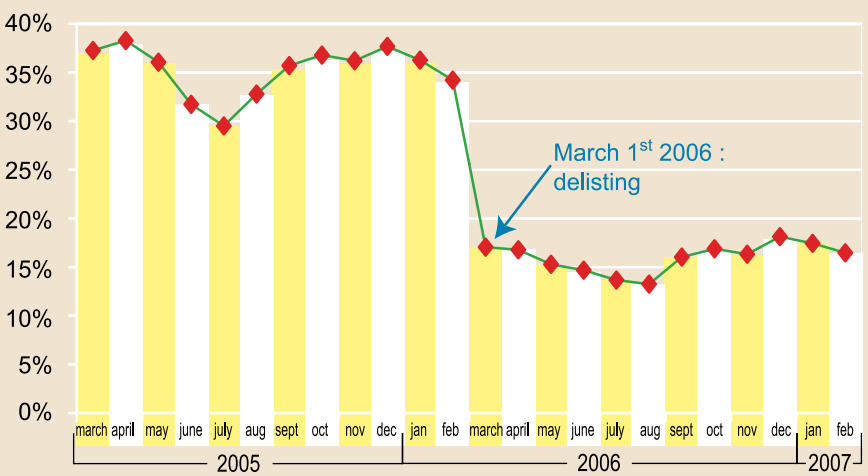
Delisting of mucolytics and expectorants: what is the impact on general practitioners' prescribing?

Marion Devaux, Nathalie Grandfils, Catherine Sermet

Following the round of delisting of March 1st, 2006, general practitioners' prescribing of mucolytics and expectorants for the treatment of upper and lower respiratory tract infections has reduced by a half. From this point of view the policy would appear to be effective. Nevertheless it seems that physicians are shifting their prescribing to other therapeutic classes, depending on the diagnosis, such as cough suppressants or bronchodilators, some non-steroidal anti-inflammatories, corticoids and otological products, without any obvious medical justification in all cases.

Because mucolytics and expectorants are inexpensive, total prescribing costs have remained stable, despite a trend of increasing costs for other drug classes.

Monthly rates of consltations with prescriptions of mucolytics and expectorants for the 8 diagnostic groups studied



Note for the reader: The monthly rate of consultations with prescriptions of mucolytics and expectorants decreased from 34% in February 2006 to 17% in March 2006, following the delisting of March 1st, 2006.

Source: IRDES - Data: IMS Health, *Disease Analyzer*

In an attempt to control pharmaceutical expenditure while maintaining quality of care, the governement has delisted drugs with lower therapeutic value. In order to do this, between 1999 and 2001 the Transparency Commission reassessed the therapeutic value (see box p.2) of reimbursable ambulatory drugs, which resulted in the delisting of 152 pharmaceutical specialties on March 1st, 2006, in particular mucolytics and expectorants[1]. These drugs, which loosen bronchial secretions or facilitate their expectoration, were widely used in the treatment of upper and lower respiratory tract infections, particularly in children and older people.

The objective of this study is to evaluate the impact on physicians' prescribing behaviour of mucolytics and expectorants[2] (see Box p. 3). Apart from the direct effect on prescribing, we try to assess the extent prescribing has shifted to other categories of drugs and evaluate the economic impact of this measure in terms of Sickness insurance expenditure.

This study is based on all prescriptions of a sample of general practitioners one year before and one year after the delisting of March 1st, 2006. Those consultations like-

1 The drugs are still reimbursed for patients with mucoviscidose.

2 Heceforth we use the term expectorants for both mucolytcs and expectorants.

ly to result in a prescription of expectorants were selected (*see box p.4*).

The prescription of mucolytics and expectorants has reduced by a half

In 2005, the Sickness Insurance General Regime[3] reimbursed approximately 50 million Euros for expectorant prescriptions, i.e. 0.37% of total reimbursements (Medic'am, 2006). Following delisting, the total number of consultations with a prescription of expectorants reduced by a half. In the year before delisting, 36% of consultations involving one of the selected diagnoses was associated with a prescription of expectorants. This percentage dropped suddenly to 17% in the month following delisting, a decrease by 53% (see figure p. 1). In addition, there is a similar seasonal change in expectorant prescribing between the two periods: a reduction in prescribing between April and August, followed by an increase during Autumn and Winter.

