Monitoring Of Reimbursement Significant Expenses

M.O.R.S.E.

Semi-annual Report (semester 1 - 2010)

data 2009

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. …) constitutes the subject 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 report on the management agreement – article 32.

This report aims at presenting the evolution of the expenditures for the pharmaceutical specialities supplied in both the public pharmacies and in hospitals to and including December 2009.

For the assessment of the expenditures, recourse is taken to NIHDI data (Farmanet for the public pharmacies, posted data for the hospitals) and to recent IMS sales figures.

For the estimation of the expenditures in the public pharmacies, MORSE combined, in an initial approach method, recent IMS sales figures with NIHDI expenditures available for public pharmacies via Farmanet. This technique was not used for this report, since sufficient data were on hand via Farmanet (to and including January 2010).

For the estimation of the expenditures in hospitals, recourse is had to recent NIHDI expenditures available for hospitals via doc PH data (billing data passed on to the NIHDI by the insurance companies, available to and including the first semester in 2009).

For the review and discussion of the measures, reference is made to the historical background data for groups (reference price, price reductions, shifts towards Chapter II …) as registered with the administration, and to the administrative databank for the individual measures /dossiers (introduction of new drugs, changes to reimbursability …).

In the present report, no projection is made for the expenditures in 2010: not enough validated data about these expenditures are available (Farmanet January 2010, IMS July 2010) to enable us to make a relevant estimation or forecast of the evolution of the expenditures, given a fairly recent number of measures (April/May: adaptation of the reference price system and the new reimbursement scheme for pharmacists) with the anticipated particular impact on that evolution.

Financial monitoring is not an exact science: the considerations are likewise being tested against the probability factors that internal collaborators (internal evaluator, dossier managers, Farmanet cell…) have decided to assign to them.
Furthermore, earlier forecasts are tested out regularly against the real expenditures as soon as relevant data for this have become available 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 reports, an attempt is made to process the relevant information gleaned from other sources: the present report was, wherever deemed useful, complemented by data gathered from the Permanent Audit (May 2010).

MORSE reports are especially meant to inspire thoughtful reflection and discussion. All commentaries in this regard are most welcome!

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

General

Table 1: MORSE dataset: net annual expenditures NIHDI for drugs 2002 – 2009

Net expenditures NIHDI x 1,000,000 €								
	2002	2003	2004	2005	2006	2007	2008	2009
Pharmacies	**1.921,6**	**2.063,3**	**2.213,0**	**2.203,6**	**2.161,1**	**2.297,9**	**2.611,1**	**2.679,2**
Hospitals					**979,4**	**1.062,3**	**1.178,5**	**1.216,1***
Total					**3.140,5**	**3.360,2**	**3.789,6**	**3.895,3**
Growth %								
		2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009
Pharmacies		**7,4**	**7,3**	**min 0,4**	**min 1,9**	**6,3**	**13,6**	**2,6**
Hospitals						8,5	10,9	3,2*
Total						7	12,8	2,9

Net expenditures NIHDI for Public pharmacies calculated on the basis of the available data to and including December 2009 (Farmanet)

Net expenditures NIHDI based on doc PH data 2006 to and including the 1st semester 2009;
* extrapolation of doc PH data semester 1 2009 for the entire year 2009
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 growth that in the previous report was for the year 2009 estimated for the public pharmacies at 9.93 % (on the basis of an extrapolation of the 2008 data – not adjusted for the effect of the changes with reference to the 'small risks for the self-employed'), was in an NIHDI press release of 8 September 2009 adjusted to an expected growth by 3.17%.
On the basis of the actually available data (Farmanet data to January 2010, IMS data to July 2010), it may be deduced that the actual growth amounted to 2.6 %.

Also in hospitals, one records a levelling off of growth, resulting in a total increase in expenditures for pharmaceutical specialities by 2.9 %.

An ever more important portion of the expenditures is to be attributed to the integration of the small risks coverage for the self-employed since 1 January 2008 (+ 6.2 %). Striking is the fact that the expenditures for drugs for the self-employed are rising more quickly that the expenditures within the general regime (see ***Table 2***).[1]
One has to take into account in this that the effect of new measures are not always immediately obvious (it is primarily a matter of accounting data), for instance, because of the fact that one is working with primarily 'posted' data and that there are 'delays' in the implementation in daily practice (amongst others, because the measures are not adequately or fully "known" amongst the parties involved, in casu = the self-employed).

