Monitoring Of Reimbursement Significant Expenses
M.O.R.S.E. semi-annual report 2008 (2)
data 2nd semester 2008

Content

INTRODUCTION

The financial follow-up of the expenditures for reimbursable drugs in function of the adopted policy measures (including new introductions of drugs in the reimbursement scheme, savings measures, etc. …) constitute the subject and topic of the MORSE-project as it is described in the Business Steering Group of the Medical Health Care Department. The results of the analysis are likewise introduced as part of the management agreement report – article 32.

It is for that purpose that a financial report is being composed on a quarterly basis. This report is aimed at drawing up the evolution of the expenditures for the pharmaceutical specialities supplied in both public pharmacies and in hospitals to and including ***semester 2 of the year 2008***, with forecast for the year 2009.

For the estimation of the expenditures, recourse is had to the NIHDI data (Pharmanet for the public pharmacies, posted data for the hospitals) and to the recent IMS sales figures.
For the estimation of the expenditures in public pharmacies MORSE combines, in an initial approach method, recent IMS sales figures (to and including December 2008) with NIHDI expenditures as available for public pharmacies via Pharmanet (to and including August 2008). Only if the correlation between both is sufficiently marked in size during the identified historical period can IMS be used to forecast recent NIHDI expenditures. In all other instances, available NIHDI-data are being extrapolated.
For the estimation of the expenditures in hospitals recourse is had to an analogous technique as used in the estimation of the expenditures for the public pharmacies: recent IMS-BHA sales figures (to and including the third quarter of 2008) compared with the NIHDI expenditures as available for hospitals via docPH data (billing data to the NIHDI as submitted by the insurance companies, available to and including 2007). In this case also, what is significant is that only if the correlation between both of them is sizeable enough within the relevant historical period can IMS data be used to forecast NIHDI expenditures. If that is not the case, available NIHDI data will be extrapolated.

For the discussion of the measures, reference is made of the historical background data for :

- Data determined by groups (reference price, price reductions, shifts towards Chapter II…) as registered with the administration
- The administrative databank for the individual measures /dossiers (introduction of new drugs, changes to the reimbursability…).

For the projection for 2009, recourse is had to at least 2 methods whereby:

- A different weight is assigned to older versions versus the recent historical data
- Different mathematical regressions are being proposed (linear and non-linear)

The financial monitoring is not an exact science: the considerations are likewise being tested against the probability that internal collaborators (internal evaluator, dossier managers, Pharmanet cell…) have decided to assign to it.
Furthermore, earlier forecasts are tested against the real expenditures as soon as relevant data for this have become available, this in order to determine the extent of the deviation.

There exist ***several financial reports*** on the subject of the expenditures for drugs: permanent audit, Infospot, cell data management, … Through the MORSE report, an attempt is made to process the relevant information that could be gleaned from other sources: this report was, wherever deemed necessary, complemented by data gathered from the Permanent Audit (November 2008 and May 2009).

MORSE reports are meant to inspire reflection and discussions. All commentary and remarks in this regard are most welcome!

I. OVERVIEW OF THE GLOBAL EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES BROKEN DOWN BY PUBLIC PHARMACIES AND HOSPITALS

I.1. General

Table I.1. MORSE dataset: net annual NIHDI expenditures for drugs 2002 – 2009, with extrapolation for 2008 and 2009

Expenditures net NIHDI x 1.000.000 €								
	2002	2003	2004	2005	2006	2007	2008	2009
pharmacies	**1.921.59**	**2.063.46**	**2.213.13**	**2.203.74**	**2.161.01**	**2.296.73**	**(*)2.600.12**	**(*)2.858.24**
Hospitals					**972.88**	**1.055.16**	**(°)1.122.69**	**(°)1.181.07**
Total					**3.133.89**	**3.351.89**	**3.722.81**	**4.039.31**
Growth %								
		2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009
pharmacies		7.38	7.25	-0.42	-1.94	6.28	13.21	9.93
Hospitals						8.46	(°°) 6.40	(°°) 5.20
Total						6.96	11.07	850

(*) Net NIHDI expenditures in public pharmacies calculated on the basis of
a. the available data to and including August 2008 (Pharmanet)
b. conversion of IMS-data (available to and including December 2008) for the categories with a correlation IMS-Pharmanet $r^2>0.75$ for September 2008 to and including December 2008
c. linear extrapolation for 2008 and 2009 for remaining data

(°) Net NIHDI expenditures for hospitals based on docPH data for 2007 and the calculated growth percentages

(°°) Growth percentages for hospitals calculated on the basis of
a. The available docPH data: first semester 2006 to and including second semester 2007 (NIHDI data), whereby total expenditures = expenditures ambulatory + expenditures outside of the fixed limit + 4 x expenditures within the fixed limit
b. conversion of IMS-data (data to and including the third quarter 2008) for the categories (ATC3 level) with a correlation IMS-doc PH $r^2 > 0.75$ for the first three quarters 2008
c. linear extrapolation for 2008 and 2009 for remaining data

The nature of the available data and the technique used (hospitals) do not allow us to generate this data set in the same manner for the period 2002 – 2005 for hospitals.

The positive growth that was estimated in the previous report for public pharmacies for 2008 at 11.9 % (Pharmanet data to and including February 2008, IMS data to and including June 2008) is being estimated on the basis of the actual available data (Pharmanet data to August 2008, IMS data to November 2008) at a growth of 13.21%. For 2009, a growth figure of 9.93% is anticipated.

A significant part of the strong rise in the increase of expenditures in public pharmacies is due to the integration of the low risks for self-employed workers as of 1 January 2008 (+ 6.2%).

For the forecasting of the growth figures in the hospital environment, a method analogous to the one used in estimating the evolution of the expenditures in public pharmacies (via combination of IMS data and docPH-data) is applied for the first time.
On the basis of this technique, a levelling-off of the growth in expenditures in hospitals is anticipated.

The global growth of the expenditures for reimbursable pharmaceutical specialities for 2009 is estimated at 8.5%.

The most recent Pharmanet data (to and including November 2008) confirm the major increase of the expenditures for drugs in public pharmacies.
For 2008, the data were extrapolated for 12 months.

Table I.2. Pharmanet dataset (update to and including November 2008): evolution of the net annual NIHDI expenditures for drugs 2002 – 2008 (November) in millions of EURO

	2002	2003	2004	2005	2006	2007	2008
net NIHDI (millions of EURO)	1.921.5	2.062.1	2.207.8	2.201.9	2.159.7	2.296.6	2.592.2
% increase compared with the previous year	***7.29***	***7.32***	***7.06***	***-0.27***	***-1.92***	***6.34***	***12.87***

The most recent IMS data indicate another evolution of the expenditures. IMS data do not, however, take into account the patients' own contributions (capped), for example. A relative higher number of 'expensive' drugs can result in faster growing expenditures for the health insurance.
The increase of the contribution in drug expenditures for self-employed workers (incorporation of 'low risks') is for 2008 in public pharmacies estimated at 143 million EURO (Table 3.1.7.2. in the permanent audit of May 2009).
Excluding this amount, the increase in the expenditures compared with 2007 would be 6.7 %, which corresponds to the increase that is also noted in the IMS data.

Table I.3. IMS dataset: evolution of the gross turnover of reimbursable drugs and 'moving annual total' 2002 – 2009, in millions of EURO

	2002	2003	2004	2005	2006	2007	2008
total	2.571.9	2.784.7	2.926.6	3.005.5	3.005.6	3.159.8	3.368.4
% increase compared with the previous year		***8.3***	***5.1***	***2.7***	***0.0***	***5.1***	***6.6***

MAT **(April)**	2002	2003	2004	2005	2006	2007	2008	2009
'Moving Annual Total'	2.451.5	2.649.9	2.829.2	2.969.3	3.000.9	3.035.5	3.253.3	3.394.9
% increase compared with the previous year		***8.1***	***6.8***	***5.0***	***1.1***	***1.2***	***7.2***	***4.4***

Likewise, the most recent NIHDI data for what concerns the posted expenditures (doc N – permanent audit of May 2009 – key Table 3.1.1.) confirm the evolution.

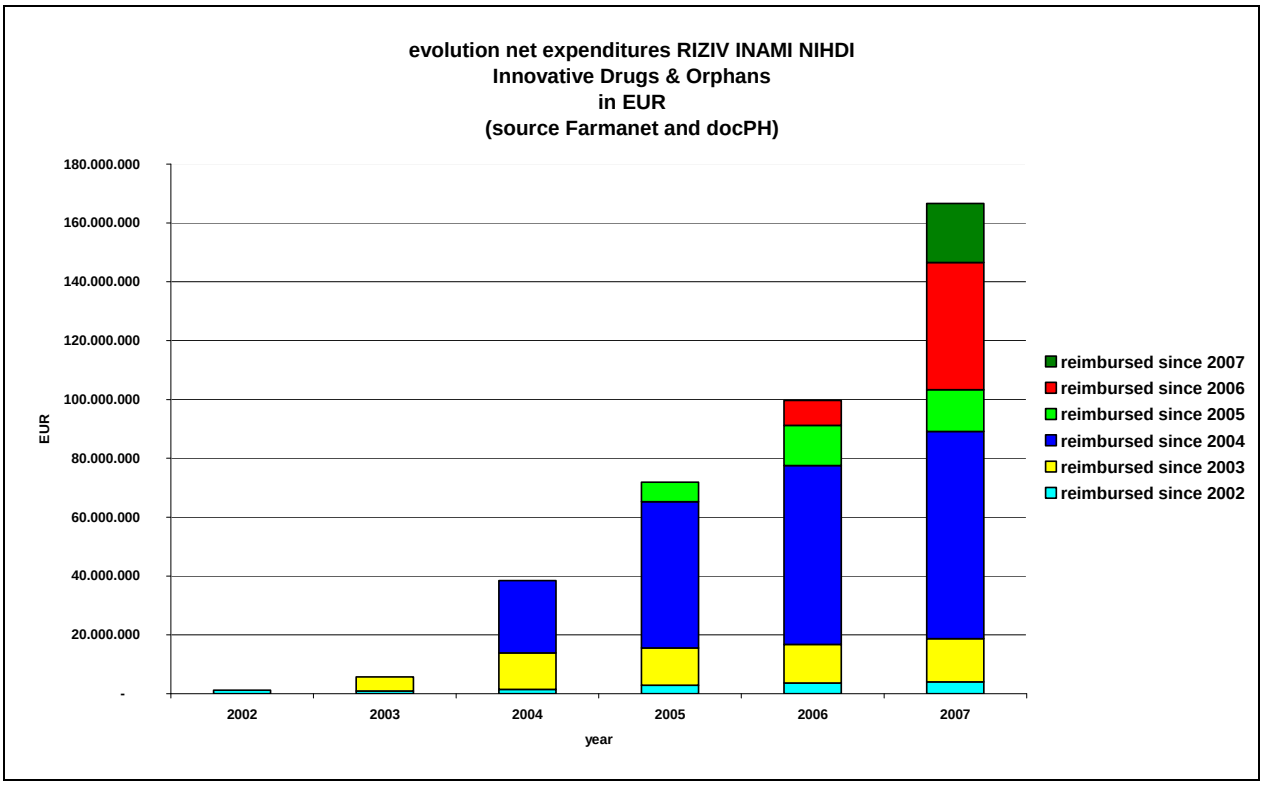
Table I.4. docN dataset: evolution of the posted expenditures on an annual basis: total specialities, in millions of EURO (source permanent audit of May 2009 – key Table 3.1.1.)

	2003	2004	2005	2006	2007	2008
public pharmacies	2.015.3	2.179.8	2.205.5	2.155.1	2.288.8	2.568.9
hospitals – ambulatory patients	326.6	404.0	451.3	477.7	570.0	671.8
hospitals – hospitalised patients	474.6	512.7	513.5	503.0	502.3	510.2
Total	**2.816.5**	**3.096.4**	**3.170.3**	**3.135.8**	**3.361.2**	**3.750.8**
evolution in %						
public pharmacies		8.2	1.2	-2.3	6.2	12.2
hospitals - ambulatory patients		2.7	11.7	5.8	19.3	17.9
hospitals – hospitalised patients		8.0	0.2	-2.0	-0.1	1.6
Total		**9.9**	**2.4**	**-1.1**	**7.2**	**11.6**

I.2. Evolution of the expenditures for class 1 drugs and orphan drugs (public pharmacies and hospitals)

From the graph that shows the expenditures of innovative and orphan drugs in public pharmacies and hospitals from 2002 to and including 2007, it may be deduced that the expenditures for this group of drugs may in 2009 increase to 230 million euro (= 8% of the entire drug budget for 2009).

Figure I.1. Evolution of the expenditures for class 1 drugs (approved class 1 qualification) and orphan drugs (public pharmacies and hospitals)



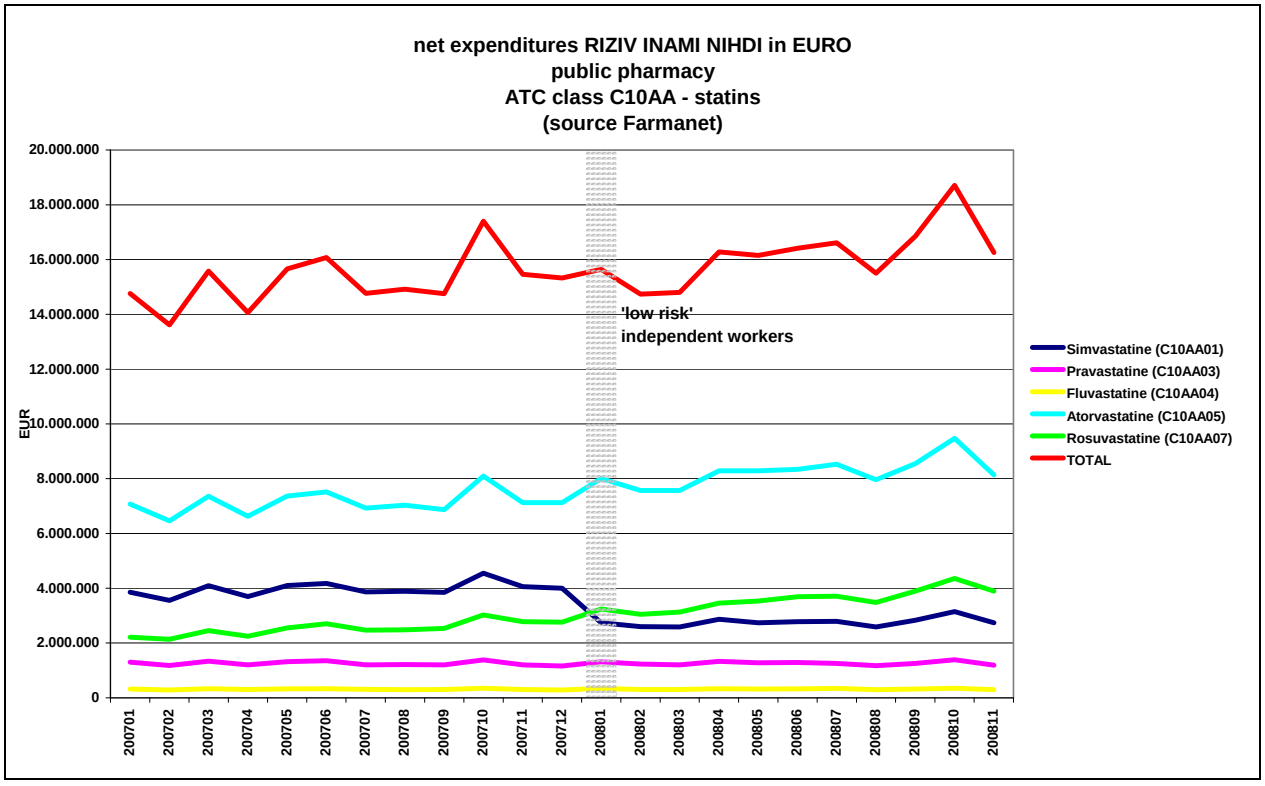
These expenditures still need to be increased with the expenditures in the public pharmacies for the orphan drug Glivec® (L01X) that in 2007 **increased to more than 20 million EUR** (net expenditures NIHDI).

I.3. Global measures and trends exerting an impact on the expenditures for drugs in public pharmacies and in hospitals, plus explanatory factors

I.3.1. Revision by group for budgetary reasons (the 'KIWI' procedure)

For the revision by group for budgetary reasons (the '**KIWI**' procedure) for the specialities containing simvastatin as an active ingredient, savings of 14.6 million euro on the drug budget were estimated as of January 2008.
Globally, the expenditures for the statins rose in 2008 compared with 2007 by 11.7 million euro (for 2007 vs. 2006 this was 16.8 million euro).
The expenditures for simvastatin decreased by 14.5 million euro; however, thess savings are cancelled out by an increase in the expenditures for atorvastatin (+ 1,4 million euro) and rosuvastatin (+ 12.7 million euro).

Figure I.2. net NIHDI expenditures for statins 2007 – 2008 (source Pharmanet)



The data available for the numbers of patients that are being treated with statins show a recurring increase since 2005 of some 10%. At this moment, more than 1 million patients are being treated with this type of drug in Belgium.