At a more detailed level, the analysis shows substantial reductions in prescribing, whatever the diagnosis. Before delisting, expectorants were prescribed in more than one in two cases of acute or chronic bronchitis ; in one in three cases of chronic infections of the upper respiratory tract and otitis ; and in about one in four cases of asthma, influenza, coughs and acute infections of the upper respiratory tract. Delisting resulted in a 50% reduction in prescriptions for each of these diagnoses. Hence, for example, 59.5% of consultations for acute bronchitis involved a prescription of an expectorant before delisting. This percentage then dropped to 30.5% (*see figure below*).

There is a decrease in prescriptions whatever the age or sex of the patient

Consultations with prescriptions of expectorants are more frequent for young and older people. The reduction in delisted expectorants affected all patients to the same degree whatever their age or sex.

3 Not including local mutualist sections, in metropolitan France.

BACKGROUND...

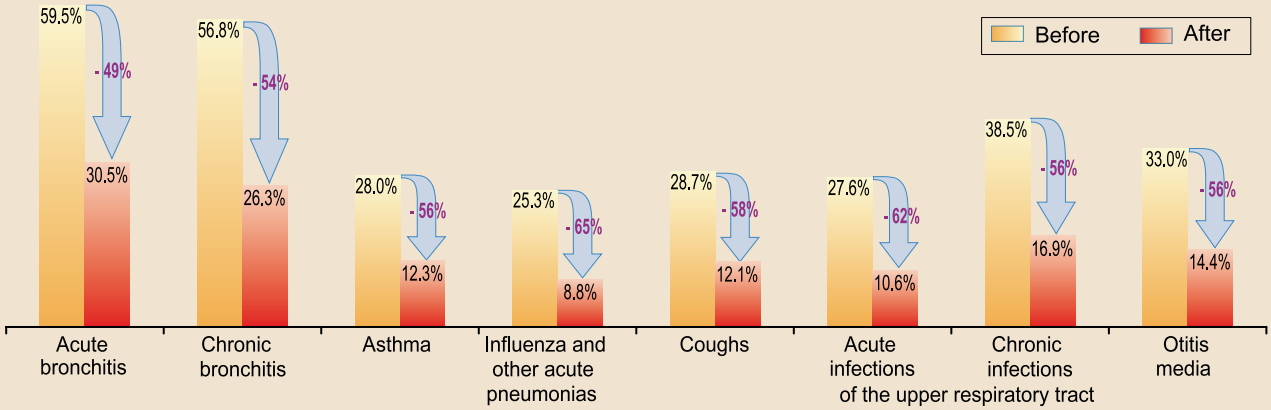
This study is part of IRDES programme of research on pharmaceutical market regulation policy .

It is one of a serie of studies on the effect of delisting, reductions in reimbursement rates and of the removal of some drugs from the market, carried out by IRDES in conjunction with DREES (Directorate of Research, Studies, Evaluation and Statistics) and AFSSAPS (French Agency for the Health Safety of Health Products. IRDES undertook to anlayse the effect of delisting of mucolytics and expectorants, while DREES studied the effect of lowering the reimbursement rate of veinotonics, and AFSSAPS is looking into the impact of the removal from the market of some classes of immunostimulants. This forms part of a collaborative study to evaluate the quality and potential utility of data from the « Disease analyzer » panel of IMS Health. The study is based on the prescriptions of 1,063 general practitioners in almost 500,000 consultations with 330,000 patients.