[1] Standardized report in application of article 51, § 4 of the GVU Law (mandatory health insurance) - Sector 3: Pharmaceutical Provisions – Posted expenditures 200912, p 3.3. table 3.1.2.2. (NIHDI, Standardized report in application of article 51, § 4 of the GVU Law – Sector 3 : Pharmaceutical Provisions – Posted Expenditures 200912, 2010 May)

Table 2: Evolution posted expenditures on annual basis per regulation: total specialities, in Mil EURO (source Permanent Audit May 2010)

	2004	2005	2006	2007	2008	2009
General regulation	2.973,8	3.042,1	3.005,3	3.215,2	3.444,6	3.569,2
Self-employed	122,6	128,2	130,5	146,0	306,3	334,6
Total	3.096,4	3.170,3	3.135,8	3.361,2	3.750,8	3.903,8
evolution in %						
General regulation		2,3	-1,2	7,0	7,1	3,6
Self-employed		4,6	1,7	11,9	109,8	9,3
Total		**2,4**	**-1,1**	**7,2**	**11,6**	**4,1**

The most recent IMS data indicate an analogous evolution of the expenditures – with the exception of the year 2008, during which, for instance, the effect of the contribution to the costs of drugs for the self-employed (integration of the 'small risks ') is not being capped.

Although this report is not meant to make a forecast of the evolution of the expenditures for reimbursable drugs for 2010, it may be noted from the available IMS data (see ***Table 3***) that in 2010 no significant rise in these expenditures is to be expected.

Figure 1 illustrates the excellent correlation between the (evolution of the) net expenditures NIHDI for pharmaceutical specialities in the public pharmacies and the (evolution of the) exfac turnover figures as available in the IMS datasets. At the same time, the "prediction value" of these IMS data is justified herewith.

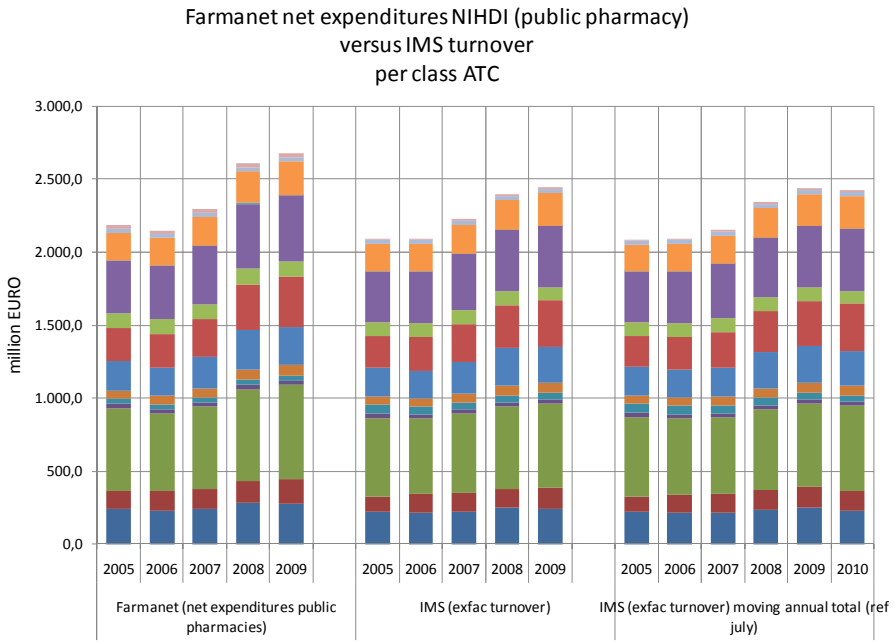
Table 3: IMS dataset: evolution of the gross turnover reimbursable drugs and 'moving annual total'[2] 2002 – 2009 (in Mil EURO)

	2005	2006	2007	2008	2009
total	2.089,3	2.094,9	2.227,1	2.396,5	2.444,5
% increase versus the previous year	0,27	6,31	7,61	2,00	0,27

MAT **(July)**	2005	2006	2007	2008	2009	2010
'moving annual total'	2.080,1	2.090,7	2.150,8	2.340,3	2.434,8	2.424,7
% increase versus the previous year		0,51	2,87	8,81	4,04	-0,41

[2] The term MAT 'moving annual total' indicates: total over a one-year period : not the (usual) calendar year but from month x (in this instance = August) of year y (for instance, 2009), to and including month x-1 (in this instance July) of year y+1 (for instance, 2010)

Figure 1: net expenditures NIHDI (public pharmacies) versus IMS turnover (2005 - 2009)



Likewise the most recent NIHDI data, for what concerns the posted expenditures (***Table 4***), confirm the extent of the expenditures and their evolution.