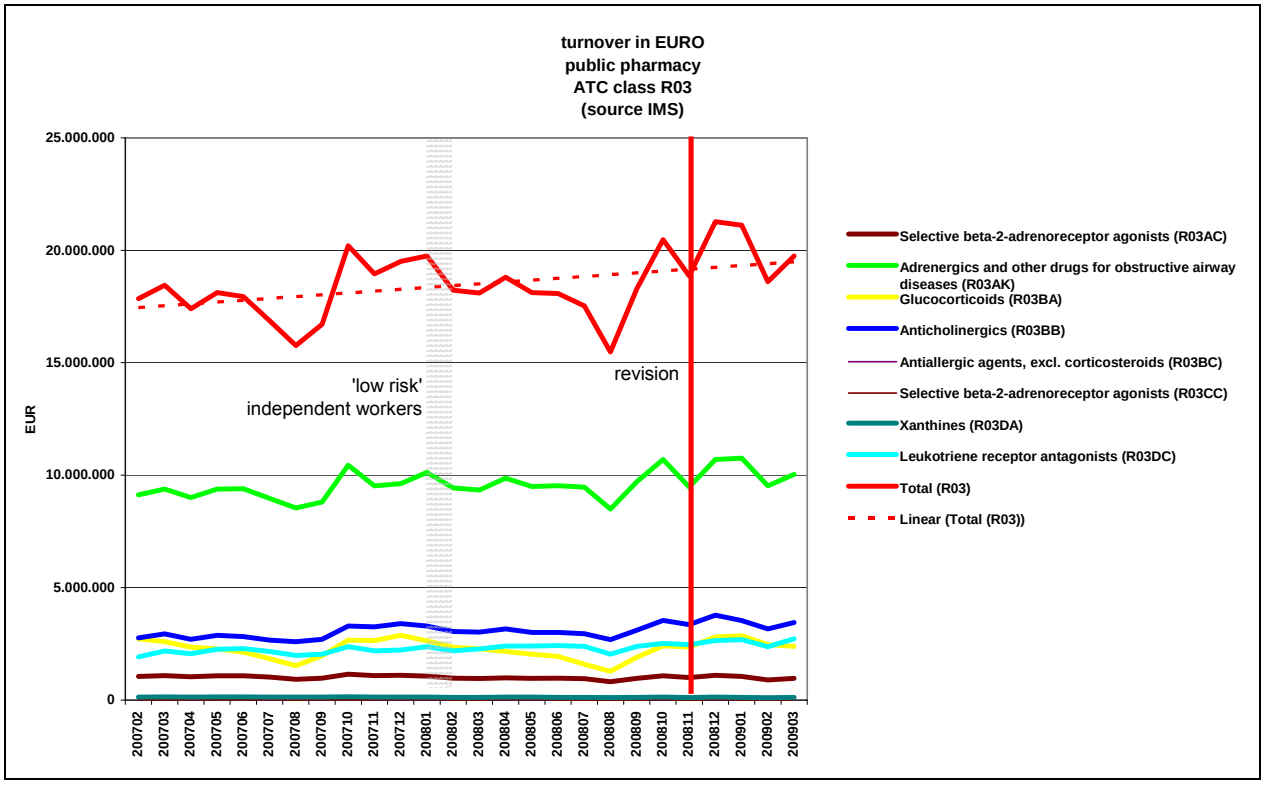
Table I.5. Evolution of the number of patients (source Cell Pharmanet)

	# patients				evolution in %		
	2004	2005	2006	2007	2004-2005	2005-2006	2006-2007
SIMVASTATINE	305.775	402.691	466.220	516.779	31.7	15.8	10.8
PRAVASTATINE	107.888	115.810	118.843	118.598	7.3	2.6	-0.2
FLUVASTATINE	26.762	2.384	20.751	20.101	-12.6	-11.3	-3.1
ATORVASTATIN	260.380	254.952	251.820	259.787	-2.1	-1.2	3.2
ROSUVASTATIN	49.556	82.437	112.163	148.279	66.4	36.1	32.2
	750.361	**879.274**	**969.797**	**1.06.544**	**17.2**	**10.3**	**9.7**

I.3.2. Chapter II – Control a posteriori

As a result of the implementation of the recommendations for specialities used in the treatment of **asthma and COPD,** the CRM (Commission for Reimbursement of Medicines) estimated a reduction in the drug and health care budget from 1 to 5% *(source: CRM budget impact estimation of the revision by group).*
From IMS data to and including March 2009, it may be deduced, however, that the expenditures for the R03 class have slightly increased since the putting into operation of the revision by group (November 2008 – scored with a vertical line on the graph), and this primarily because of the increase in the expenditures for the combinations sympathicomimeticum-corticosteroid (Seretide ®, Symbicort ®). Taking into account the seasonal effect, it is too early to be able to make an assessment of the ultimate effect of the revision by group.

Figure I.3. Total expenditures R03 class for 2007 – March 2009 (source IMS)



I.3.3. Other

- The fixed reimbursement of the specialities used in the treatment of female sterility, in effect since 1 January 2009, will lead to a better management and a stabilisation of the expenditures for these specialities.

- The budgetary impact as a consequence of the inclusion of the speciality Avastin® (December 2008) on the list of reimbursable drugs is estimated at 12.5 million euro for the first year, 15.8 million euro for the second year, and 21.4 million euro for the third year.

- As a result of the inclusion of the speciality Asaflow® on the list of reimbursable drugs (September 2008), net savings on the expenditures for the speciality Plavix® could be realized of up to 6 million euro on an annual basis. From IMS-data, it appears that the expenditures for Plavix® remain stable. The expenditures for Asaflow® and generic drugs are dropping as a result of the significant price decrease at the moment of inclusion on the

list of reimbursable specialities; however, the use of these specialities has increased, primarily, or even exclusively, because of the growing use of Asaflow® 80 mg 168 pills.

Figure I.4. Total expenditures for Plavix® and Asaflow® (originators + generics) (source IMS)

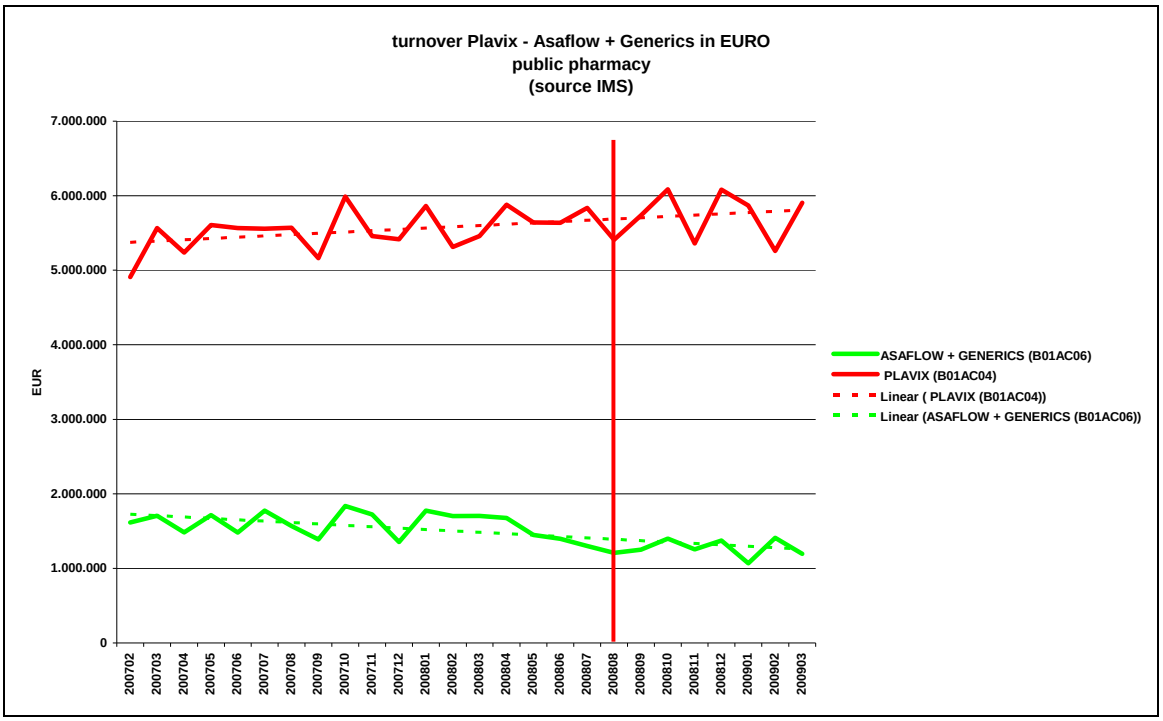
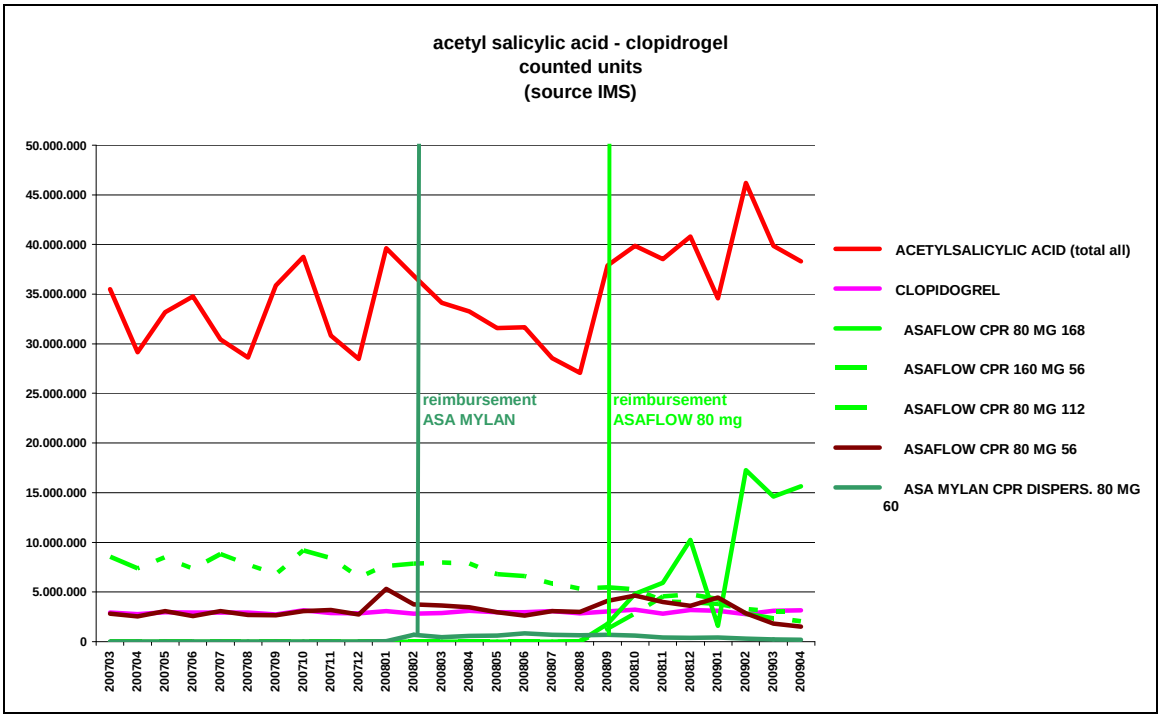


Figure I.5. Total use (in 'counted units') for Plavix® and acetyl salicylic acid (source IMS)



- The molecular entities below are/will be included in the reference reimbursement scheme and, by steady and unchanged used, will result in the stated savings for the speciality.
  The total savings in case of unchanged use amount to 49.1 million EURO:

Magnegita	Magnevist®	January 2009	1 million euro
Epirubicin	Farmorubicine®	January 2009	1.8 million euro
Ropinirol	Requip®	January 2009	1.1 million euro
Perindopril	Coversyl®	January 2009	7.9 million euro
Octreotide	Sandostatine®	January 2009	3.6 million euro
Pantoprazole	Pantozol®	May 2009	11.2 million euro
Irinosin	Campto®	May 2009	3.3 million euro
Midazolam	Dormicum®	May 2009	0.6 million euro
Venlafaxine	Efexor-exel®	May 2009	3.2 million euro
Aceclofenac	Biofenac®	May 2009	1.5 million euro
Montelukast	Singulair®	August 2009	5.9 million euro
Topiramate	Topamax®	October 2009	1.7 million euro
Piperacillin/tazobactam	Tazocin®	October 2009	6.3 million euro

  Comment: The savings resulting from the entering into operation of the reference reimbursement scheme for pantoprazole could be voided by the transfer of the generic drugs from Chapter IV to Chapter II. To this effect, the generics have, in fact, been subject to an additional 40% lowering of the price.

- Article 159 of the Programme Law states that, on 1 May 2009, the reimbursement base of the pharmaceutical specialities needs to be lowered (subject to modularisation) so that savings of 1.95% can be realized on the turnover of 2007 for every applicant.
  The savings effected by this measure are estimated at 90.5 million euro (including the specialities for which on 1 May 2009 a reference pricing scheme was implemented – 11.2 million EURO – and further including the additional lowering of the reimbursement base rate by 2.5% of specialities for which on 1 May 2009 the reference pricing system had already been of application for a period of 2 years – 15.2 million EURO)).

- The physicians-health insurance funds agreement 2009-2010 (the Medico-Mut agreement), point 6, states that as far as there exists no indication to the contrary and the therapeutic goals are realized, in at least 8 out of 10 cases at the start of a treatment, a choice be made for one of the least costly molecular entities from the drug class in question (list of molecular entities: see NIHDI website – 04-05-2009 - Physicians: Feedback drugs ingevolge akkoord artsen-ziekenfondsen).
  The savings that can be realized by this method are estimated at 42 million euro.

I.4. Comparison of the budget impacts as estimated by CRM with the real expenditures for innovative and orphan drugs

With his or her reimbursement application, the applicant provides data concerning the anticipated use and the costs of the speciality. Based on these data, an estimation will be made of the budget impact. The budget impact estimation can be carried out both for the drug budget and for the global health insurance budget, whereby generally no distinction is made between the cost of the reimbursement of the product and the incremental cost (that is to say, taking into account the alternatives that are to replace the new product) on the drug budget and the possible net increased cost for the budget of the health insurance.

From the annual reports for the orphan drugs (internal data), it may be concluded that the forecast expenditures per patient are fairly well in line with the real expenditures per patient.

For the class 1 drugs, greater deviations are observed between the estimated and the real expenditures. Roughly, the under-estimations are being compensated for by the over-estimations, by which the total forecast corresponds with the total real expenditures; only in some instances can there be question of an accurately estimated budget impact. Chronic disorders are, it appears, more readily under-estimated.
Globally, it may be concluded that in approximately 80% of the applications for reimbursement, or applications to change the reimbursement modalities, the budget impact estimations do not correspond to the ultimately realized expenditures.
It is also to be noted that the drugs for which, in contrast, a reliable budget impact estimation was advanced, cannot be confined to one single area of application but they belong to all therapeutic classes.

This then confirms how difficult it is, even following a variety of (mathematical) models and exercises, to predict the future. These findings are in line with those of a Dutch study (Scientific platform 2008;2(9): 212-16 Costs of drugs are difficult to predict): this study mentions a deviation for the real expenditures vis-à-vis the estimated budget impacts situated between 1 to 1132%. Where a comparison of the real expenditures with the budget impacts as estimated by CRM is possible, (that is to say, when the estimated budget impacts are represented as the net increased cost of the new drug), deviates are calculated that are lying between 1 and 400%.

There is clearly a need for unambiguous guidelines concerning budget impact estimation. In the literature, one finds a limited number of guidelines, and, recently, ISPOR published the results of the working group on budget impact concerning cost-effective analysis (Value Health. 2007 Sep-Oct;10(5):336-47); yet, from a pragmatic/practical standpoint, it seems advisable to already advance a number of points on the basis of the herein described findings.

The determination of the product-related budget impact was in the analyses of CRM not always equally evident. Sometimes, the budget impact was indirectly expressed in terms of savings for the NIHDI. When a figure was given concerning the use of the product, this was not always done per year and, likewise, not always for the first three years. Furthermore, not all information concerning the budget impact was always taken directly from the original dossier.

Summarized, the following advice may be formulated:
Both for the evaluation and for the setting up of the budget impact analyses, and irrespective of the method used to arrive at figures, the following elements are desirable:

- It must be possible to relate the proposed figures directly to the drug, broken down per available packaging.
- The budget impact analysis must be presented on an annual basis and for a minimum of three consecutive years (starting as of the reimbursement)
- The figures need to be provided, both in terms of value (ex factory) and of units, (this is to simplify recalculations in the event of any possible price adjustments later on)
- The anticipated budget impact needs to be broken down in hospital and ambulant use
- The anticipated number of treatments and patients treated per year needs to be estimated.

II. EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES IN THE PUBLIC PHARMACIES

II.1. General

Table II.1. Net annual expenditures NIHDI for drugs 2002 – 2009

	2002	2003	2004	2005	2006	2007	*2008	*2009
Net annual expenditures NIHDI x 1.000.000 €	**1.921.59**	**2.063.46**	**2.213.13**	**2.203.74**	**2.161.01**	**2.296.73**	**2.600.12**	**2.858.24**

	2001-2002	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009
growth %	**7.25**	**7.37**	**7.25**	**-0.42**	**-1.94**	**6.28**	**1.21**	**9.93**

Table II.2. Net annual expenditures NIHDI for drugs in public pharmacies top 80%

	Denomination	Growth 2006-2007	Growth 2007-2008	Net NIHDI 2008	Growth 2008-2009
	TOTAL	6.3%	13,2%	2.600.12,685	9,9%
C10A!	LIPID MODIFYING AGENTS, PLAIN	11.0%	6,0%	209.831.456	6,5%
N06A	ANTIDEPRESSANTS	6.7%	10.6%	158.379.932	7,3%
L04A	IMMUNOSUPPRESSANTS	18.9%	30.9%	147.748.187	22.8%
A02B!	DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE	2.5%	17,9%	140.585.229	12.4%
B01A	ANTITHROMBOTIC AGENTS	2.2%	12.6%	106.770.052	10.3%
R03A	ADRENERGICS, INHALANTS	2.9%	8,9%	10,704.249	8,1%
N05A	ANTIPSYCHOTICS	8.9%	4,9%	94.364.340	6,3%
A10A	INSULINS AND ANALOGUES	6.7%	13,3%	67.69,447	9,4%
L03A!	IMMUNOSTIMULANTS	3.0%	9,2%	65.059.177	6,6%
C07A!	BETA BLOCKING AGENTS	2.7%	11.4%	62.811.201	8,4%
C09A	ACE INHIBITORS, PLAIN	6.4%	12.7%	62.292.041	8,3%
J05A	DIRECT ACTING ANTIVIRALS	14.2%	14,3%	61.257.529	10.9%
J07B!	VIRAL VACCINES	216.7%	146,7%	61.150.106	47,6%
C09C!	ANGIOTENSIN II ANTAGONISTS, PLAIN	3.7%	7,6%	60.630.036	5,1%
N02A	OPIOIDS	0.8%	11.5%	59.748.069	8,8%
N03A	ANTIEPILEPTICS	12.9%	14,4%	54.957.171	12.4%
J01C	BETA-LACTAM ANTIBACTERIALS, PENICILLINS	9.1%	13,1%	51.116.146	6,6%
A10B	BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	4.4%	13,8%	51.075.638	11.0%
M05B	DRUGS AFFECTING BONES AND MINERALIZATION	9.8%	6,1%	50.757.842	0.7%
R03B	OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS	8.6%	7,2%	49.506.966	9,9%
M01A!	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	-0.7%	6,4%	49.080.501	3,5%
C08C!	SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	4.9%	12.3%	48.659.842	8,8%
C09D	ANGIOTENSIN II ANTAGONISTS, COMBINATIONS	16.8%	28,0%	48.01,523	19,1%
B02B!	VITAMIN K AND OTHER HEMOSTATICS	9.4%	12.6%	46.079.244	9,6%
L02B	HORMONE ANTAGONISTS AND RELATED AGENTS	18.2%	21.3%	41.756.253	15,3%
C01D	VASODILATORS USED IN CARDIAC DISEASES	-5.3%	0.2%	37.456.128	-0.5%
N06D	ANTI-DEMENTIA DRUGS	13.2%	15,0%	30.849.321	11.7%
L02A!	HORMONES AND RELATED AGENTS	-0.9%	1.4%	29.447.176	-0.6%
N04B	DOPAMINERGIC AGENTS	11.0%	9,9%	27.242.194	7,3%
L01X!	OTHER ANTINEOPLASTIC AGENTS	11.6%	22.5%	26.751.610	15,2%

The overview of the expenditures and the *anticipated* growth per ATC3-class (Table II.2) shows that **30 of the 172 classes** are accountable for **80% of the expenditures** in public pharmacies**.**