The therapeutic value of a drug

The Transparency Commission advises on whether a drug will be reimbursed by Sickness Insurance and assesses the therapeutic value (SMR: Service medical Rendu) of a drug among other things. There are five levels of SMR: 'insufficient', 'low', ' moderate', 'important' or 'major', which, according to the Decree of 27th October 1999, determines the level of reimbursement, ranging form 0% to 65%. A drug with a major or important SMR with an indication for a serious disease is reimbursed at 65% by Sickness Insurance. A drug with a major or important SMR for a non-serious disease or a moderate or low SMR is reimbursed at 35%. Finally, a drug with an insufficient SMR is not in theory reimbursed; this assessment of an insufficient SMR does not indicate that the drug is ineffective but that its therapeutic value in relation to medical progress and the development of scientific knowledge is no longer considered sufficiently important for its reimbursement by national insurance. We note that exceptions were made by granting a temporary reimbursement rate of 15% for some drugs, notably veinotonics. We also note that some ambulatory drugs are considered irreplaceable and particularly expensive by the Ministry of Health and the Ministry of Social Security and are hence reimbursed at 100%.

Annual rates of consultations with the prescriptions of mucolytics and expectorants before and after delisting, by diagnosis



Note for the reader: In the case of acute bronchitis, the annual rate of consultations with a prescription of mucolytics or expectorants exceeded 59.5% before delisting and 30.5% after the delisting, a reduction by 49%.

Source: IRDES - Data: IMS Health, *Disease Analyzer*

Percentage change in the average number of different drugs prescribed before and after delisting for the eight diagnostic groups studied

	Acute bronchitis	Chronic bronchitis	Asthma	Influenza and other acute pneumonias	Coughs	Acute infections of the upper respiratory tract	Chronic infections of the upper respiratory tract	Otitis media
Analgesics and antipyretics	10%	3%	13%	4%	18%	11%	-4%	4%
Antibiotics	7%	0%	-11%	-5%	10%	8%	-4%	-1%
Cough suppressants and bronchodilators	11%	8%	1%	7%	6%	-2%	1%	9%
Corticoids	2%	8%	5%	10%	-3%	12%	7%	7%
Mucolytics and expectorants	-41%	-42%	-50%	-52%	-48%	-53%	-47%	-48%
Other drugs	-3%	2%	6%	-15%	18%	3%	12%	1%
Total	**-3%**	**-4%**	**-2%**	**-3%**	**0%**	**-3%**	**-6%**	**-4%**

Note for the reader: For the consultations for chronic bronchitis, the average number of mucolytics and expectorants prescribed has decreased by 42% following delisting the while the number of cough suppressants and bronchodilators has increased by 8%.

Source: IRDES - Data: IMS Health, *Disease Analyzer.*

Substitution of mucolytics and expectorants

In order to cover the range of mucolytics and expectorants, we have used the WHO therapeutic class ATC[1] , code R05CA for « expectorants », code R05CB for « mucolytics », and the pharmaceutical industry classification therapeutic class Epharma[2], code R05C for « expectorants ». 200 specialties prescribed in our data i.e. 29 molecules, are thus classified as mucolytics or expectorants.

Before the delisting of March 2006, there were two categories of mucolytics and expectorants : reimbursed (99% of prescribed expectorants) and non-reimbursed (1%). In fact, certain specialties were not reimbursed prior to March 2006, either because they had been delisted during a previous round of delisting (in 2003), or because pharmaceutical companies had never requested reimbursement. The effect of delisting is different for each of the categories. For the group of diagnoses studied, the rate of consultations with prescriptions for mucolytics and expectorants fell by 59% for specialties which were reimbursed and then delisted, while it fell by 2% for non-reimbursed specialties. Mucolytics and expectorants reimbursed before March 2006 and then delisted on March 1st, 2006 (HAS 2006) represent 118 specialties prescribed in our data, namely 16 substances. 82 specialties non-reimbursable before March 2006 were excluded from our data because they were rarely prescribed.