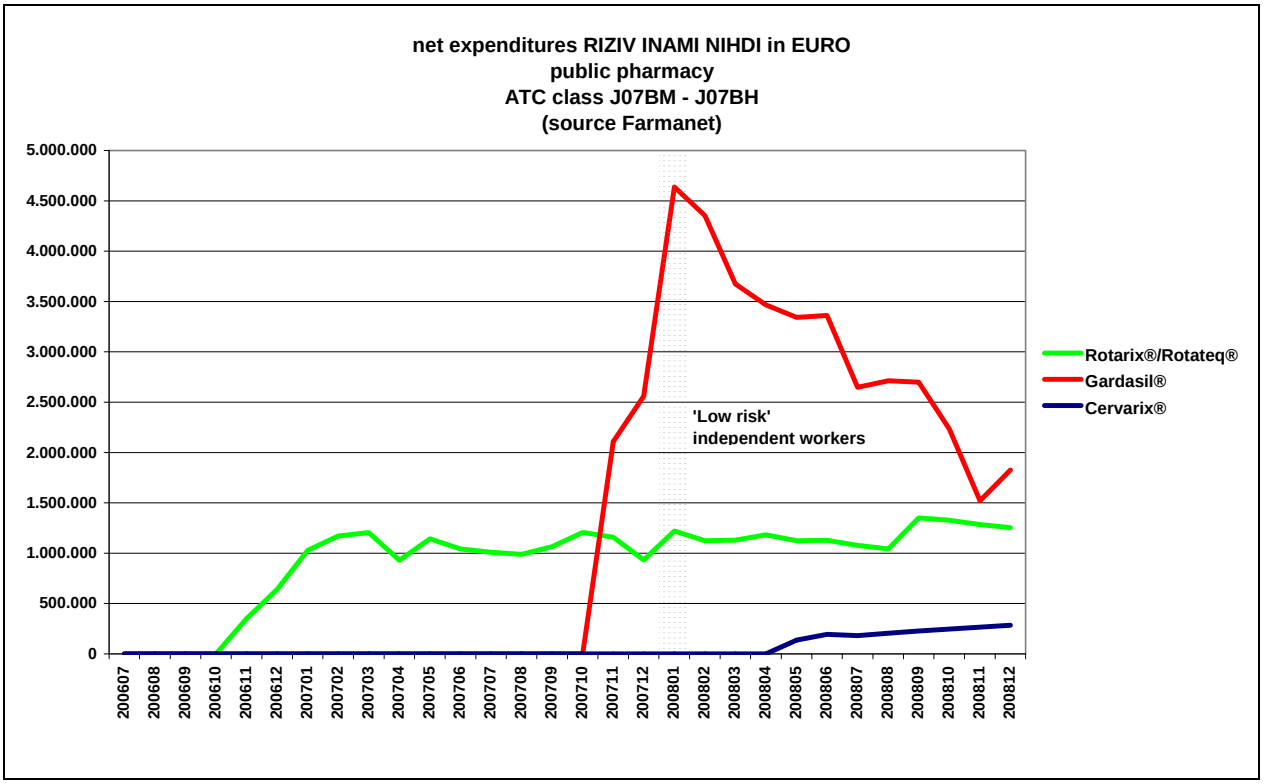
(*) Net NIHDI expenditures in public pharmacies calculated on the basis of
a. the available data to and including August 2008 (Pharmanet)
b. conversion of IMS-data (available to and including December 2008) for the categories with a correlation IMS-Pharmanet $r^2>0.75$ for September 2008 to and including December 2008
c. linear extrapolation for 2008 and 2009 for remaining data
The categories with a correlation IMS-Pharmanet $r^2<0.75$ are indicated with an exclamation mark !

In Section II.2., a number of these categories of drugs with a significant evolution in the expenditures will be discussed in more detail.

II.2. Analysis

II.2.1. Vaccines HPV/rotavirus

Figure II.1. Net expenditures for vaccines HPV/rotavirus in public pharmacies



Gardasil®/Cervarix® (vaccines HPV – J07BM)

Within the context of the inclusion of the vaccines for the prevention of cervical cancer on the list of the reimbursable pharmaceutical specialities - ATC 4 J07BM - (GARDASIL in November 2007 and CERVARIX in May 2008), additional expenditures of 45 million euro were foreseen for the year 2008. The most recent estimation of the expenditures for 2008 gives a figure of 38 million euro (- 15% vis-à-vis the forecasts): a new trend towards a decrease in the expenditures has become noticeable as of June 2008. This trend will in all likelihood not be continued in 2009, given the expansion of the reimbursements on 01.12.2008 (to and including 18 years).

Rotarix®/Rotateq® (vaccines rotavirus – J07BH)

The budget impact of the reimbursement of the vaccine for the rotavirus, for first three years of its commercialisation, was upon submission of the dossier estimated as follows:

year 1	2.029.821 EURO
year 2	4.567.098 EURO
year 3	5.861.109 EURO

For the third year, the applicant used a vaccination ratio of 50% of the children to demonstrate these estimations.
In contrast, in the maximisation hypothesis, where 90% of the children would be vaccinated against the rotavirus, the expenditures were estimated at 13.627.800 euro/year (113.000 children x 134 euro x 90%).

The High Council for Public Health, whose recommendations concerning the vaccination against the rota- virus were not yet available during the evaluation of the Rotarix® reimbursement dossier, has taken on this vaccination in its basic vaccination calendar for the children.

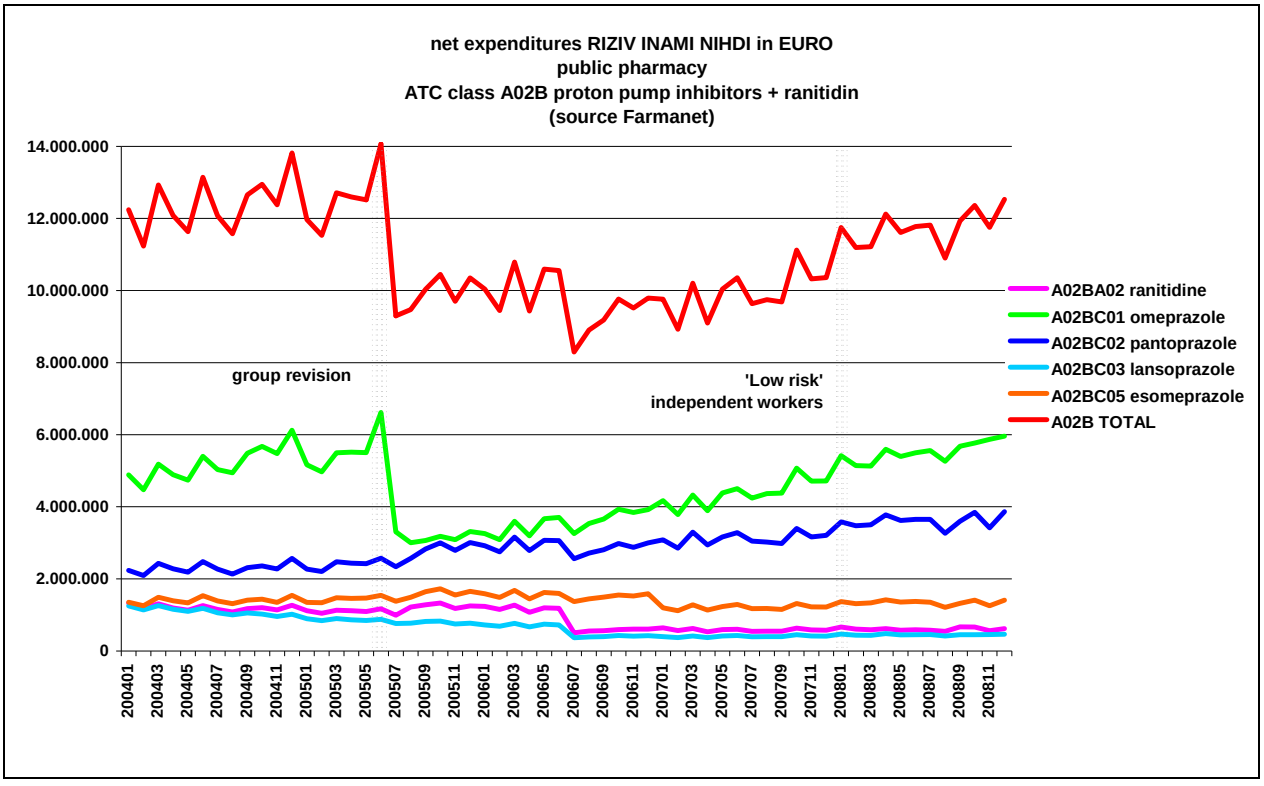
The real expenditures (with extrapolation for 09-11/2008) approximate the maximal estimations, which means that the vaccination ratio of the infants approaches 90%:

Year 1 (11/2006-11/2007) 11.785.053 EURO
Year 2 (11/2007-11/2008) 13.807.919 EURO

In France and in the Netherlands, the vaccinations against the rotavirus have neither been introduced into the vaccination calendar, nor are they reimbursable.
France : 'In view of the current epidemiology, the CSHPF (High Council of Public Hygiene in France**)** does not recommend the systematic anti-rotavirus vaccination for infants under 6 months of age. On the contrary, they advise people to rather take necessary actions to provide optimum care in the case of acute gastro-enteritis' (12/2006).
the Netherlands : 'the CFH (Commission for Pharmaceutical Aid) has also decided that there are still too few data available to be able to determine an added therapeutic value. The Commission concludes that the claimed effectiveness of the rotavirus vaccine is not adequately supported by the findings in the model study used (report CFH Rotarix, 22-10-2007).

II.2.2. Gastric acid secretion inhibitors

Figure II.2. Net expenditures for gastric acid secretion inhibitors in public pharmacies

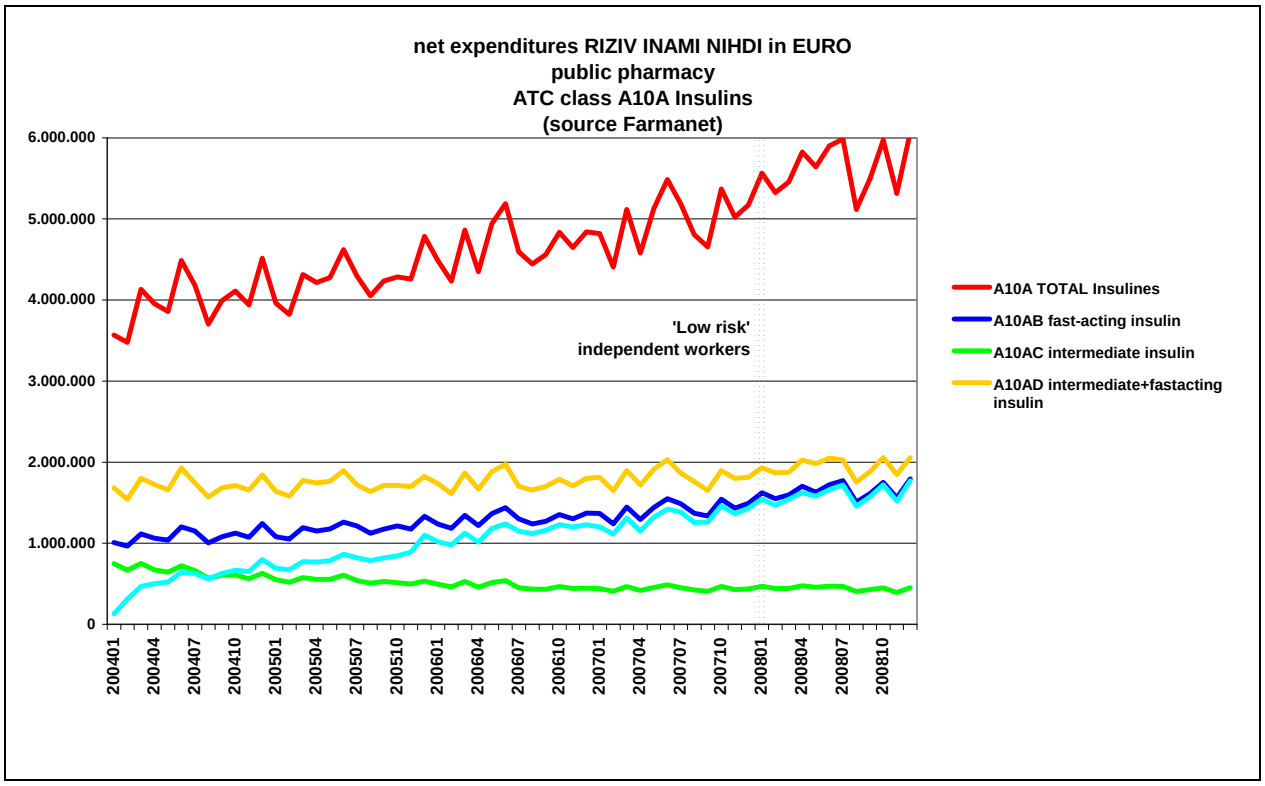


The notable rise of 13.7 million € that was forecast for 2008 for the class of the 'gastric acid secretion inhibitors' (A02B), will, on the basis of recent figures up to and including August 2008, even be exceeded further. For 2008, the net NIHDI expenditures for this class are being estimated at 140.6 million € instead of the anticipated 135.5 million €.

This persistent rise is almost entirely attributable to the PPIs omeprazole and pantoprazole. The evolution of the pantoprazoles for 2009 will on the one hand, be influenced by the reimbursement of the generics as of May 2009. At that moment, the conditions for reimbursement will change as these specialities are to be entered into Chapter II with the same recommendations as applied to the omeprazoles; on the other hand, the reference pricing scheme for pantoprazole will enter into operation on 01-10-2009.

II.2.3. insulin analogues

Figure II.3. Net expenditures for insulins in public pharmacies



For 2008, the expenditures for the insulins keep rising considerably (67.5 million €), with a real increase of 13.3% for 2007-2008, which remains in line with the estimated increase of 14.4% from the previous MORSE-report. The expenditures for the NIHDI for the long-acting insulin preparations (Levemir® and Lantus®) equal those for the fast-acting insulins (Novorapid®, Actrapid®, Apidra® and Humalog®).

Upon evaluation on the molecular level (ATC-5), the major drivers of the increase in the expenditures for 2008 are Lantus®, Novorapid®, and Humalog Mix®. The combination preparation of traditional insulins - Mixtard® - demonstrates a strong decline while Levemir® remains rather at a constant level.
For 2008, the annual expenditures for Lantus® are estimated at 15 million €, while, on inclusion in the list (on January 04), for a constant number of patients, an additional expense of 4.6 million € was earmarked as of the 4th year.

In general, it may be held that the rising expenditures can be attributed to the fact that:
- insulin preparations are used for a lifetime;
- there are many new diagnoses of diabetes mellitus;

- there is a trend to ever more frequently treat diabetes with the more costly types of insulin-analogues (e.g., Novorapid®, Lantus® and Humalog ® (Mix)), and ever less frequently with the human insulin preparations (e.g., Mixtard®, Actrapid®, Humulin®), knowing that the insulin analogues have been included in the list in Chapter IV with specific reimbursement conditions, and that the human insulins are reimbursable in Chapter I.

The French Transparency Commission has decided that the long-acting insulin-analogues Lantus® and Levemir® are to be used
- for type 1-diabetics in the first line
- for type 2-diabetics in the second line for which alternatives are available.
Their alternatives in Belgium are *human* insulin preparations NPH, specifically insulins with an intermediate acting duration.
In contrast to France, Belgium currently only reimburses Levemir® for type 1-diabetics and not for type 2-diabetics in second line, which, however, is the case for Lantus®.

Table II.3. Number of reimbursed DDDs for insulin preparations (ATC class A10A – source Pharmanet) per annum, and observed growth vis-à-vis the previous year

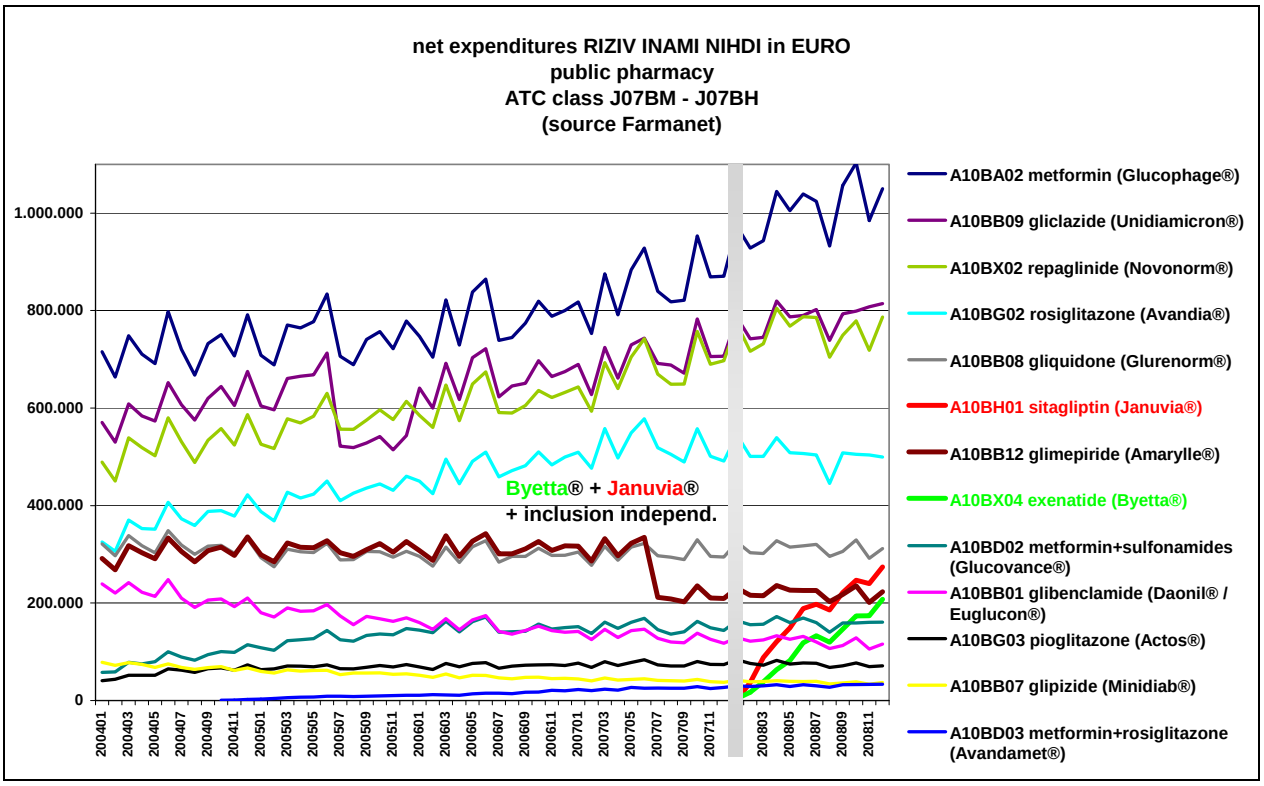
DDD 2004	DDD 2005	DDD 2006	DDD 2007	DDD 2008 (extrapolation 8 months)
43.916.359	45.543.982	48.905.286	52.245.955	57.938.448
7.9%	3.7%	7.4%	6.8%	10.9%

II.2.4. Oral anti-diabetics

Table II.4. Number of reimbursed DDDs in oral anti-diabetics (ATC class A10B – source Pharmanet) per annum and observed growth vis-à-vis the previous year

DDD 2004	DDD 2005	DDD 2006	DDD 2007	DDD 2008 (extrapolation8 months)
107.728.476	110.903.335	115.885.021	121.531.946	134.515.268
5.19%	2.95%	4.49%	4.87%	10.68%

Figure II.4. net expenditures for oral anti-diabetics in public pharmacies – detail



Given that the expenditures of the oral anti-diabetics for 2008 (51 million €) are increasing during 2007-2008 at a rate of 13.8%, and the increase in the DDDs for the oral anti-diabetics amounts to 10.7 %, this indicates that there is a shift in use towards the more expensive, newer oral anti-diabetics. Aside from the notable increase in the use of new anti-diabetics, there is also a strong rise in the use of metformin, a first-choice preparation when medication is necessary to treat type 2-diabetes, certainly in the case of obese patients.

The rising expenditures in 2008 for metformin are due, on the one hand, to the growing number of new diabetes type 2-patients, and, on the other hand to the reimbursement of the new specialities Januvia® and Byetta® since 01/01/2008, which do require an advance and simultaneous treatment with respectively metformin and metformin plus a sulfamide. In 2008, the hypoglycemite sulfamides are, for the first time in many years, again registering an increase in the number of used DDD.

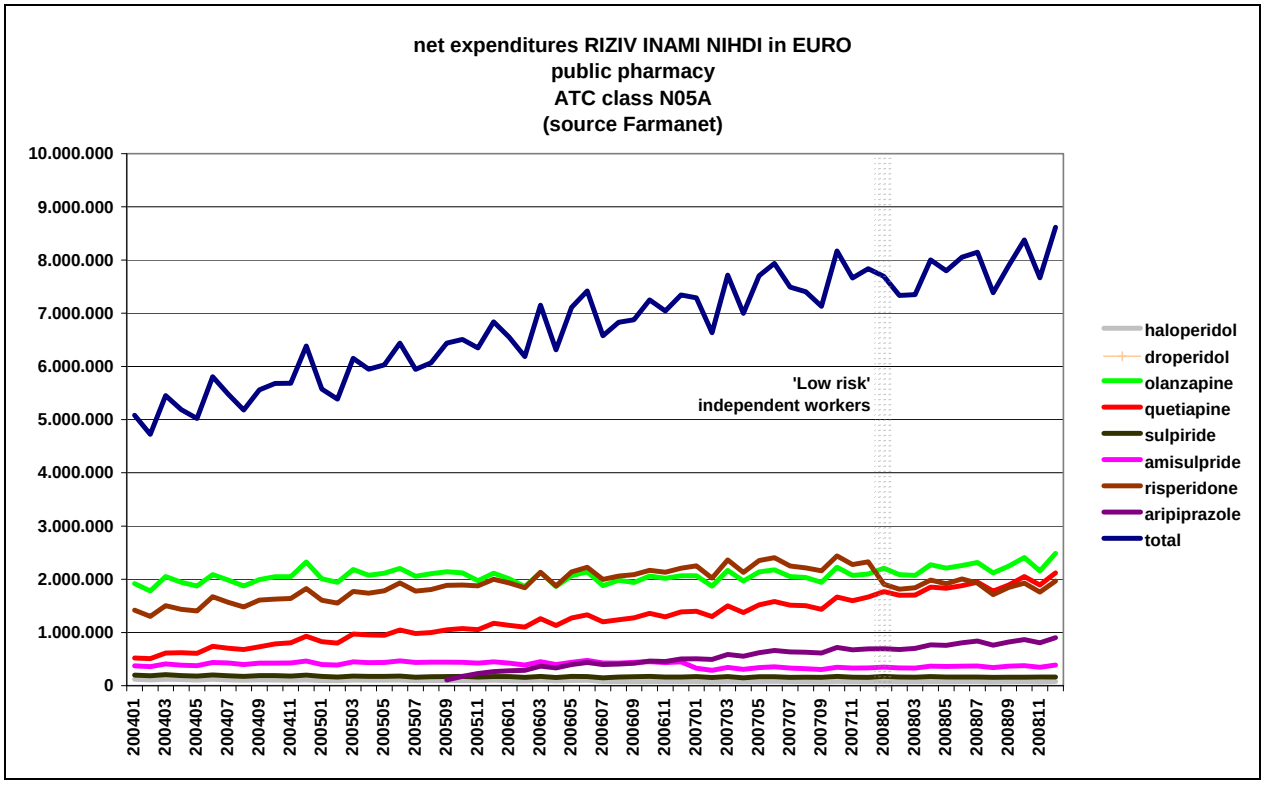
Diabetes is a typical disease associated with western civilization that is the subject of continuous discussions, leading to the introduction of varied and various measures to create personal awareness in patients (diabetes registration card, treatment regime for diabetes patients…).

The class of the glitazones (A10BG) registered a slight decrease in expenditures for 2008 (-3%). This decline is almost completely explainable by a reduced use of rosiglitazone (Avandia®).

The American Food and Drug Administration (FDA) issued on 21 May 2007 a warning regarding the heightened risk of cardiovascular incidents due to rosiglitazone (Avandia ®). According to recent advice from the scientific European and American Diabetes Associations (American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)), rosiglitazone has no place in the treatment of type-2 diabetes, given its unfavourable risk-benefit ratio and the availability of therapeutic alternatives. This advice is based primarily on the results of the ACCORD study, where an increase in the mortality of patients under very intense treatment was recorded. As a consequence of this observation, at the start of 2008, a procedure to change the reimbursement modalities was started whereby, in advance of the treatment, the physician has to certify that he has evaluated the importance of the cardiovascular safety of Avandia® within the context of the global treatment of the patient in question.

II.2.5. Anti-psychotic drugs

Figure II.5. Net expenditures for anti-psychotic drugs in public pharmacies (ATC class N05A – source Pharmanet)

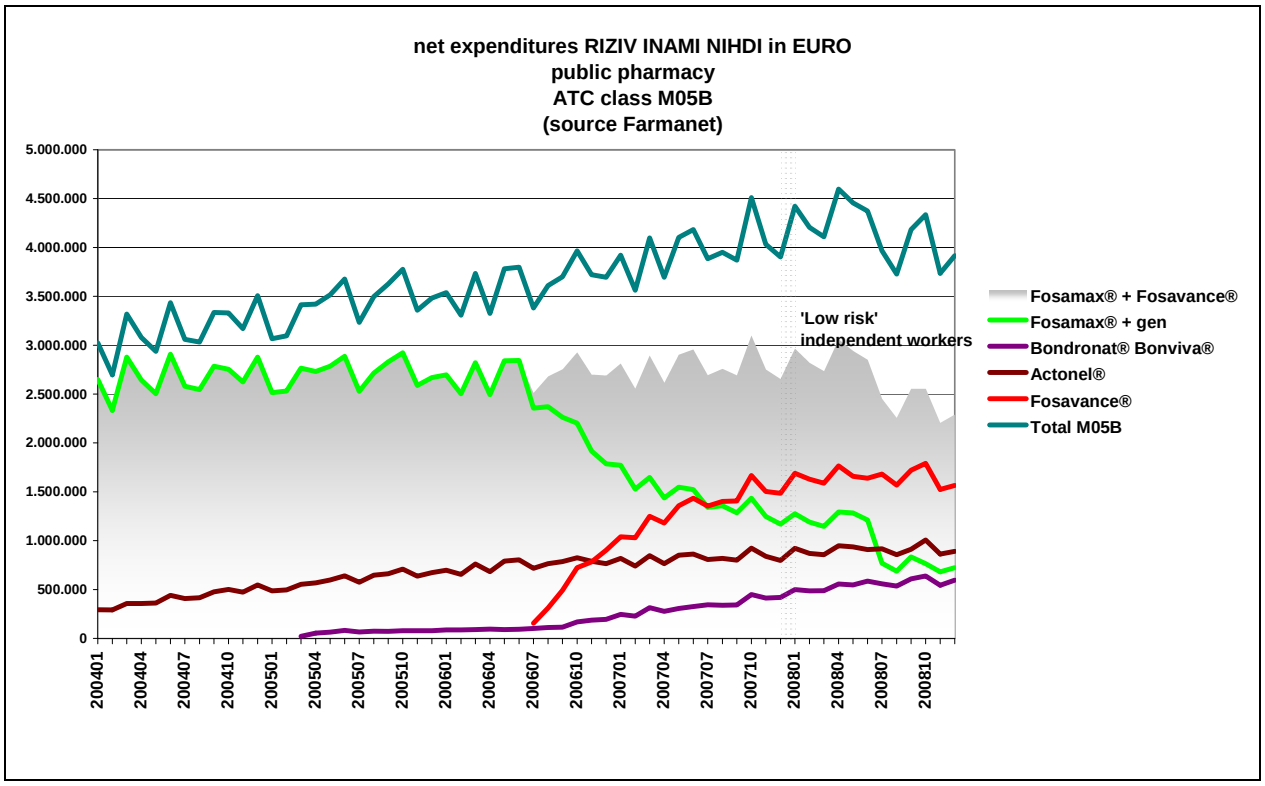


After a slight levelling in the growth of the anti-psychotic drugs (N05A) at the start of 2008, due to the entering into effect of the reference reimbursement scheme for risperidone on 1.01.2008, a growth in total expenditures for this group was again noted (for 2009: + 6 million € or + 6.3 %). The savings thus generated by the reference reimbursement for risperidone have been retained for the entire 2008 year. The expenditures for the other atypical anti-psychotic drugs (Seroquel®, Abilify® and Zyprexa®) keep rising (+ 9%: 2nd semester 2008 versus 2nd semester 2007), and in this way nullify the savings on risperidone at the class level. The introduction of Invega® (paliperidon, metabolite, or risperidone), a new atypical anti-psychotic drug reimbursable since

01.03.2009, makes a further follow-up and monitoring of the expenditures in this drug class desirable.

II.2.6. Drugs affecting bones and mineralisation

Figure II.6. Net expenditures for drugs affecting bones and the mineralisation in public pharmacies (ATC class M05B – source Pharmanet)



For the class M05B, the estimation of the increase of the expenditures was revised downwards. A rise of 6.1% was noted for 2007-2008 (in contrast to 12.7% that was forecast for the previous MORSE report), while for 2008-2009, a stabilisation of the expenditures is anticipated: + 0.7% (versus + 10.3% forecast in the previous MORSE report).

The total expenditures for alendronates (Fosamax® + generics + Fosavance®) rose between 2004 and 2008 only very slightly. On 01.07.2008, the entering into effect of the reference reimbursement scheme for the alendronates in mono-preparation (M05BA04) induced a reduction of 30% in the expenditures for this class, but this exerted merely a limited impact on the total expenditures for the group M05B, given the expansion of the expenditures, in particular, for Bonviva® and Actonel®.
For the purpose of the next report it will be useful to further monitor these expenditures, given that the considerable reductions in the reimbursement base within this group still have to take place in the 2nd semester of 2009.

The specialities Zometa®, Aclasta® (M05B08), and Aredia® (+ generics, M05BA03) are largely supplied in hospitals. The estimation of the expenditures demonstrates a slight drop (- 7% between 2006 Q4 and 2007 Q4) for these specialities.

Table II.5. Expenditures for drugs affecting bones and the mineralisation in hospitals (source docPH)

	2006 Q3	2006 Q4	2007 Q1	2007 Q2	2007 Q3	2007 Q4
ZOMETA	3.953.226	3.816.255	3.792.958	3.623.900	3.599.853	3.536.818
ACLASTA	27.471	33.617	28.804	28.481	36.699	37.374
AREDIA + G	260.470	194.403	189.544	194.403	185.787	187.476

The more recent IMS-data (up to 11/2008) confirm this evolution for Zometa® and Aredia®. Nevertheless, for the speciality Aclasta® we note a strong rise in sales volume between mid-2008 and the end of that year: the expansion of the reimbursement to the treatment of osteoporosis in menopausal women has been in effect since 01.07.2008.
The reimbursement conditions provide since July 2008 only for the reimbursement in cases of contra-indication for oral bifosfonates. In May 2009 (in principle entering into effect on 1 August 2009), the Minister of Social Affairs decided, at the request of the company, to lift this restriction. In addition, in the same decision of the Minister, the reimbursement of Aclasta I.V. for the treatment of osteoporosis in males was granted. Consequently, further monitoring of the expenditures is desirable.

Table II.6. Expenditures for drugs affecting bones and the mineralisation in hospitals (source IMS)

	200801	200802	200803	200804	200805	200806	200807	200808	200809	200810	200811
ZOMETA	1.241.247	1.133.732	1.117.622	1.189.500	1.195.639	1.171.450	1.243.033	1.182.734	1.193.843	1.226.166	1.115.952
ACLASTA	18.785	23.029	23.715	26.455	8.647	18.861	45.000	78.405	120.099	147.692	131.332
AREDIA+G	111.756	106.886	105.550	107.242	96.631	104.762	85.283	95.658	91.553	102.187	87.057

III. EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES IN HOSPITALS

III.1. General

Table III.1. Net annual NIHDI expenditures for drugs in 2006 - 2007 (docPH), with an estimation of the expenditures for 2008 and 2009, based on IMS-BHA data

Net NIHDI expenditures x 1.000.000 EUR

	2006	2007	(°)2008	(°)2009
Hospital	972.88	1.055.16	1.122.69	1.181.07

Growth %

		2006-2007	(°°)2007-2008	(°°)2008-2009
Hospital		8.5	6.4	5.2

(°°) Growth percentages 2008 vs 2007 and 2009 vs 2008 arrived at following the technique as described under point III.4
(°) Net NIHDI expenditures, based on docPH data for 2007 and the calculated growth percentages

Table III.2. Top 80% for drugs in hospitals

Rank 2008	Rank 2007	Fixed	ATC 3		Growth (%) 07-06	total 2008 MORSE (virtual) (*)	Growth (%) 08-07	Growth (%) 09-08
1	1	No	L01X	OTHER ANTINEOPLASTIC AGENTS	42	163.620.071	16.7	14. 3
2	2	No	B03X	OTHER ANTIANEMIC PREPARATIONS	-3.7	90.719.966	-4	-4.7
3	4	No	L04A	IMMUNOSUPPRESSANTS	22.2	67.243.553	17.2	14.3
4	3	Yes	B05B	I.V. SOLUTIONS	-3.1	59.707.693	-1	-3.2
5	8	Yes	V08A	X-RAY CONTRAST MEDIA, IODINATED	-0.5	38.847.407	10.1	8.3
6	5	No	J06B	IMMUNOGLOBULINS	6.8	37.784.008	-1.8	-7.3
7	7	No	L01C!	PLANT ALKALOIDS AND OTHER NATURAL PRODUCTS	-1.9	36.635.216	1.3	1.8
8	10	No	B02B!	VITAMIN K AND OTHER HEMOSTATICS	15.9	36.101.201	8.7	7.9
9	6	Mix	B01A	ANTITHROMBOTIC AGENTS	0.5	35.602.872	-2	-3.4
10	9	Yes	N01A	ANESTHETICS, GENERAL	-1.5	35.488.104	3.6	1
11	11	Yes	J01C!	BETA-LACTAM ANTIBACTERIALS, PENICILLINS	0.6	32.900.370	1.2	2.4
12	12	Mix	J01D	OTHER BETA-LACTAM ANTIBACTERIALS	-0.8	31.228.170	1.2	-0.6
13	13	No	L03A	IMMUNOSTIMULANTS	8.9	27.806.930	4.6	5
14	15	No	L01B	ANTIMETABOLITES	31.5	26.640.191	19.1	16.2
15	17	Mix	A16A	OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	43.3	25.47.105	34.3	27.7
16	14	Yes	N05A!	ANTIPSYCHOTICS	0.2	24.680.543	-0.3	-1.2
17	18	Mix	V03A	ALL OTHER THERAPEUTIC PRODUCTS	0.1	21.172.513	22.6	16.5
18	16	yes	M05B	DRUGS AFFECTING BONES AND MINERALIZATION	-14.1	18.886.144	-1.1	-0.2
19	19	mix	J02A	ANTIMYCOTICS FOR SYSTEMIC USE	-1.1	17.146.782	5.9	4.2
20	20	No	L01D!	CYTOTOXIC ANTIBIOTICS AND RELATED SUBSTANCES	6.6	16.371.995	1.6	0.6
21	21	No	B05A	BLOOD AND RELATED PRODUCTS	-6.9	15.872.639	0.7	-0.3
22	38	No	S01L	OCULAR VASCULAR DISORDER AGENTS	1.5	14.680.522	268.3	59.8

The classes with a correlation IMS-doc PH r2 < 0.75 are identified with the exclamation mark !

(*) expenditures calculated on the basis of (see also under point III.4):

- The available docPH data: first semester 2006 to and including the second semester 2007 (NIHDI data) where total expenditures = expenditures ambulant + expenditures outside of the fixed amount + 4 x expenditures falling within the fixed amount
- Conversion of IMS-data (data to and including the third quarter 2008) for the classes (ATC3 level) with a correlation IMS-docPH $r^2 > 0.75$ for the first three quarters of 2008
- linear extrapolation for 2008 and 2009 for remaining data

The overview of the (virtual) expenditures and the *expected* growth per ATC3-class (Table III.2.) shows that **22 of the 158 classes** are responsible for **80% of the expenditures** in hospitals.

In Section III.3., the evolution of the expenditures for the oncolytic drugs is discussed.

III.2. Fixed budget for drug reimbursements: "forfait"

III.2.1. General

Since 1 July 2006, in the acute hospitals a **fixed budget for drug reimbursement (called "forfait")** for hospitalised patients has been introduced. For these patients, the rule is that, in principle, all drugs fall under the "forfait" scheme.

Nonetheless, a list of exceptions has been published (based on the ATC5 code).
Drugs are excluded either statutorily (such as the orphan drugs, cytostatics. … cf. art 95 §3 b) 3rd paragraph of the Royal Decree of 21.12.2001) or by proposal of the "permanent working group on *forfait* specialities" (if, on the one hand, the active component is of great importance in the medical practice, and on the other hand, the cost might severely limit their administration in the event of a *forfait* reimbursement).

The national *forfait* for drugs in hospitals is determined by means of a link between the Minimal Clinical Data (MKG) and the Financial Data (AZV data).
The reference period for the determination of the amount for the period 1/7/2006-30/6/2007 was 2003. Hence, the reported MKGs coupled to the financial data in 2003 have led to a national drug budget for the drugs included in the *forfait* scheme.
This means that via a total national fixed budget one can arrive at a national drug *forfait* scheme for a well-defined diagnose (APRDRG, All Patients Refined Diagnosis Related Groups) and degree of severity. The total fixed drug budget that is to be allocated to a hospital is thus calculated on the basis of the individual casemix (as reported via MKG).
The casemix of a hospital pertains to the number of hospitalisations per diagnosis and 'severity' level per annum for that particular hospital.