[1] *Anatomical Therapeutical Chemical.*

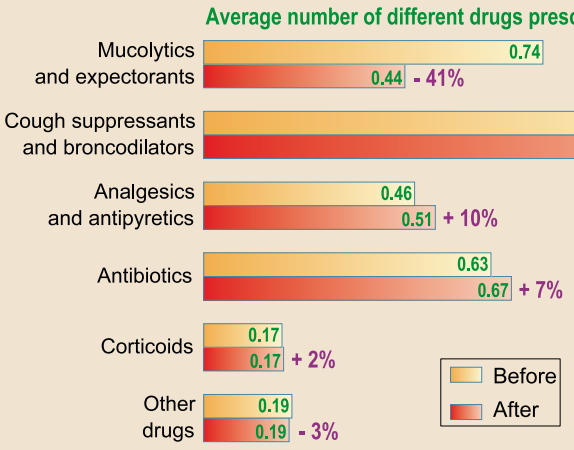
[2] *European Pharmaceutical Marketing Research Association.*

The decrease in prescribing is not related to age or sex of the physician, but is a function of his level of activity and area of practice

56% of physicians reduced by at least a half the number of consultations with a prescription for expectorants. 36% of physicians reduced it by between 5% and 50%. 4% of physicians did not change their behaviours ,with a change in the number of prescriptions of between -5% and 5%), and 4% increased their prescriptions by more than 5%.

The change in prescriptions for expectorants is not related to age or sex of the physician. However it is related to activity levels and area of practice. Furthermore, 77% of physicians of the North region reduced their prescriptions for expectorants by at least a half, whereas this rate was only 40% for physicians from the Parisian region. These differences may be explained by income differences between regions. In fact the North region has both low levels of household income (INSEE 2003) and a low density of physicians (Eco-Santé, 2007), and hence high volumes of activity among physicians. By contrast in the Parisian region both density of physicians and gross disposable household income are higher.

Change in the average number of different drugs prescribed for acute bronchitis before and after the delisting



The total number of different drugs prescribed is 3.4% before the delisting and 3.3% after, a decrease of 3%.

Note for the readre: For consultations for acute bronchitis, the average number of mucolytics and expectorants prescribed decreased from 0.74 to 0.44 following the delisting, a decrease of 41% while the number of cough suppressants and bronchodilators increased from 1.18 to 1.31, an increase of 11%.

Source: IRDES - Data: IMS Health, *Disease Analyzer*

Prescribing content changes following the delisting

The average number of different medicines prescribed per consultation is identical before and after the delisting. For all diagnoses studied, one consultation results on average in a prescription for 3.4 different drugs before the delisting and 3.3 after.

The proportion of expectorants in the number of drugs prescribed is low overall and is a function of the presenting diagnosis : before the delisting it varies from 8% for consultations for influenza to 19% for consultations for acute bronchitis. After the delisting in March 2006, these proportions are 3% and 10% respectively.

For diagnoses resulting in prescriptions of expectorants, both before and after the delisting the majority of products prescribed are decongestants and cough suppressants (Ephmra R03 and R05 classes), antibiotics (J02), analgesics and antipyretics (N02) and corticoids (H02). Consultations for otitis also involve a high proportion of otological products (12%) classified in the « other medicines » group. This group includes all therapeutic classes not cited above. They are very infrequent in prescriptions for the diagnoses studied here.

In general we note an increase in prescriptions for many therapeutic classes following the delisting (*see the table and figure on p. 3 for the example of acute bronchitis*). Hence prescriptions for cough suppressants and bronchodilators (Epharma classes R05 and R03) increase for bronchitis, coughs and influenza ; those for analgesics/antipyretics (N02) for all diagnoses except chronic infections of the upper respiratory tract ; those for antibiotics (J02) for acute respiratory tract infections and for coughs ; those for corticoids (H02) for all diagnoses except influenza ; and finally prescriptions for « other medicines » for chronic infections of the upper respiratory tract and for coughs.

The selection of consultations and classification of diagnoses

This study is based an all prescriptions issued one year before and one year after the delisting of March 1st 2006 (i.e. between March 1 2005 and 28th February 2007) by 1063 general practitioners from the « Disease analyzer » data panel of IMS Health. These physicians send data regularly on all of their consultations : age, sex, area of practice, age and sex of patients, diagnoses or reasons for consultation and related pharmaceutical prescriptions (see table opposite). Based on data from the permanent survey of medical prescribing (EEPM) of IMS Health, we have identified the reasons for consultations which resulted in prescriptions for expectorants, before the delisting. From these we selected 19 diagnoses reclassified in 8 major diagnostic groups (see table below). Prescriptions associated with these 19 diagnoses represent approximately 90% of prescriptions of expectorants.