For the period July 2006 (introduction of the *forfait*) until June 2007, the established national budget of the hospital *forfait* is set at 258.9 million EURO (given the start of the introduction of the *forfait* halfway through the year, the amounts are not determined per calendar year but for semester 2 of year x and semester 1 of year x+1)
Depending on the reported casemix (MKG), a hospital will receive one fixed budget (*forfait)*per admission. Indirectly, this means that a hospital will, for a given APRDRG, receive an annual fixed budget (*forfait)*.
The enveloppe that is allocated for the *forfait* is an open enveloppe, meaning that there is no claim for refund and no compensation. The *forfait* is therefore meant rather as an administrative management mechanism than as a means to effect savings.
Also, account is taken of outliers that are to be taken out of the normal *forfait*. This pertains to outliers on the basis of the duration of the hospitalisation.

Also needs to be noted that only the general hospitals with at least a C, D, or E Department qualify for the *forfait* regulation. This therefore excludes the psychiatric hospitals and the so-called isolated chronic Sp and G-hospitals.
In addition, currently only the standard hospitalisation, that is to say, at least one overnight stay, is eligible for the *forfait* (there is therefore no *forfait* for one-day clinics).

The regulation stipulates that for the specialities that fall under the *forfait*, 25% of the reimbursement base will still be billed per speciality. The remaining portion will be covered by a *forfait* per admission.

Because of the partial reimbursement (25% of the reimbursement base is still being billed according to the conventional method, namely billing by number of units used), it is possible to follow the real drug use without it being absorbed by a drug *forfait* total based on APRDRG.

III.2.2. *Forfait* in hospitals: analysis

Currently, three datasets are available that enable an analysis of the evolution of the expenditures for drugs in hospitals:

1. IMS data: commercial data – sales in EURO (ex-factory) on the basis of a (selective) sampling in hospitals
2. docN data: consolidated billing data without differentiation in terms of speciality - net NIHDI expenditures
3. docPH data: consolidated billing data with differentiation per speciality packaging and per type of patient (hospitalised (either entered into the *forfait* scheme or not) – ambulatory) - net NIHDI expenditures

The combination of the IMS and docPH-data makes it possible to conduct detailed analyses.

Table III.3. Quarterly figures net NIHDI expenditures for period 2006-2007 (source docPH – in millions of EURO)

	2006q1	2006q2	2006q3	2006q4	2007q1	2007q2	2007q3	2007q4
Ambulatory	116.5	117.9	118.3	126.0	131.8	135.8	142.0	149.9
hospitalised non- *forfait* pharmaceuticals	127.2	117.9	48.2	40.4	40.6	39.1	39.4	40.4
Hospitalised *forfait* pharmaceuticals	0.0	0.0	16.1	19.5	20.2	19.0	18.0	20.1
Forfait per hospitalisation	0.0	0.0	59,9	64,9	67,7	63,9	60.8	66,5
Total hospitalised	127.2	117.9	124.1	124.8	128.5	121.9	118.1	127.0
Total hospital	**243.7**	**235.9**	**242.5**	**250.8**	**260.3**	**257.8**	**260.1**	**276.9**

Figure III.1. Net NIHDI expenditures for period 2006-2007 (source docPH)

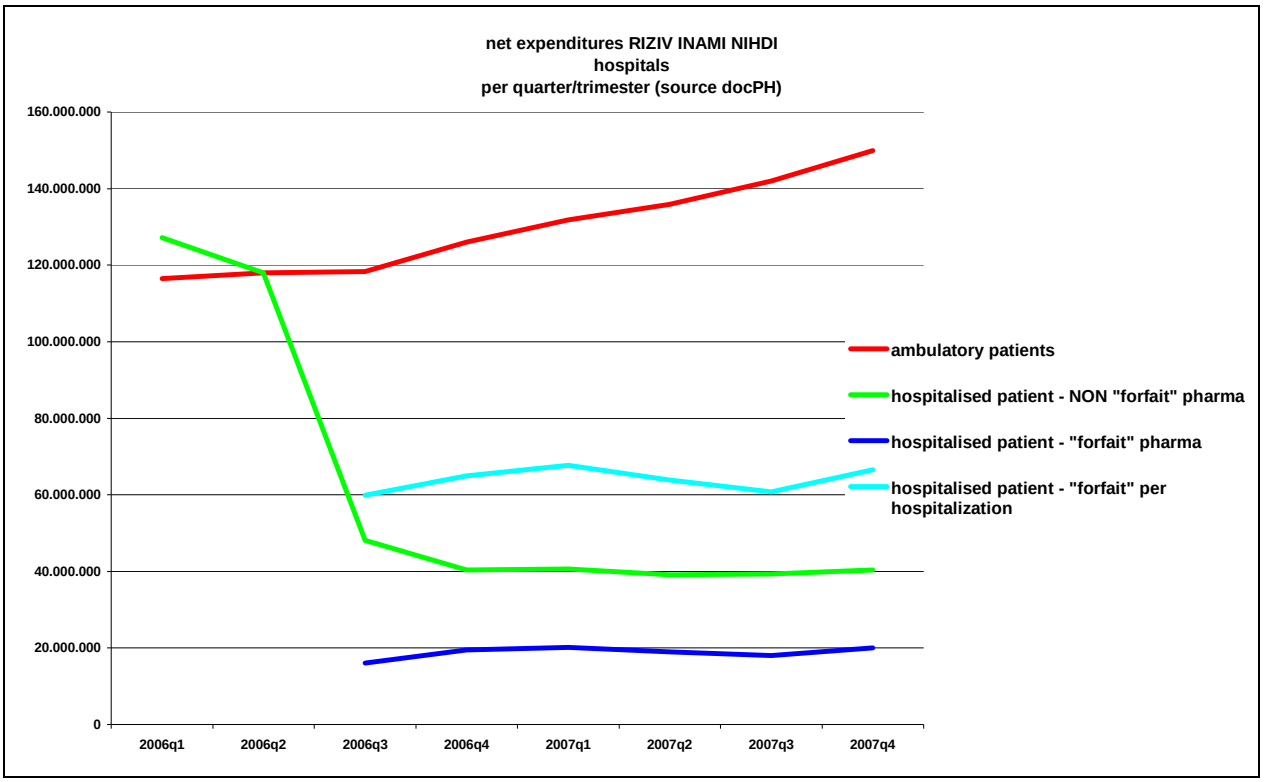


Table III.4. net expenditures NIHDI period 2006-2007 (source docPH – in EURO) – break-down of expenditures hospitals

	2006	2007
Ambulatory patients[1]	478.752.241	559.541.108
Hospitalised patients – NON-*forfait* pharmaceuticals [2]	33.719.541	159.537.774
Hospitalised patients – *forfait* pharmaceuticals [3]	35.588.038	77.195.423
Forfait per admission[4]	124.818.276	258.882.375
Total for hospitalised patients	494.125.855	495.615.572
Total for hospitals	**972.878.096**	**1.055.156.680**

[1]*Ambulatory patients*	*Administered to ambulatory patients in the hospitals, always outside of the forfait (reimbursement base rate 100% of the payment according to the reimbursement category)*
[2]*Hospitalised patients – NON forfait pharmaceuticals*	*Administered to hospitalised patients where the reimbursement falls outside of the forfait* *- it pertains to a drug outside of the forfait (included in the list of exclusions)* *- it pertains to a drug that was administered to a patient:* *- admitted prior to 1.07.2006 (start of the forfait)* *- admitted to a non-acute hospital* *(base for reimbursement 100%, contribution according to the reimbursement category)*
[3]*Hospitalised patients – forfait pharmaceuticals*	*Administering to hospitalised patients in an acute hospital (admission date after 1.07.2006) of a drug included in the forfait* *(payment = 25% of the reimbursement base rate; cancellation of the contribution according to the reimbursement category)*
[4]*Forfait per admission*	*Fixed budget per admission*

Before 1/7/2006, the contribution paid by the NIHDI for <u>all</u> drugs in the hospital was based on a reimbursement category. Except for the reimbursement category A, a portion of the cost price of the administered drug ("non-reimbursable part") was charged to the hospital:
- class A: 0 EURO
- class B: 0.37 EURO per tariff tranche
- class C: 50 % of the reimbursement base rate
- class Cs: 60 % of the reimbursement base rate
- class Cx: 80 % of the reimbursement base rate

These latter non-reimbursable portions are no longer applied for reimbursable drugs delivered within the *forfait* context. These non-reimbursable portions are taken into account (as reductions) on the annual determination of the national budget.

Moreover, the hospitalised patient pays for the reimbursable drugs that may (or may not) be administered to him or her during his or her admission the sum of 0.62 euro per day of hospitalisation.

Generally, it is accepted that the patients' own total contributions compensate for the total amount of the "own contributions" charged to the hospital.

The amount of 0.62 euro per diem remains unchanged after the introduction of the hospital *forfait*. As this amount (0.62 x total hospitalised days; "patient's own contribution") pertains to the patient's contributions for all reimbursable specialities, both those that fall within and without the *forfait*, only the fraction that pertains to the reimbursable pharmaceutical is to be taken into account.

In 2007, the expenditures for reimbursable pharmaceuticals for hospitalised patients eligible for the *forfait* scheme (*Hospitalised patients – forfait pharmaceuticals*) amounted to 77.20 million euro (contribution of 25% of the reimbursement base).
In addition, the expenditures for the *forfait* per admission for 2007 amounted to 258.88 million euro.

This means that the total contribution by the NIHDI for the use of *forfait* pharmaceuticals for the year 2007 amounted to 336.08 million euro.

If the *forfait* scheme had not been applied, the contribution by the NIHDI for an identical use of drugs would provide for a reimbursement base of 100% (or 308.78 million euro), reduced by the "own contribution" to be paid by the hospital, as was the case prior to the introduction of the *forfait* scheme.
For 2007, the *theoretical own contribution* amounted to 6.1 million euro [b].
Prior to the introduction of the *forfait*, the use of pharmaceuticals in 2007 would have carried a cost of 302.69 million euro in net NIHDI expenditures.

Hence, for the year 2007, the surplus balance for all hospitals combined, when compared to the situation without the application of the *forfait*, amounts to 33.4 million euro.

Table III.5 Calculation of the difference in the NIHDI contribution for the *forfait* pharmaceuticals for 2007 as a result of the introduction of the *forfait* scheme for the year 2007

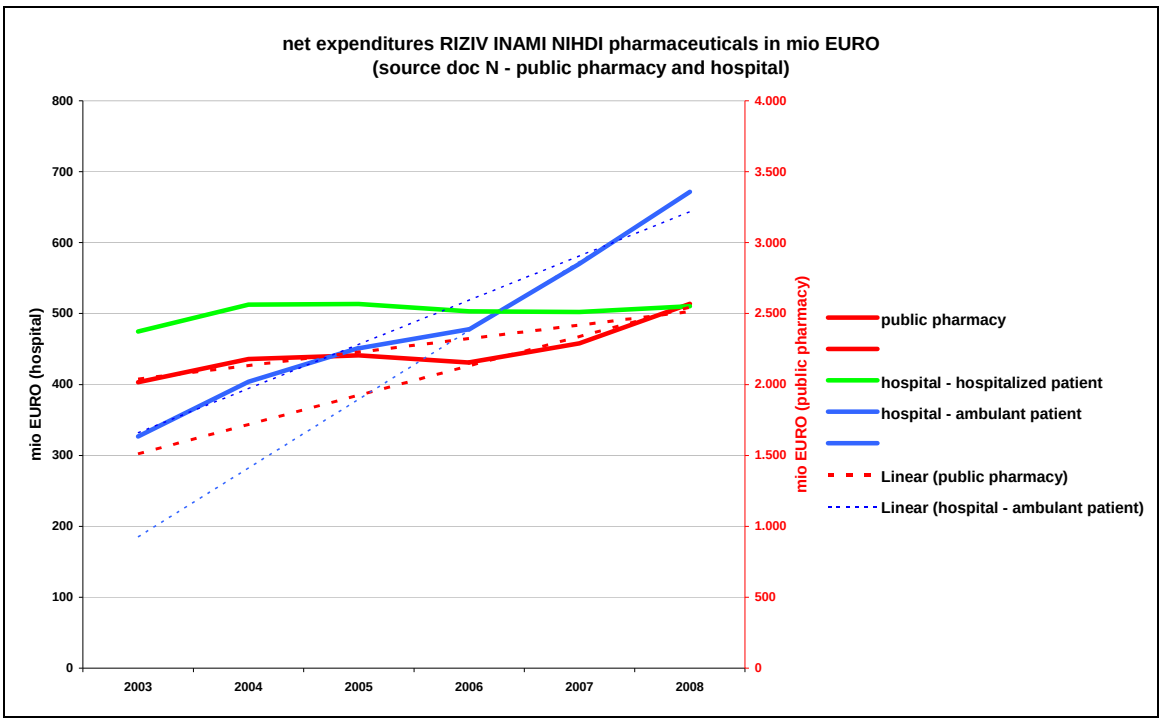
	Real amounts 2007 AFTER introduction of the *forfait*	**Theoretical amounts - 2007 PRIOR to the *forfait***	**Difference**
forfait per hospitalisation	258.882.375	0	
reimbursement base	77.195.423	308.781.692[a]	
own contribution	0	-6.084.000[b]	
Total	**336.077.798**	**302.693.692**	**33.380.106**

[a] the amount of the expenditures for *forfait* pharmaceuticals at a reimbursement base rate of 25% converted to a 100% reimbursement base rate.
[b] average of the theoretical patient's own contribution for the *forfait* pharmaceuticals for the period 1/7/2006-30/06/2007 (6.159 million euro) and that for the period 1/7/2007-30/06/2008 (6.009 million euro), source note of the General Council 2009-35.

The expenditures for ambulatory patients in hospitals manifest a faster increase as of the fourth quarter 2006 (Figure III.1.), which could create the impression that the introduction of the *forfait* scheme for hospitalised patients has brought about a shift of the expenditures towards ambulatory patients. However, an evaluation of long-term general data does not necessarily demonstrate a change in the trend towards an evolution of the expenditures for ambulatory patients in the hospital (Figure III.2.):

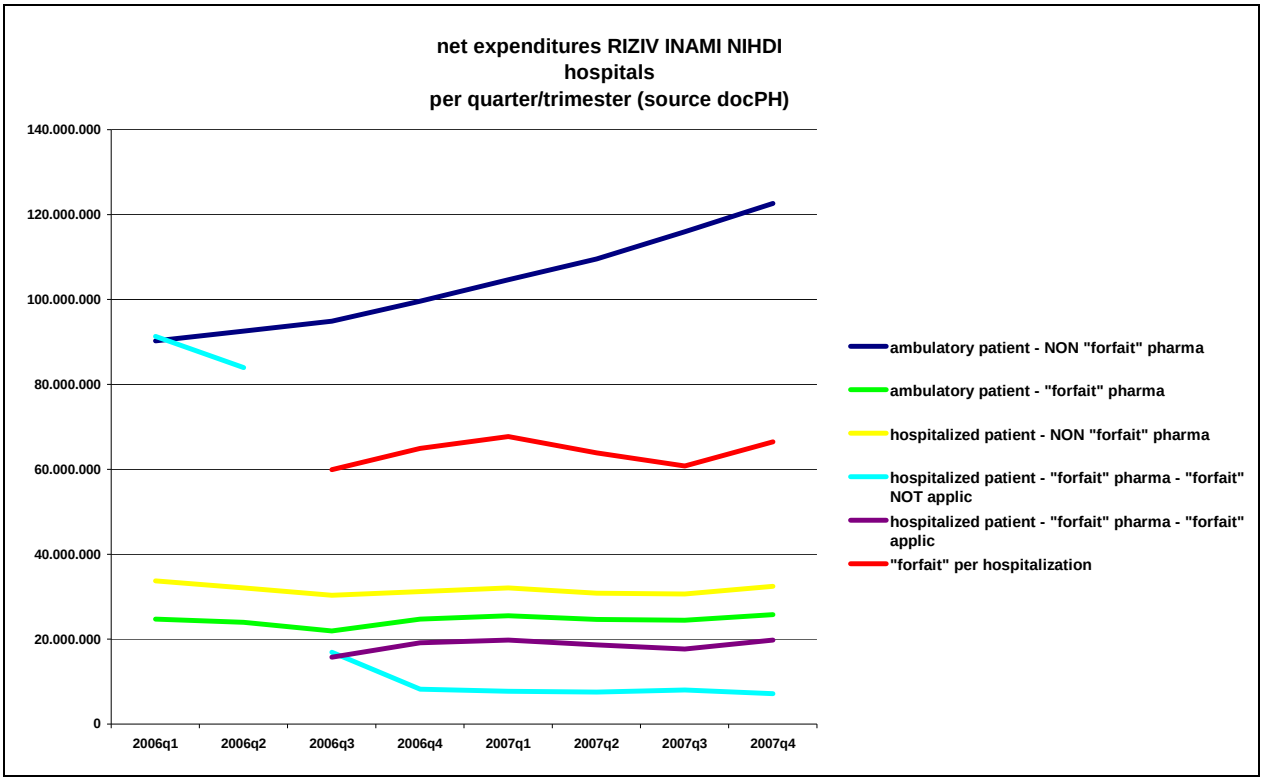
- also for ambulatory patients in public pharmacies, an renewed accelerated increase in the expenditures for drugs as of 2006/2007 is noted
- growth (speed) of the expenditures for ambulatory patients in hospitals as of 2006 is analogous to that up to 2005, just as it is for the drugs supplied to ambulatory patients in public pharmacies

Figure III.2. Evolution of the posted expenditures on an annual basis: total specialities in the hospitals – in millions of EURO (source permanent audit May 2009, heading 3.1.1. key Table – doc N)



Since the data are available at the speciality level, it was possible to check whether or not all of the expenditures pertained to *forfait* drugs, that is to say, drugs that fall within the reimbursement scheme if they are supplied within the *forfait* context.

Figure III.3. Net expenditures hospitals – break-down of the expenditures depending on whether of not it pertains to a *forfait* drug



Explanation of the concepts:

Forfait pharmaceuticals	*Drugs that fall within the forfait scheme if they are supplied to hospitalised patients in acute hospitals;* *On supply to these patients, the reimbursement base is 25%; on supply to other patients, these drugs always fall outside of the forfait scheme and the reimbursement base is 100%*
NON forfait pharmaceuticals	*Drugs that fall outside the forfait scheme for every patient (reimbursement base is 100%)*
Forfait NOT applic	*Drugs that fall within the forfait scheme but are not supplied under forfait conditions (for instance, in psychiatric hospitals)*

While the expenditures are generally stable for hospitalised patients, both for patients that fall within and outside of the *forfait* scheme, one notes a sharp increase in the expenditures for ambulatory patients (growth in expenditures for ambulatory patients: 16.9% growth for 2007 versus 2006).
It is the rise of the expenditures for the ambulatory patients that is responsible for the growth rate of the hospital expenditures (growth in total hospital expenditures: 8.5% for 2007 versus 2006).

From the evolution of the expenditures for ambulatory patients (both types drugs: within and outside of the *forfait* scheme*)* it may be deduced that – if one were to consider also a *forfait* for

ambulatory patients – the list of drugs for which an exception is allowed to the *forfait*, will have to be based on other principles or criteria in order to be able to properly manage the (growth of) expenditures. The expenditures for *forfait* drugs that are being supplied to ambulatory patients are, in fact, fairly stable (these drugs are being reimbursed at 100 %); the expenditures for non-*forfait* drugs continue to rise steadily.

The expenditures for *forfait* drugs for patients that fall within the *forfait* scheme remain more or less stable.

A global analysis of the available data does not show indications that would make us assume that, within the hospitals, the use of *forfait* drugs is being transferred out of the hospitalised setting to the ambulatory setting or to the non- *forfait* drugs.

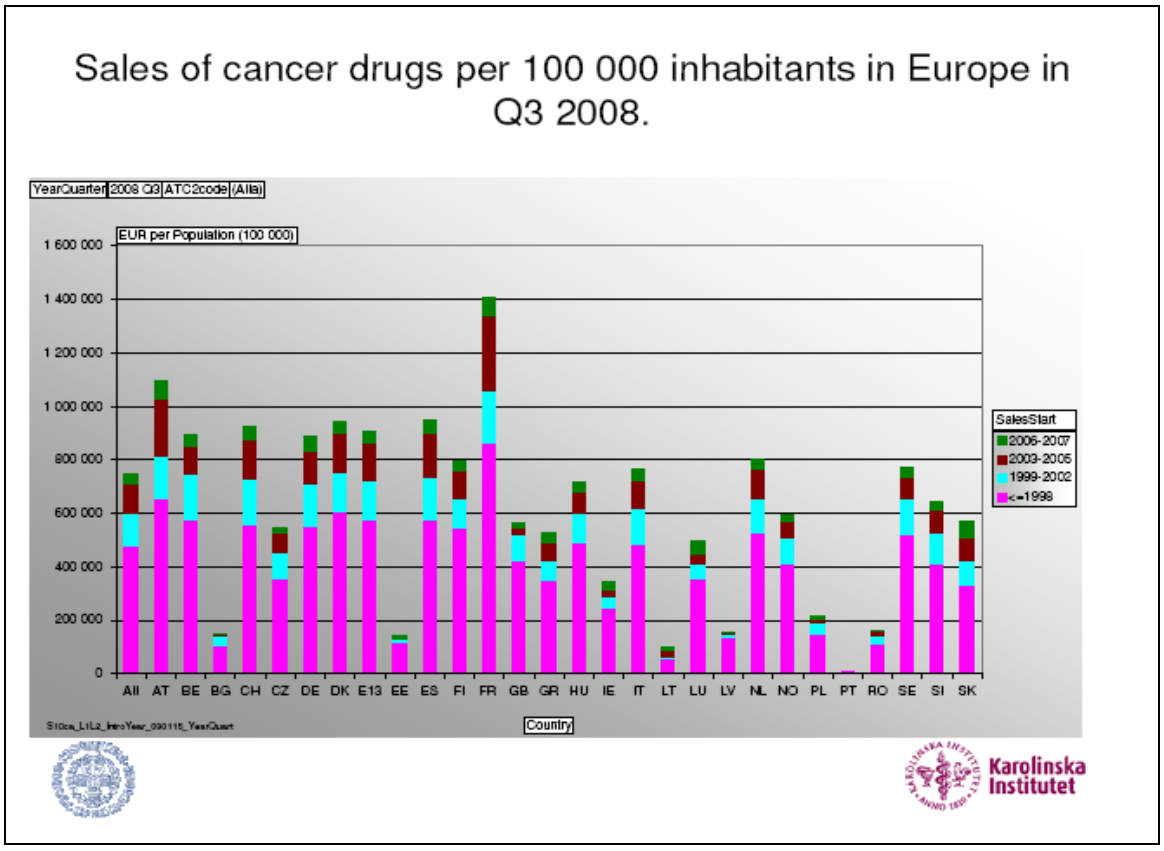
III.3. Expenditures for drugs in hospitals: analysis of oncolytic drugs

In January 2009, the Karolinska Institute in Stockholm, Sweden, published a report about the access to cancer drugs in Europe (*).
This report examined this access to cancer preparations by means of sales figures for these drugs (€ per 100.000 inhabitants or mg per 100.000 – third quarter 2008) in the various countries. A comparison was then drawn up of the global figures amongst these various European countries.

The sales figure for cancer drugs per 100.000 inhabitants in Europe for the third quarter of 2008 is 750.000 €. Since in a number of "new" EU member states a significant catch-up movement is needed to have them attain to the level of the "more affluent EU-nations" (e.g., the countries that already belonged to the EU before the "demolition of the Berlin Wall"), it is useful to also test out the comparison amongst the countries against the figure for the E-13 nations (Belgium, Austria, Germany, the Netherlands, Luxembourg, France, Spain, Italy, Greece, Portugal, Finland, Sweden, Denmark, Norway).
The turnover figure for the E-13 nations is **910.000 €**.

Out of this E-13 group, Austria and France register sales that respectively lie 21% and 54 % higher than the figure of the E-13, Belgium, Sweden, Germany, Denmark and Spain are in line with the E-13 sales figures.
Greece, Finland, the UK, Ireland, Italy, and the Netherlands register sales figures that are significantly below the E-13 figures.

Figure III.4. Sales of cancer drugs in Europe (source Corporate Report on Patient Access to cancer drugs in Europe" by the Karolinska Institute in Stockholm, Sweden (January 2009)



In breast cancer, Taxotere® and Herceptin® were analysed. In colorectal cancer, Avastin® and Erbitux®, in CML Glivec®, and in non-Hodgkin lymphoma, Mabthera® were analysed.
From these analyses (mg/100.000 inhabitants), it appears that the sales figures for **Taxotere®** in Belgium lie 36% above the E-13 figure, this being the third highest after Denmark and France.

Herceptin® registers sales in Belgium of 23.000 mg/100.000 inhabitants. This figure is 15% above the E-13 figure and lies within the same range as that of France and Switzerland.

The sale of **Erbitux®** in Belgium rose in 2008 36% above the E-13 figure, in spite of the limited reimbursement. In the Netherlands, this speciality drug was used very sparingly (only 20% of the E-13 figure). In contrast, France, however, registered sales that lie 9 % above the average sales within the E-13.

For **Glivec®,** Belgium lies above the E-13 figure (+ 6%). The sales of this speciality drug are distributed less heterogeneously across the various countries.

For 2 specialities, Belgium registered sales below those in E-13 countries, namely for **MabThera®** (-22%) and **Avastin®** (-95%).

Summarized, it appears that the use (as may be deduced from the sales figures) of oncolytic drugs in Belgium lies at the level of the average use in the EU-13 countries and thus unquestionably higher than the average figure for the whole of Europe.
These figures may even rise further in Belgium since, in 2008, there was a catch-up movement for the reimbursement of Mabthera® and Avastin® (part of the National Cancer Plan 2008).
These products register notably lower sales in Belgium than in the other European countries.
Significant is the great difference in the use of Erbitux® amongst the various European countries.

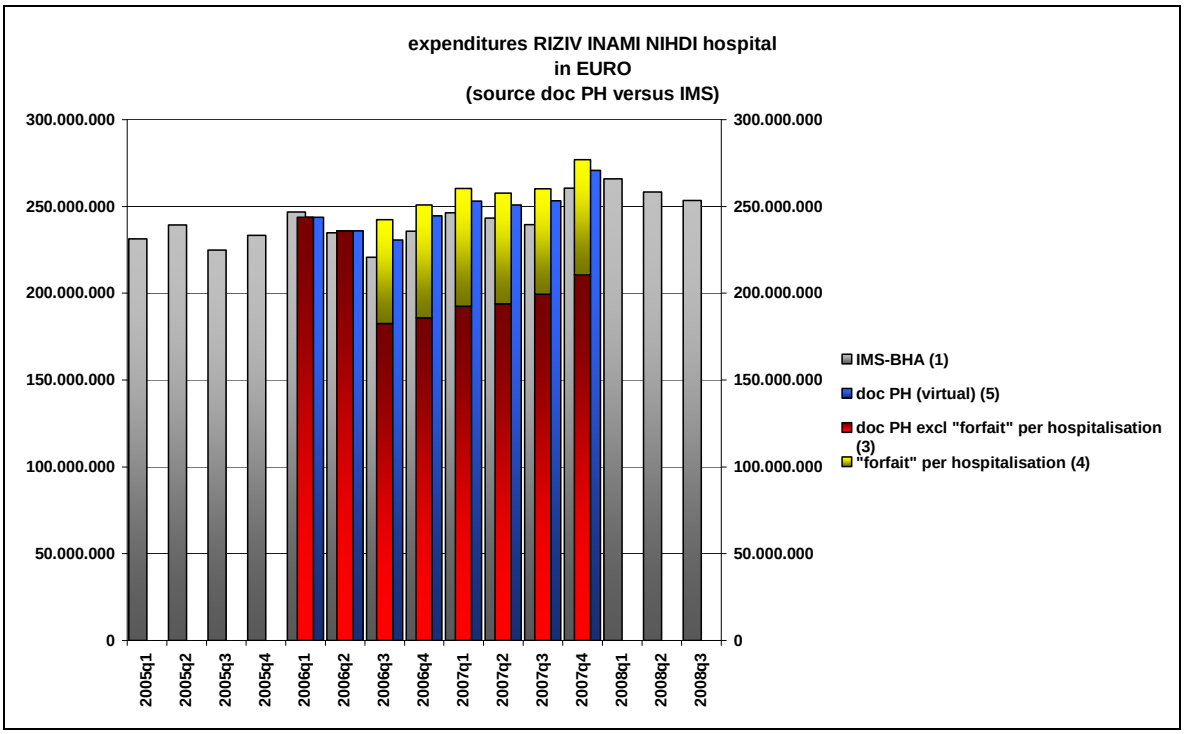
The other more global findings of this report for Europe are :

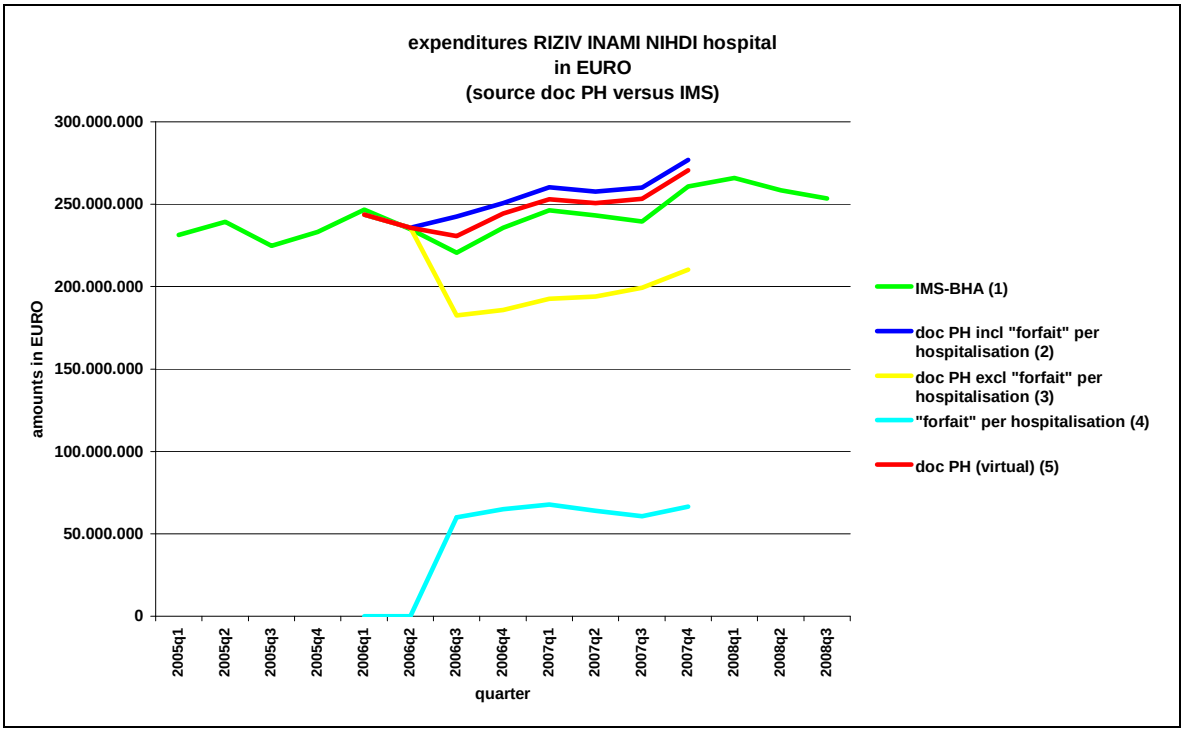
- The incidence of cancer cases is on the rise, but the mortality rate is declining.
- Survival chances in most cancer cases are improving notably, albeit there is a great variability amongst the various countries.
- The European countries are spending ever larger budgets on the screening of cancer cases, cancer prevention, and cancer treatment.
- It is estimated that the expenditures on cancer take up approximately 6 to 8% of the health care budget, but this still remains below the relative “burden of the disease”: 16% loss in DALYs (Disability Adjusted Life Years).
- There exists a trend towards ambulatory care with subsequent decline in the number of hospitalisation days, this in spite of the rise in the number of patients.
- The indirect costs are being lowered.
- The cost for the pharmaceutical specialities registers a very sharp increase, but a slower rise in the cost price is anticipated.

(**) Corporate Report on Patient Access to cancer drugs in Europe” by the Karolinska Institute in Stockholm, Sweden (January 2009)

III.4 Forecast of the expenditures for drugs in hospitals

Figures III.5. and III.6. Expenditures for drugs in hospitals: basic data: quarterly figures docPH (net NIHDI expenditures, expenditures for drugs including and excluding the expenditures for *forfait* pharmaceuticals per hospitalisation) and IMS-BHA (sales figures)





Figures III.5. and III.6. show the basic data that serve for the forecasts. If we were to base ourselves solely on the available data regarding the expenditures for specialities (docPH excl. *forfait* per hospitalisation, curve 3), we would, by extrapolation of those data, get the impression that the increase in the expenditures follows an upward linear trend.
Curve 3, however, only pertains to the expenditures for the drugs (mix. of the reimbursement base at 25% and at 100%).

The total drug expenditure in the hospitals is represented by curve 2 or by the sum of curve 3 (docPH excl. *forfait* per hospitalisation) and curve 4 (*forfait* per hospitalisation). When we compare the movement of curve 2 with the movement of the curve that shows us the IMS sales figures, we note their similarity (good correlation). From this we may deduce that the rise of the expenditures will experience a levelling-off.

By means of the available data, it is now possible, for the estimation of the evolution of the expenditures for 2008 and 2009 (for which no docPH data are available as yet), to apply an analogous approach as the one applied for the estimation of the evolution of the expenditures in public pharmacies.

To this end, we are examining what the correlation is between the docPH data and the more recent IMS data. In case the correlation is deemed adequate ($r^2 \geq 0.75$), the IMS-data will be converted; if not, the docPH data will be extrapolated in linear fashion. For the period Q4 2008 up to the end of 2009, the data established earlier will be extrapolated by linear method.

To check the correlation between IMS – docPH, for the docPH data, the expenditures for ambulatory patients in hospitals and the in and out *forfait* expenditures for hospitalised patients are all tallied together. Since the *forfait* drugs are being reimbursed at 25% of the reimbursement base, this amount is multiplied by 4, so the total expenditures for hospitalised patients = expenditures ambulatory + 4 expenditures *forfait* + expenditures non- *forfait*.

This will give us merely an approximation of the real expenditures (virtual total) and the amounts (for instance, as presented in the top 80 – Table III.2.) ought not to be read as absolute ones.

Table III.6. Forecast of the evolution of the expenditures for drugs in hospitals 2006 – 2009

	total 2006 (virtual)	total 2007 (virtual)	total 2008 (virtual)	total 2009 (virtual)
	954.823.935	1.027.860.574	1.093.796.985	1.150.701.679
evolution		2007-2006	2008-2007	2009-2008
Hospital		+ 7.6 %	+ 6.4 %	+ 5.2 %

expenditures calculated on the basis of :

- The available docPH data: first semester 2006 to and including second semester 2007 (NIHDI data), where total expenditures = expenditures ambulatory + non- *forfait* expenditures + 4 x *forfait* expenditures.
- conversion of IMS-data (data to and including the third quarter of 2008) for the classes (ATC3 level) with a correlation IMS-doc PH $r^2 > 0.75$ for the first three quarters of 2008
- linear extrapolation for 2008 and 2009 for the remaining data.

This is an under-estimation (general: this is not the case for the ATC3 class where all specialities fall outside of the *forfait* scheme) given that the expenditures for *forfait* drugs for hospitalised patients have been extrapolated from 25% to 100%.

From the data shown under point III.2.2., it may be concluded that, in 2007, in reality 27.3 million EURO more was paid out (258.9 – 3 x 77.2 = 27.3 million euro or 2.6% of the total hospital expenditures) than the theoretical 3 x 25 %.

We also note from Figures III.5 and III.6 that the virtual 'docpH' expenditures (curve 5) do indeed follow that same trend, yet that the expenditures are below the real expenditures of docpH, including the *forfait* per hospitalisation (curve 2).

IV. COST OF DRUGS

In this Chapter, the price level of drugs in Belgium is tested against the level in (the) various European countries. Given the particulars of the different price regulations (with or without price control), remuneration systems for the distribution (wholesale and pharmacies) and reimbursement schemes (restricted versus general access), every evaluation of a price comparison amongst various countries needs to be treated with a certain degree of circumspection and reservation.

IV.1. Belgium within Europe

In November 2008, the European Commission invited the EU member states and the EEA-AFTA countries to participate in a voluntary price-comparison exercise for drugs, under the aegis of the 'Transparency Committee'.

The exercise is in full implementation on 12 'blockbuster' drugs (taking into account feasibility, practicability, and continuity) and in the meantime, 30 countries are cooperating in this exercise (so far, 4 'deliveries' have been carried out):
For the exercise 1-2009, the results of which are stated infra,
- 19 countries (63.3 %) provided the selling prices ex-factory
- 27 countries (90 %) provided the wholesale prices
- 29 countries (100 %) provided the public/retail prices

For reasons of 'data protection', it is ruled that national administrations may use only 'neutralised' graphs and information in public communications, meaning they must delete mention of the brand names of the specialities.

The coordination of the exercise is conducted by ÖBIG - Österreichisches Bundesinstitut für Gesundheitswesen (Mrs. Claudia Habl). Explicit permission was asked, and granted, from and by ÖBIG and the representative of the 'Transparency Committee' to include the following graphs into this report.

Under the same reservations that are applicable to every price comparison for drugs in Europe, it may be summarized that the prices of drugs in Belgium (for off-patent drugs) globally approach the average European prices, with the exception of specific molecules (such as simvastatin) for which special measures (in casu the 'KIWI'-procedure) have exerted a special impact on the price.