In Disease Analyzer data, each drug, even if prescribed for two different indications, can only be associated with one diagnosis. Hence we excluded consultations with more than one diagnosis from our study. For example consultations involving one of the diagnoses selected for study and another illness (for example depression) have been excluded ; similarly consultations for two of the selected groups have been excluded : for example code J00 (cold) and H65 (otitis). However, consultations for two diagnoses belonging to the same group have been retained (for example J00 (cold) and J01 (sinusitis)). In addition, all consultations for any diagnosis plus "cough" have been retained because a cough is a symptom not an illness.

Descriptive statistics

	BEFORE	AFTER
Number of physicians	**1,063**	
Average age of physicians	49.6 years	
Percentage of female physicians	12.30%	
Average annual number of consultations	4,520 (+/- 1 725)	
Percentage of physicians in the region...		
Centre	6%	
Centre-East	14%	
East	12%	
North	12%	
West	16%	
Parisian region	8%	
South East	19%	
South West	13%	
Number of patients	**341,219**	**333,708**
Average age of patients	29.2 years	28.2 years
Percentage of female patients	53%	53%
Number of consultations	**487,244**	**474,813**
Percentage of consultations for...		
Chronic infections of the upper respiratory tract	59%	56%
Acute bronchitis	8%	8%
Chronic bronchitis	8%	8%
Influenza and other acute pneumonias	7%	9%
Otitis media	6%	6%
Chronic infections of the upper respiratory tract	5%	5%
Coughs	4%	4%
Asthma	3%	4%
Number of prescriptions	**1,664,105**	**1,567,307**

Selected diagnoses

Groupes of diagnoses	Diagnoses (International classification of Diseases 10th revision)
Acute infections of the upper respiratory tract	J00, J01, J02, J04, J06
Chronic infections of the upper respiratory tract	J31, J32, J34
Acute bronchitis	J20, J21
Chronic bronchitis	J40, J42, J44
Asthma	J45
Otitis media	H65, H66
Influenza and other acute pneumonias	J11, J18
Coughs	R05

Source: IRDES - Data: IMS Health, *Disease Analyzer*

Percentage difference in the annual change in the number of prescriptions of the substitution group and the reference group for the eight selected diagnoses

	Acute bronchitis	Chronic bronchitis	Asthma	Influenza and other acute pneumonias	Coughs	Acute infections of the upper respiratory tract	Chronic infections of the upper respiratory tract	Otitis media
Analgesics and antipyretics	-7%	-5%	-27%	11%	-12%	14%	-6%	6%
Antibiotics	-3%	-10%	-56%	-30%	-17%	-3%	-17%	-3%
Cough suppressants and bronchodilators	43%	47%	16%	39%	59%	25%	24%	-6%
Corticoids	6%	-11%	-39%	NS	30%	8%	-1%	-6%
Other drugs	-8%	-5%	36%	81%	6%	25%	19%	31%

Note for the reader: For consultations for acute bronchitis, the before/after difference in the number of cough suppressants and bronchodilators prescribed is +49% in the substitution group and +6% in the reference group, a difference of 43 points. NS indicates that the difference is not significant (less than 0.005 drugs per prescription).

Source: IRDES - Data: IMS Health, *Disease Analyzer*

There are various possible interpretations of these increases. They may reflect a general increase in pharmaceutical prescribing, or substitution by other therapeutic classes following delisting, or a combination of both.

Expectorants have been changed for bronchodilators and cough suppressants

To distinguish between a general increase in prescribing from any increase due to substitution, a « reference group » was created of physicians who, both before and after the delisting, are infrequent prescribers of expectorants (see the box opposite). In this group we may observe any changes in pharmaceutical prescribing in physicians who in theory have had no reason to change their behaviour. Any change here may therefore be attributed to general changes in prescribing behaviour. Then we compare the prescriptions of this group with those physicians who prescribed expectorants in the period « before » and who greatly reduce their prescription of expectorants in the period « after » i.e. those physicians who change their prescribing behaviour. We refer to this group as the substitution group. The observed difference approaches the volume of substitutions resulting from the delisting of expectorants (*see table below*).