Figure IV.1. EU-price comparison – proton pomp inhibitor: off-patent originator (source INFOPRICE 1/2009 delivery)

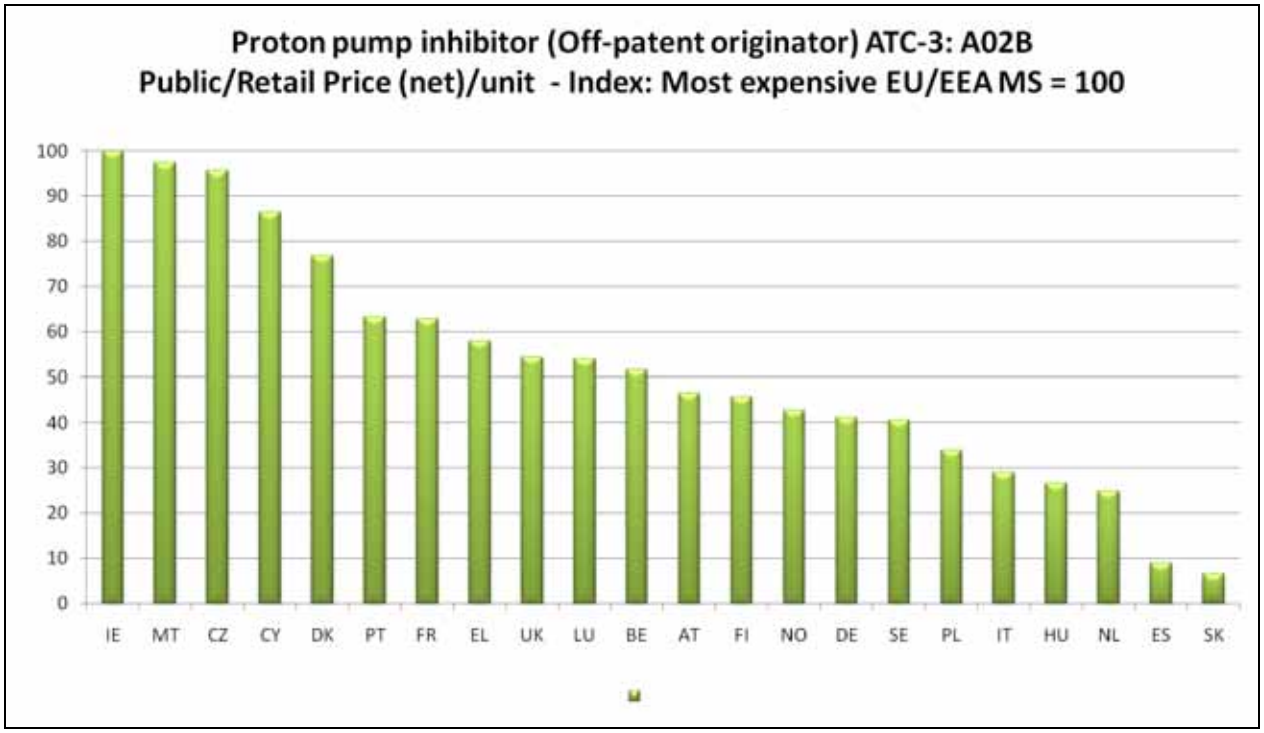


Figure IV.2. EU-price comparison– anti-depressant: off-patent originator (source INFOPRICE 1/2009 delivery)

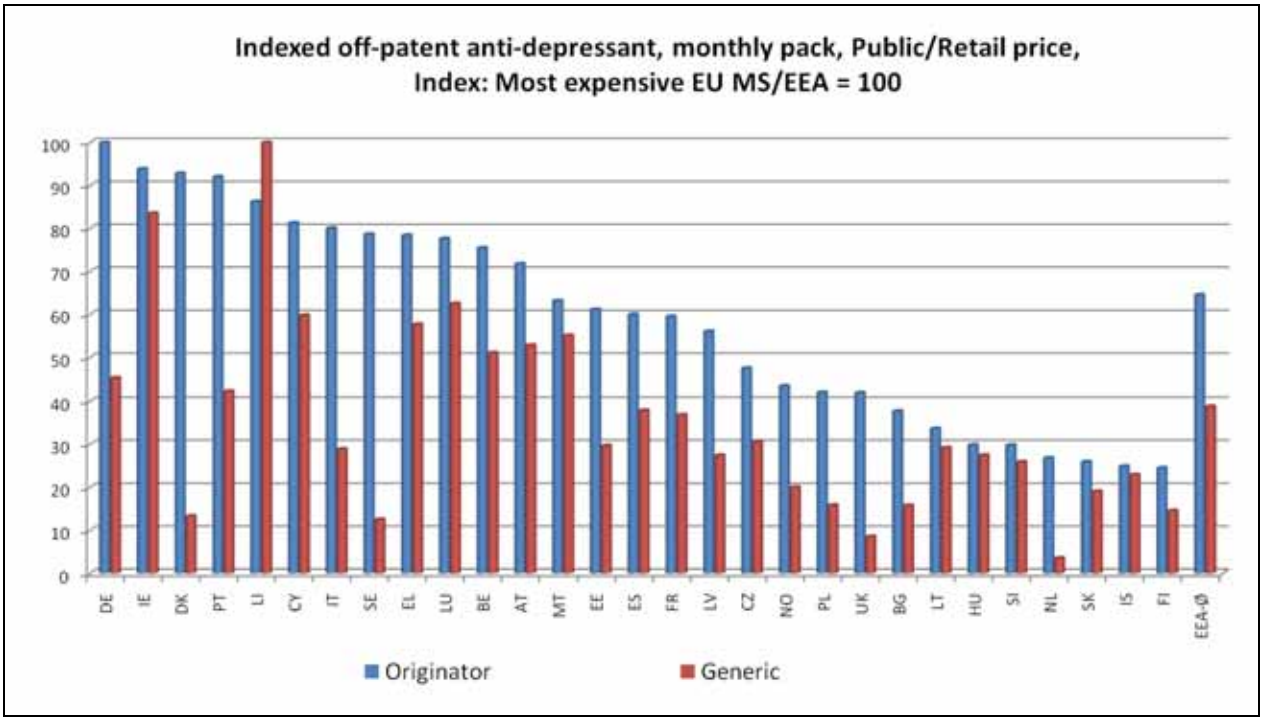


Figure IV.3. EU-price comparison – simvastatin: off-patent originator versus least expensive product (source INFOPRICE 1/2009 delivery)

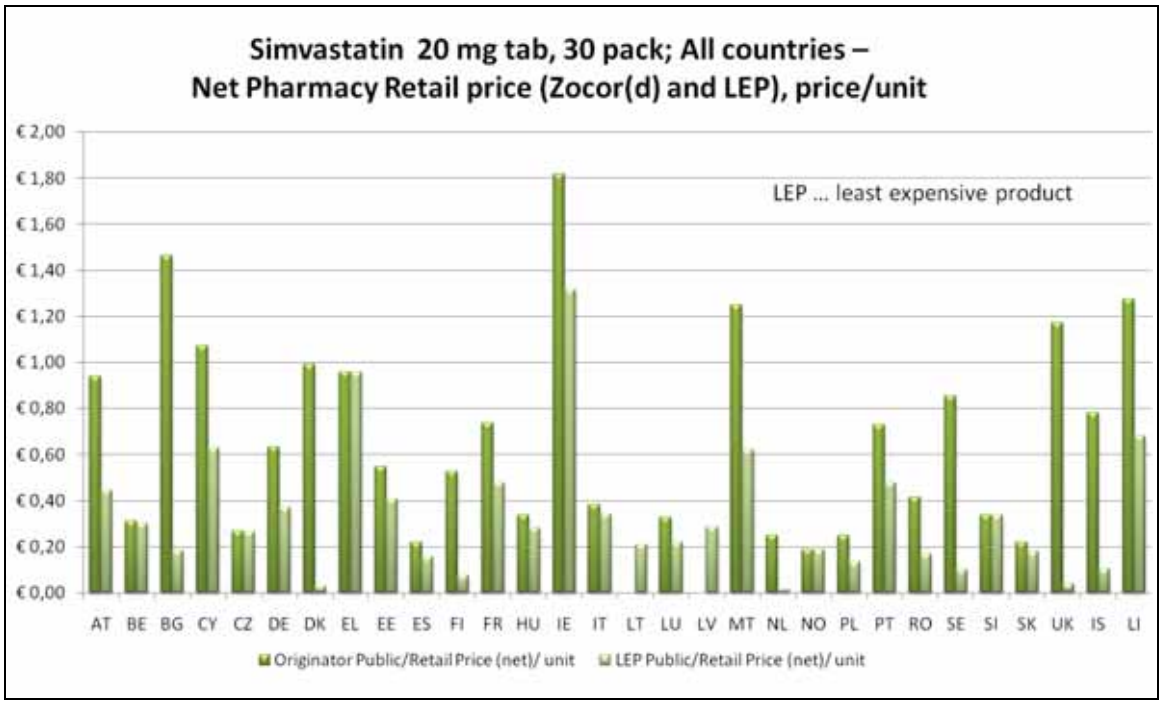
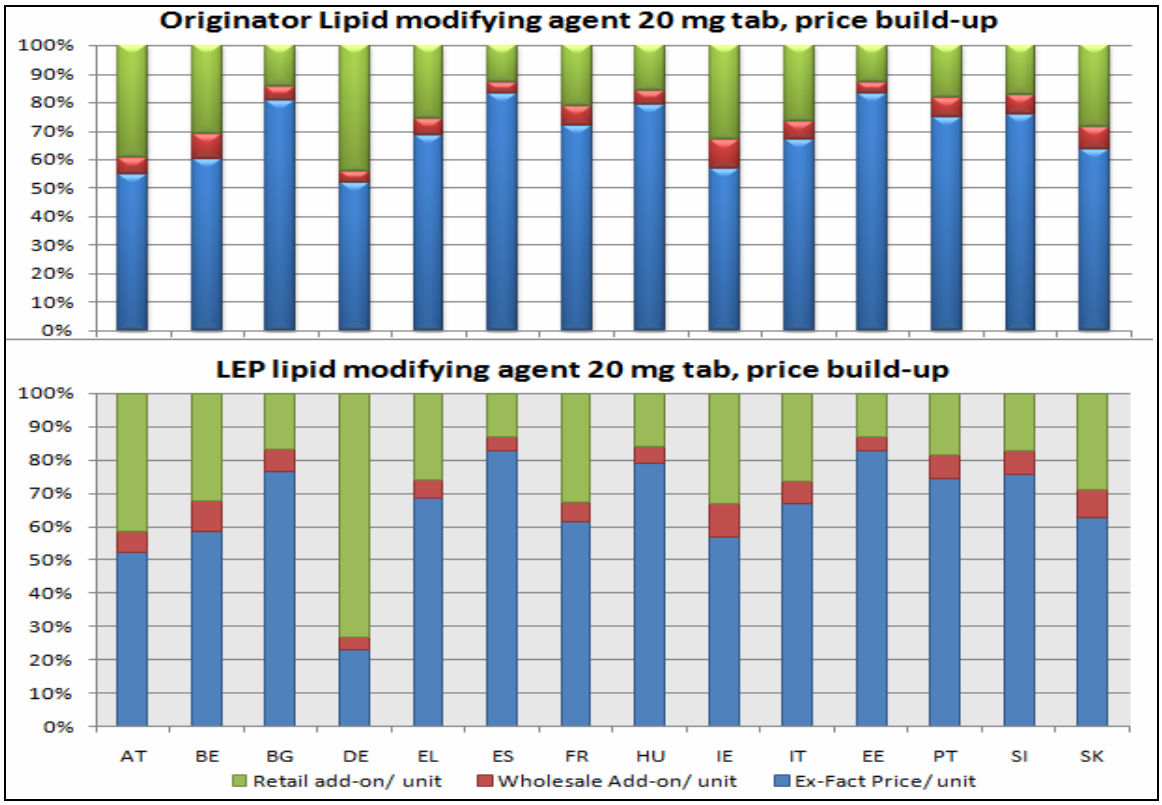


Figure IV.4. EU-price structure comparison– hyperlipidemic drug (source INFOPRICE 1/2009 delivery)



IV.2. Belgium– the Netherlands

The newspaper 'De Morgen' of 26 January 2009 featured the article: 'Pharmacy at the Dutch border offers drugs at rock-bottom prices'.

The article discussed a price comparison between various drug specialities in the Netherlands and in Belgium. Since 1 July 2008, a notable drop in price has been registered in the Netherlands for some thirty-odd prescription drugs as a result of a tender organized by the private health care insurance companies.
This system (preference system) provides only for a reimbursement of drugs from the firm that is offering the lowest prices.

Unfortunately, it was not possible to reconstruct either these prices or the comparison since:
- the source of the Dutch prices was unknown and could not be traced: did not correspond to the list prices or the prices listed on the site www.medicijnenkosten.nl
- there were no data relating to the compared dose,
- there were no data relating to the compared size of packaging
- the methodology used to arrive at these prices is unknown
- Other observations about these prices:

the Netherlands: - additional reimbursement / delivery fee
- no patient's own contribution

Belgium: - pharmacist's remuneration is included in the reimbursement base rate
- patient pays the patient's own contribution

As a result of the said article, the exercise was repeated independently, based on the following premises :
- Identical treatment term of 15, 30, or 90 days for these specialities in both countries
- Comparison based on the standard dose (DDD: Daily Defined Dose) as determined by the WHO

Prices in the Netherlands: Table IV.1	Reimbursement base rates in Belgium: Table IV.2
Exclusive of Delivery rate[1] - cost for health care insurance company - cost for patient : 0 EURO **unless** drug falls within the preference system of the private health care insurance company	Inclusive of margins for wholesaler and pharmacist - cost for NIHDI + patient's own contribution (ratio : 70 actives/30 omnio)

Table IV.1. Cost for insurance company (the Netherlands)

	Term of treatment		15 days		30 days		90 days	
			min	max	min	max	min	max
omeprazole	20	Mg	0.46	7.26	0.91	14.51	2.74	43.54
citalopram	20	Mg	0.58	4.09	1.16	8.18	3.47	24.53
risperidone	4	Mg	2.07	31.21	4.13	62.43	12.4	197.54
pravastatin	20	Mg	0.9	7.22	1.8	14.45	5.39	43.34
lisinopril	20	Mg	0.21	1.36	0.43	2.73	1.29	8.19
Alendronate	10	Mg	0.68	10.24	1.36	20.49	4.07	61.47
tamsulosin	0.4	Mg	0.6	10.54	1.21	21.08	3.63	63.25

[1] The current maximum delivery rate is 6,78 euro (incl VAT) for a standard delivery. For delivery of packages of weekly doses, the delivery rate is 3,17 EURO (incl. VAT).

Table IV.2. Reimbursement base (cost NIHDI + patient's own contribution, Belgium)

Term of treatment			15 days		30 days		90 days	
			min	max	min	max	min	max
omeprazole	20	Mg	6.2	18.5	12.4	37	37,2	111
citalopram	20	Mg	5.3	11.1	10.6	22.2	31.8	66.6
risperidone	4	Mg	25.4	40.5	50.8	81	152.4	243
Pravastatin	20	Mg	5.4	23.7	10.8	47.4	32.4	142.2
Lisinopril	20	Mg	2	3.5	4	7	12	21
Alendronate	10	Mg	6.7	16	13.4	32	40.2	96
tamsulosin	0.4	Mg	Non-reimbursable – cost to patient see Table 4					

Table IV.3. cost for the NIHDI (Belgium)

Term of treatment			15 days		30 days		90 days	
			min	max	min	max	min	max
omeprazole	20	Mg	4.7	14.5	9.4	29	28.2	87
citalopram	20	Mg	4.2	8.7	8.4	17.4	25.2	52.2
risperidone	4	Mg	22.2	31.6	44.4	63.2	133.2	189.6
Pravastatin	20	Mg	4.2	18.5	8.4	37	25.2	111
Lisinopril	20	Mg	1.5	2.8	3	5.6	9	16.8
Alendronate	10	Mg	5.2	12.5	10.4	25	31.2	75
tamsulosin	0.4	Mg	0	0	0	0	0	0

Table IV.4. cost for the patient (Belgium)

Term of treatment			15 days		30 days		90 days	
			min	max	min	max	min	max
omeprazole	20	Mg	1.4	8.4	2.8	16.8	8.4	50.4
citalopram	20	Mg	1.2	10.2	2.4	20.4	7.2	61.2
risperidone	4	Mg	3.1	8,9	6.2	17.8	18.6	53.4
pravastatin	20	Mg	1.2	5.2	2.4	10.4	7.2	31.2
lisinopril	20	Mg	0.4	0.8	0.8	1.6	2.4	4.8
alendronate	10	Mg	1.5	3.5	3	7	9	21
tamsulosin	0.4	Mg	3.75	20.23	7.5	40.45	22.5	121.35

Based on this exercise, it may only be concluded that the prices for the specialities are less high in the Netherlands. An absolute price comparison is difficult, however, since the real cost (including the pharmacist's remuneration) is not known for the Netherlands.

IV.3. 'In-patent' drugs

A study conducted by L. Garattini of the Italian Mario Negri Institute for Pharmacological Research (published in Health Policy in 2008 – abstract infra) compared :

- the selling price ex-factory
- distribution margins
- and selling prices to the public (payers' prices) for a series of pharmaceutical specialities (792 packages in total),

on the basis of 20 active in-patent compounds *(Anastrazole Atorvastatin Bicaltamide Candesartan(cilexetil) Celecoxib Enoxaparin Esomeprazole Fluvastatin Irbesartan Latanoprost Lercanidipine Losartan Montelukast Nebivolol Olanzeapine Pantoprazole Rabeprazole Telmisartan Valsartan Venlafaxine)* in seven European countries *(Belgium, the Netherlands, France, Germany, the Unitred Kingdom, Spain, and Italy)*.

As far as the ex-factory price concerns, Belgium rates somewhere in the middle (France, Spain, and Italy register lower ex-factory prices). However, Belgium assumes a higher ranking because of its relatively higher distribution margins and payers' (public) prices.