For most diagnoses, the change in the prescription of cough suppressants and bronchodilators in the substitution group is considerably greater than in the reference group, which suggests some substitution in favour of these classes for all diagnoses except otitis. Similarly, the data seem to show substitution with corticoids for coughs and with other drugs, such as otological products, for otitis, and non-steroidal anti-inflammatories[4] for asthma, influenza and infections of the upper respiratory tract. We have not observed any substitution towards antibiotics and the antalgic/antipyretic class.

From a medical point of view, it is difficult to explain some of these changes: cough suppressants should be administered for dry coughs while expectorants are for wet coughs (coughs with mucous). On the other hand anti-inflammatories and corticoids may be appropriate for the treatment of bronchial inflammation underlying the production of mucous. Finally, the huge decrease in oral corticoids and the reduction in antibiotics for diagnoses of asthma is more difficult to explain and is probably due to imprecise diagnoses on the part of physicians (most are unspecific asthma) ; the inclusion of antibiotics in some prescriptions would suggest that some diagnoses are for asthma with related infection. Antihistamines in other prescriptions probably indicate allergic asthma. A more detailed study would be necessary to analyse changes in prescribing behaviour by type of asthma, following the delisting of expectorants.

4 Some anti-inflammatories from the Ephmra M01 class.

Analysis of the substitution of mucolytics and expectorants by other drugs

In order to distinguish between general trends in pharmaceutical prescribing and any increase due to possible substitution, a control group or « reference group » was created. This group consists of consultations without expectorants before and after realised by physicians who did not prescribe expectorants before the delisting (87 physicians). A physician is a non-prescriber if he prescribes expectorants in less than one in ten consultations. For this group of physicians we measure change in the content of prescriptions before and after the delisting, after excluding prescriptions with expectorants. Hence in this group the before/after difference in the average number of prescribed drugs represents the general tend in prescribing.

A second group was constructed based on consultations with expectorants before the delisting, and without expectorant following the delisting, by physicians prescribing expectorants before the delisting (974 physicians). Hence we are measuring change in prescription content for consultations with expectorant before the delisting and those without in the period after, which enables us to focus on prescribing behaviour. In this group any change in prescribing behaviour before and after may be attributable to substitution ; which is why this group is called the « substitution group ».

Two physicians have been excluded from this analysis because more than 10% of their consultations involved expectorants before and after the delisting.

The different rates of change between these two groups is close to the volume of substitution resulting from the delisting of expectorants : a difference of more than 15% is worthy of note ; below this threshold, the difference should not be thought of as substitution.

The age and sex distribution is similar for both groups, for patients and for physicians. However there is a significant difference in yearly volume of activity which is higher for the substitution group than for the reference group.

The cost of prescribing has not changed following the delisting

The total cost of prescribing, for all diagnoses, is estimated at €29.40[5], before and after the delisting (see box below). The excess for the patient or his Supplementary Insurance if he has this, is approximately €14 for the two periods while the proportion covered by Sickness Insurance is on average €15.40.

The cost of expectorants represents 6% of the total cost of prescribing, that is €1.80, before the delisting, and 3% after, i.e. €0.90. The cost of expectorants within the total prescribing cost before the delisting is so low that a 50% decrease in this cost, together with an increase in other classes, whether they reflect a general trend or change resulting from substitution, has no effect on the total cost of prescribing.

5 In current euros.

Calculating the cost of prescribing

In order to estimate the total cost of prescribing, two sources of information were used : the number of boxes prescribed and the price of drugs. Packaging-specific drug prices are monthly public prices for the period March 2005-February 2007, from the SEMPEX/VIDAL® database. For prescriptions with a International Non-Proprietary Name (INN), an average monthly cost for the product was estimated for the group of corresponding active ingredients present in the SEMPEX/VIDAL® database.