> *Prices and distribution margins of in-patent drugs in pharmacy: a comparison in seven European countries.*
> *Garattini Livio; Motterlini Nicola; Cornago Dante*
> *Health policy (Amsterdam, Netherlands) 2008;85 (3):305-1,*
>
> *Abstract:*
>
> *OBJECTIVES: To compare prices of in-patent active ingredients (AIs) in Europe at three levels (ex-factory prices, net distribution margins and third party payers' prices). METHODS: We compared the prices in seven EU countries (Belgium, France, Germany, Italy, the Netherlands, Spain and the UK) of the 20 in-patent AIs most sold on the Italian retail market in 2004, based on "sell in" sales data. We calculated the average ex-factory price per unit of each compound in each of the seven countries, weighted by the volumes of all reimbursable package sizes and strengths. We estimated net distribution margins according to the 2004 domestic regulations by deducting any type of mandatory discount. Finally, we added VAT to calculate "third party payer's prices". All prices were expressed in index numbers (Italy=100). RESULTS: Italy had the lowest average ex-factory prices, the Netherlands and particularly the UK had by far the lowest distribution margins, while Germany had by far the highest third party payers' prices. The Netherlands and particularly the UK showed a steep decrease from ex-factory to third party payers' prices, while Belgium, Italy and Spain gave the opposite pattern. CONCLUSIONS: Our study suggests that public authorities can deal with drug prices both by strictly controlling ex-factory prices and by establishing appropriate distribution margins. The latter might be facilitated by liberalizing the distribution sector.*

V. THE COMMISSION FOR THE REIMBURSEMENT OF MEDICINES

V.1. General

This analysis evaluates two of the objectively measurable variables that are co-determinants for the (speed of) access to new innovative or non-innovative drugs in Belgium: **number of submitted applications** for reimbursement (dossiers) and **speed of reimbursement** of new drugs for which an application was submitted.
In the evaluation and the interpretation of the data, account has to be taken of a number of significant elements:

1. general

- the reimbursement of drugs in Belgium is **supply-related**, this means that it is dependent on applications for reimbursement by pharmaceutical companies. This is absolutely determinant for the package of reimbursable pharmaceutical specialities and their reimbursable indications, and to a significant measure determinant for the speed of the reimbursement of new innovative or non-innovative drugs.
- for orphan drugs and class 1 applications, the application may already be submitted as of the moment the applicant has been given a positive opinion by the Commission for drugs for human consumption with EMEA (RD 20 November 2007).
For the time being, this possibility was used only sparingly (1 finished dossier and 1 dossier in procedure)

2. specific to this analysis

- the data that have been processed originate from the **administrative database** that is used by the Secretariat of the Commission for the Reimbursement of Medicines in the ongoing monitoring of procedures and process time delays. For the analysis of the numbers of dossiers, and the analysis of the Time of Submission of the application, all applications are taken into account (including the procedures in progress and those that have been deferred to a later date, plus finished and withdrawn dossiers,…) between 1 January 2003 and 1 January 2009. For the analysis of the speed of reimbursement of new drugs, obviously only the dossiers that are effectively eligible for reimbursement (positive decision or absence of a decision from the Minister) are being taken into account.
- for this analysis, only **unique dossiers** are taken into account. That means that in the event of simultaneous applications for different doses /packaging for specialities, dossiers are being pooled when the contracting party, type of dossier, day 0, active compound, proposal by the Commission and decision by the Minister are identical.
- the analysis draws no distinction between **first or renewed applications** (limited number). In other words, every unique dossier is being considered as a 'new dossier'. In effect, no objective distinction can be made between renewed applications of dossiers following a negative decision by the Minister and renewed applications following the withdrawal of the dossier on the initiative of the company. The reason for this initiative is, in fact, unknown (for instance, 'avoidance' of a negative notification because of 'reputational risk').
- the analyses do not take into account the dossiers that are processed **administratively** (RD 15 February 2007), which means without the intervention of the Commission, and for which the procedure is limited to 60 days. During the period 01.04.2007 to and including 31.12.2008, 345 dossiers were submitted in this manner, 207 of which were submitted in a valid fashion. In the meantime, 173 of these dossiers have been processed. On 1 January 2009, of these, 151 pharmaceutical specialities qualified for reimbursement.

V.2. Number of dossiers

The number of dossiers that has been submitted via the CRM-procedure (RD 21.12.2001) in 2008 is slightly higher than the fairly constant number noted for the previous years, nonetheless with important differences depending on the type of application (see Figure V.1):

It is to be noted that:

- The number of class 1 applications (on the average some 25 per annum up to 2006) appears to be declining slightly since the first semester of 2006 and in 2008 attained the lowest number – 7 (seven) - ever. This negative trend appears significant.
  Is it as a result of a declining number of registrations, for instance, a mere 14 by FDA approved *New Molecular Entities* in 2007 (Figure V.2)? Or is there a shift towards new indications rather than towards new products?

- The number of applications for orphan drugs was 11 (eleven) in the year 2008. It has remained stable since 2006 and closely coincides with the number of new registered orphan drugs with EMEA (approximately 15 per annum).

- The declining trend in class 2 and 3 applications has ceased in 2006 and, in effect, ever since that time, has reversed itself once again.

- The recent increase in applications for modifications to the reimbursement modalities appears to be stabilized; however, it is to be noted that this pertains to both an expansion of indications and more technical corrections that are being dealt with via article 38. Therefore, care needs to be exercised in the interpretation of the figure for the second semester of 2007, which includes all simvastatin revisions and modifications from class C towards class B!

Figure V.1: Number of applications per annum (unique dossiers)
(including finished procedures, withdrawn applications, procedures in progress)

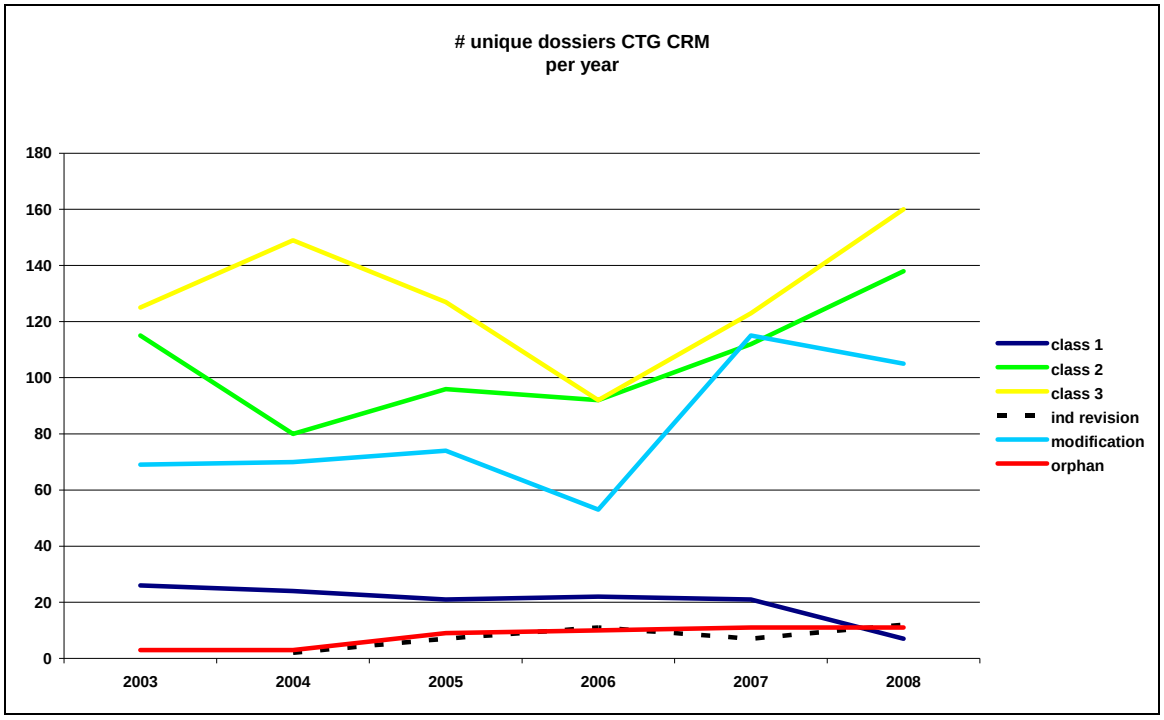
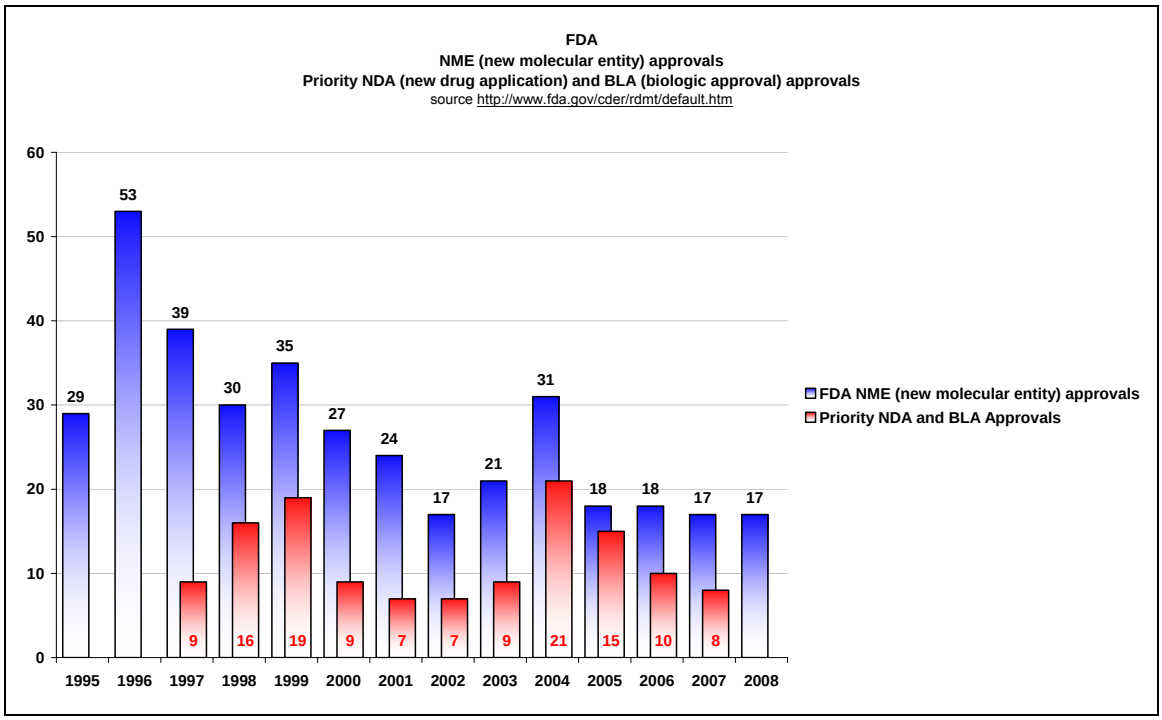


Figure V.2: Number of new molecular entities and new biological entities approvals by the FDA since 1995



V.3. Processing times and time delays for reimbursement of new drugs

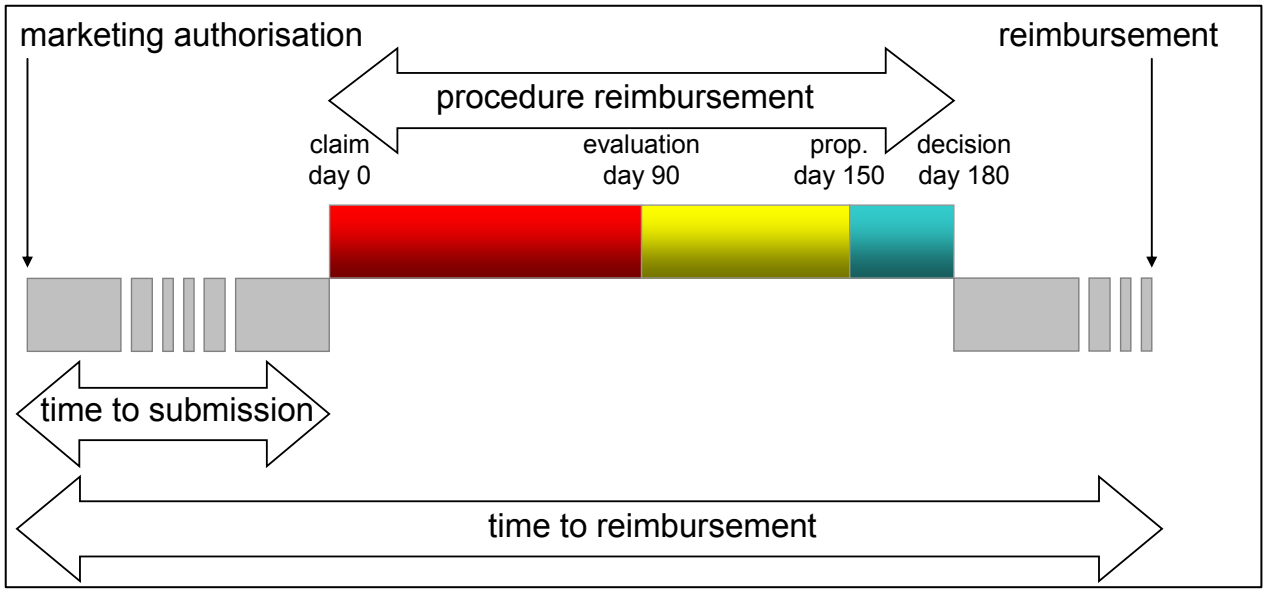
The Royal Decree dated 21 December 2001 concerning the determination and establishment of the procedures, processing terms, and conditions pertaining to the reimbursement of the mandatory insurance for medical health care and the payments of the costs of pharmaceutical specialities provides that Ministerial decisions about applications for reimbursement of new specialities need to be notified to the applicants within a delay of **180 calendar days following the submission of the application**, without account taken of possible suspensions of the procedures. Except for the suspension for reason of the insustainability of the dossier, these suspensions are only possible at the initiative of the company. In the event that this term is not adhered to, the drug will be reimbursed in accordance with the conditions advanced in the company's most recent proposal.
In this way, these procedures are coherent with the EU-Directive 89/105, which allows a maximum term of 90 (for the price setting) + 90 days (for the reimbursement decision).

V.3.1. Methodology

The following variables have been calculated:
Time to Reimbursement: the time in days between the Marketing Authorization date and the date of the effective implementation of the reimbursement (including all suspension of the reimbursement procedures by the company).
Time to Submission: the time in days between the Marketing Authorization date and the date of the application.

The variables have been calculated for all applications/claims, applications/claims for added therapeutic value class 1, applications/claims for analogue therapeutic value class 2 and class 3, orphan drugs, and drugs of the ATC class L ('ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS' – all added value classes and orphan drugs).

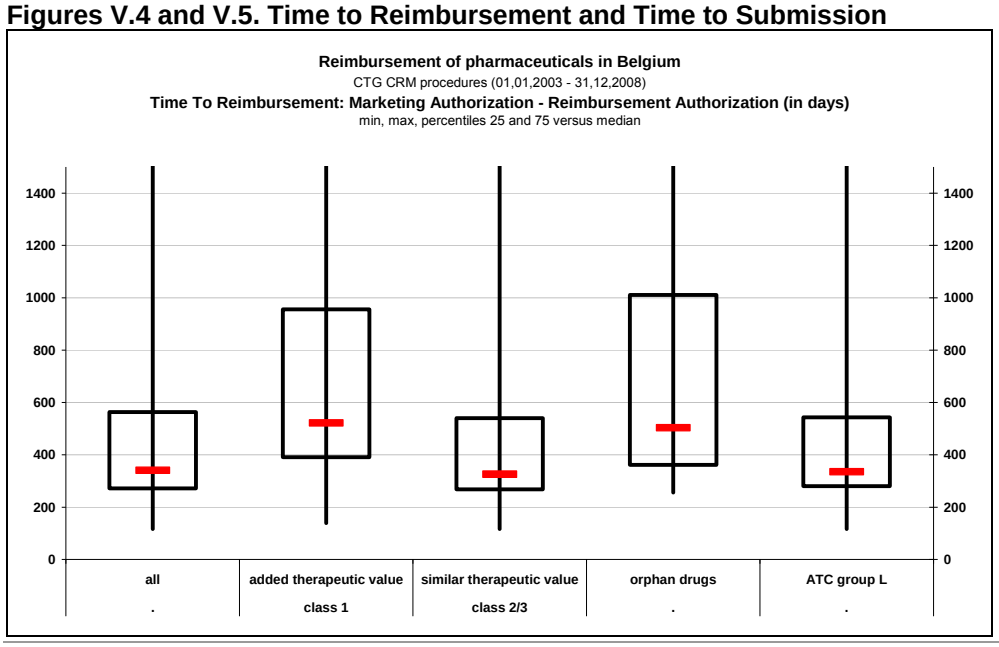
Figure V.3. Procedure for reimbursement of drugs

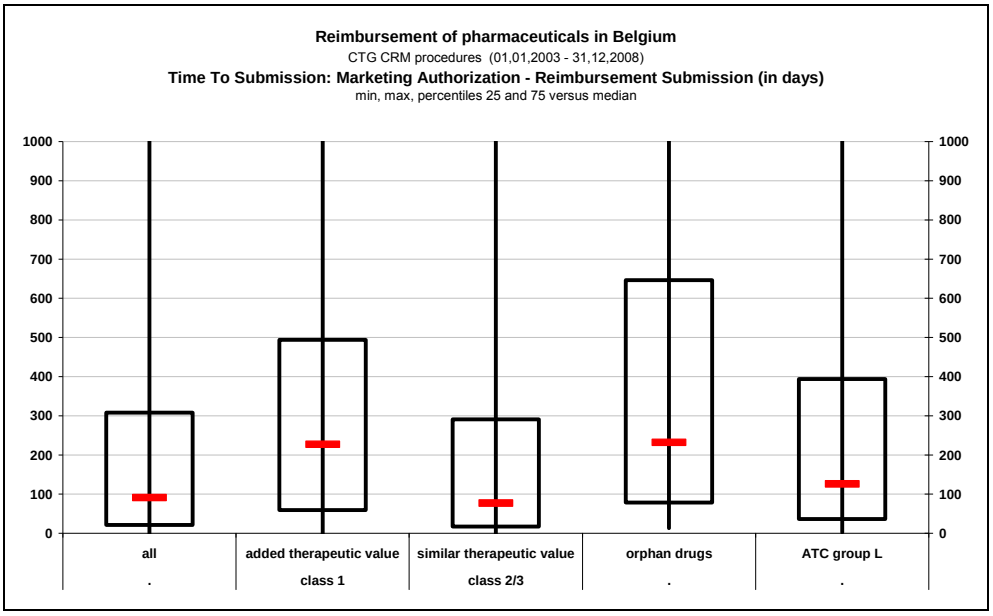


V.3.2. Results

	Time to Submission median in days	**Time to Reimbursement** median in days
All applications	**91**	**340.5**
Added value class 1	227	522
Added value class 2 and 3	77	326
orphan drugs	232	503
ATC class L	126	335

Figures V.4 and V.5. Time to Reimbursement and Time to Submission





V.3.3. Conclusions

For applications for reimbursement of new specialities, submitted since 2003, the median processing time between Marketing Authorization and the actual reimbursement was 340.5 days. However, in this, account has to be taken of the fact that the applicant needs a median of 91 days following the Marketing Authorization of the drug before the application for reimbursement is submitted.

For drugs distinguished by a special therapeutic value (orphan drugs and applications for added therapeutic value class 1), both the Time to Submission and the Time to Reimbursement are significantly longer.

Possible explanations for this – to be confirmed, corrected, or refuted by means of specific research – may for instance be the need for additional data – evidence of added therapeutic value and pharmaceutical-economic data, the more complex evaluation process, strategic choices of pharmaceutical companies for sequencing the marketing and commercialisation (including application for price reimbursement) in the various countries …

For the drugs of the ATC class L (primarily oncolytic pharmaceuticals) – all added value classes, including 20 orphan drugs - the processing times are not significantly different from the global values.

VI. AUTHORS OF THIS REPORT

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VII. COMPLEMENTARY USEFUL SOURCES OF INFORMATION

The following persons have supplied useful comments and information:

Catherine Adriaens, Marc Van De Casteele, Mickaël Daubie, Ri De Ridder, Minne Casteels

Report "Permanent audit":

Actuarial Department

Report "Infospot"

Objective: Every third month, a current subject about drugs shall be discussed and elucidated on the basis of the Pharmanet - data.

Link : http://inami.fgov.be/drug/nl/statistics-scientific-information/pharmanet/info-spot/index.htm