We used a method of imputation based on the average because data on the number of boxes prescribed was missing and could not be calculated. We replaced the missing data by the average rounded up, calculated for sub-groups of products with the same galenic form. Where it was not possible to impute, we replaced the missing data by one box.

The cost of prescribing by Sickness Insurance was estimated using the theoretical monthly reimbursement rates available for the product.

This estimation does not correspond to the actual cost for Sickness Insurance because some patients are reimbursed at 100%, notably those with chronic long-term illness which reimbursed at 100%. Because this information is not available in our data, changes in costs to Sickness Insurance are underestimated ; however this bias exists before and after the delisting and therefore does not affect our interpretation of any resulting changes in expenditure.

The first aim of the delisting has clearly been achieved because physicians have substantially changed their prescribing behaviour for mucolytics and expectorants. However substitution is clearly taking place, particularly with cough suppressants and bronchodilators for all diagnoses except otitis. This is in line with results published by the Commission for Social Security (2007). Substitution with corticoids for coughs, with otological products for otitis and with some non-steroidal anti-inflammatories for influenza is also taking place. Nevertheless, this policy of delisting expectorants has had a negligible impact on expenditure. There has been no change in the cost of prescribing, for Sickness Insurance, for the patient or for his Supplementary Insurance. This analysis has not considered expenditure related to self-medication nor to advice from pharmacists. Hence it underestimates costs for the patient, particularly given that, following reimbursement the price of these medicines is no longer controlled and has increased. In fact, according to a study by French Mutual (2007), the average price of delisted medicines, for all classes, has increased by 36%, and for over the counter drugs by 33%.

Lastly, prescriptions for respiratory physiotherapy sessions were not included in the database, although this practice is recommended by the National Authority for Health (HAS,2000). It would be interesting to analyse these data in order to assess the extent of substitution of these sessions for the prescription of expectorants, in order to assess the financial impact of such substitution on Sickness Insurance.

FURTHER INFORMATION

- Commission des comptes de la Sécurité sociale (2007), Déremboursements et reports de prescriptions, fiches éclairage de la Commission des comptes de la Sécurité sociale, consulté le 20/11/07 sur http://www.securite-sociale.fr/comprendre/dossiers/comptes/2007/ccss200710_fic_9-3.pdf
- Eco-Santé 2007 : http://www.EcoSante.fr
- HAS (2006), Liste officielle des médicaments déremboursés au 1er mars 2006, consultée le 11/12/07 sur http://www.has-sante.fr/portail/types/FileDocument/doXiti.jsp?id=c_514379
- HAS (2000), Prise en charge de la bronchiolite du nourrisson, consulté le 20/11/07 sur http://www.has-sante.fr/portail/upload/docs/application/pdf/bronc.pdf
- INSEE (2006), Revenu disponible brut des ménages en 2003 par région, consulté le 11/12/07 sur http://www.insee.fr/fr/ffc/chifcle_fiche.asp?ref_id=CMRSOS04238&tab_id=486
- Medic'AM (2006), consulté le 20/11/07 sur http://www.ameli.fr/fileadmin/user_upload/documents/Tableau_medicaments_rembourses_2002__2005.xls
- Mutualité française (2007), Impact économique de la modification des conditions de remboursement des SMRi en 2006 consulté le 20/11/07 sur http://www.mutualite.fr/content/download/18608/314391/file/EtudeSMRi.pdf

IRDES INSTITUTE FOR RESEARCH AND INFORMATION IN HEALTH ECONOMICS - Online on www.irdes.fr
10, rue Vauvenargues 75018 Paris - ✆ : 01 53 93 43 02/17 - Fax : 01 53 93 43 50 - document@irdes.fr
Director of the publication: Chantal Cases
Technical senior editor: Nathalie Meunier
Translator: Marian Craig - Dummy maker : Khadidja Ben Larbi
ISSN : 1283-4769 - Diffusion by subscription: €60 per annum - Price of number: €6 - 10 to15 numbers per annum.