Table 4: Evolution of the posted expenditures on annual basis: total specialities, in Mil Euro (source Permanent Audit May 2010)[3]

	2004	**2005**	**2006**	**2007**	**2008**	**2009**
Public pharmacies	2.179,8	2.205,5	2.155,1	2.288,8	2.568,9	2.670,1
Hospitals – ambulatory patients	404,0	451,3	477,7	570,0	671,8	736,3
Hospitals - hospitalised patients	512,7	513,5	503,0	502,3	510,2	497,4
Total	3.096,4	3.170,3	3.135,8	3.361,2	3.750,8	3.903,8
evolution in %						
Public pharmacies		1,2	-2,3	6,2	12,2	3,9
Hospitals – ambulatory patients		11,7	5,9	19,3	17,9	9,6
Hospitals - hospitalised patients		0,2	-2,1	-0,1	1,6	-2,5
Total		**2,4**	**-1,1**	**7,2**	**11,6**	**4,1**

[3] Standardized report in application of article 51, § 4 of the GVU Law (mandatory health insurance) - Sector 3: Pharmaceutical provisions – Posted expenditures 200912, p 3.2. table 3.1.2.1. (NIHDI, Standardized report in application of article 51, § 4 of the GVU Law – Sector 3 : Pharmaceutical Provisions – Posted Expenditures 200912, 2010 May)

Similar recent NIHDI data for 2010, each time for the first five months (***Table 5***), extrapolated out of the permanent monitoring of data for these expenditures by the NIHDI actuarial department, confirm the assumption (on the basis of the IMS-dataset) that for 2010, one may at the most expect a minor increase in expenditures for 2010.

Table 5: Evolution of the posted expenditures (accumulated per year to and through May), in Mil EURO (source note Insurance Committee, Evolution of the monthly expenditures)[4]

	2007	**2008**	**2009**	**2010**
Public pharmacies	928.637	1.052.794	1.126.966	1.133.023
Hospitals – ambulatory patients	224.441	265.416	291.705	319.859
Hospitals - hospitalised patients	218.368	219.789	216.651	204.617
Total	1.371.446	1.537.999	1.635.322	1.657.499
evolution in %		**2008/2007**	**2009/2008**	**2010/2009**
Public pharmacies		13,4	7,0	0,5
Hospitals – ambulatory patients		18,3	9,9	9,7
Hospitals - hospitalised patients		0,7	-1,4	-5,6
Total		12,1	6,3	1,4

[4] (NIHDI, note CGU 2010/303 Evolution of the monthly expenditures on insurance for medical care. MAY 2010, p.7, 2010 September).

Global measures and trends with an impact on the expenditures for drugs in the public pharmacies and in hospitals and explanatory factors

Changes to the caps on the contributions made by patients – abolition of the ATC4 level

On 1 May 2008, the ATC4 patients' own contributions caps in reimbursement class B for the drugs for which an inexpensive alternative is available on the market were abolished. The patients' own contributions amount was brought back to the level of the patients' contributions for a drug in the reimbursement class B for which *no* inexpensive alternative is available (small or large-size packaging). This measure has resulted in an additional expenditure of 16 million Euro.

The caps for patients' own contributions were adapted on 1 July 2009. This measure has resulted in the additional expenditure of 14.1 million Euro.

Price reductions for old drugs

The total savings resulting from the mandatory price reduction for old drugs on 01-07-2008, 01-01-2009 and 01-07-2009 amount to 13.4 million Euro.

Effective implementation of the reference reimbursement system

The effective implementation of the reference reimbursement system on 01-07-2008; 01-01-2009, 01-05-2009, 01-07-2009 and 01-10-2009 will in the event of unmodified application in the future result in a savings of 95.6 million Euro. This savings represents the sum total of the savings realized on the initial implementation of the new reimbursement base and the subsequent additional reduction of the reimbursement base after 2 and 4 years.

Savings within the context of article 159 of the Programme Law

Article 159 of the Programme Law held that on 1 May 2009 the reimbursement bases of the pharmaceutical specialities had to decrease (modular), so that a savings of 1.95% can be realized over the turnover figure of 2007 for each applicant. The savings thus realized by this measure amount to 59.3 million Euro.

EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES IN THE PUBLIC PHARMACIES

General

Table 6: net annual expenditures NIHDI for drugs in 2002 – 2009

	2002	2003	2004	2005	2006	2007	2008	2009
NIHDI net expenditures x 1,000,000 €	**1.921,6**	**2.063,3**	**2.213,0**	**2.203,6**	**2.161,1**	**2.297,9**	**2.611,1**	**2.679,2**

	2001-2002	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009
growth %	**7,3**	**7,4**	**7,3**	**min 0,4**	**min 1,9**	**6,3**	**13,6**	**2,6**

Table 7: net annual expenditures NIHDI for drugs in public pharmacies top 80%

	Denomination	Growth 2007-2008	Growth 2008-2009	Net NIHDI 2009
	Total	13,63	2,61	2.679,2
C10A	LIPID MODIFYING AGENTS, PLAIN	7,49	10,52	235,3
L04A	IMMUNOSUPPRESSANTS	32,07	19,94	178,9
N06A	ANTIDEPRESSANTS	10,33	-7,48	146,2
A02B	DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	18,89	-5,12	134,6
B01A	ANTITHROMBOTIC AGENTS	13,35	9,82	118,0
R03A	ADRENERGICS, INHALANTS	8,47	3,67	107,1
N05A	ANTIPSYCHOTICS	4,91	9,67	103,5
A10A	INSULINS AND ANALOGUES	13,36	4,36	70,7
J05A	DIRECT ACTING ANTIVIRALS	15,11	13,09	69,8
L03A	IMMUNOSTIMULANTS	9,25	-0,71	64,6
C07A	BETA BLOCKING AGENTS	11,61	-0,45	62,6
N03A	ANTIEPILEPTICS	14,63	12,81	62,1
N02A	OPIOIDS	11,46	2,61	61,3
C09C	ANGIOTENSIN II ANTAGONISTS, PLAIN	7,42	-2,65	58,9
A10B	BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	14,46	4,69	53,8
C09A	ACE INHIBITORS, PLAIN	13,28	-14,21	53,7
C09D	ANGIOTENSIN II ANTAGONISTS, COMBINATIONS	27,96	9,79	52,7
J01C	BETA-LACTAM ANTIBACTERIALS, PENICILLINS	14,05	-0,03	51,5
R03B	OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS	6,54	4,01	51,2
C08C	SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	11,99	1,14	49,1
B02B	VITAMIN K AND OTHER HEMOSTATICS	11,61	4,14	47,6
M01A	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	7,13	-4,09	47,4
J07B	VIRAL VACCINES	138,06	-24,03	46,0
M05B	DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	6,39	-11,61	45,0
L02B	HORMONE ANTAGONISTS AND RELATED AGENTS	21,59	-2,62	40,8
C01D	VASODILATORS USED IN CARDIAC DISEASES	0,03	-5,35	35,4

N06D	ANTIDEMENTIA DRUGS	16,25	8,01	33,7
N04B	DOPAMINERGIC AGENTS	12,21	4,52	29,1
L01X	OTHER ANTINEOPLASTIC AGENTS	20,64	4,41	27,5
L02A	HORMONES AND RELATED AGENTS	2,04	-7,39	27,4

The overview of the expenditures and the *established* growth per ATC3-class (***Table 7***) indicates that **30 of the 180 classes** account for **80% of the expenditures** in the public pharmacies**.**

Later on in this report, a number of these classes of drugs that have seen a significant evolution in the expenditures will be discussed in greater detail.

DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE

Figure 2: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class A02B for Peptic Ulcer and Gastro-Oesophageal Reflux disease

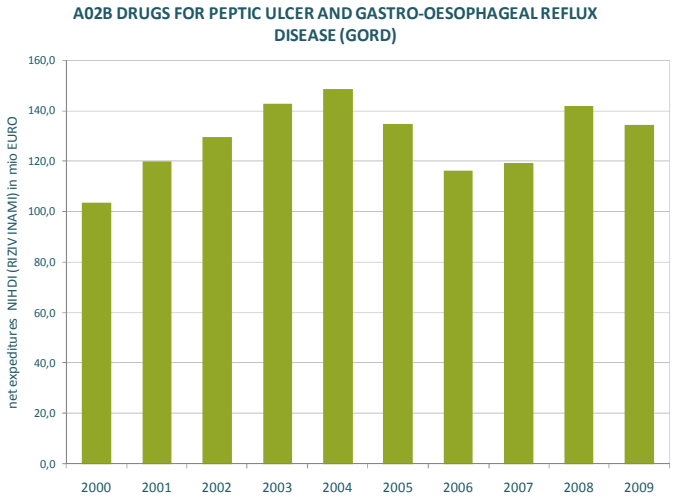
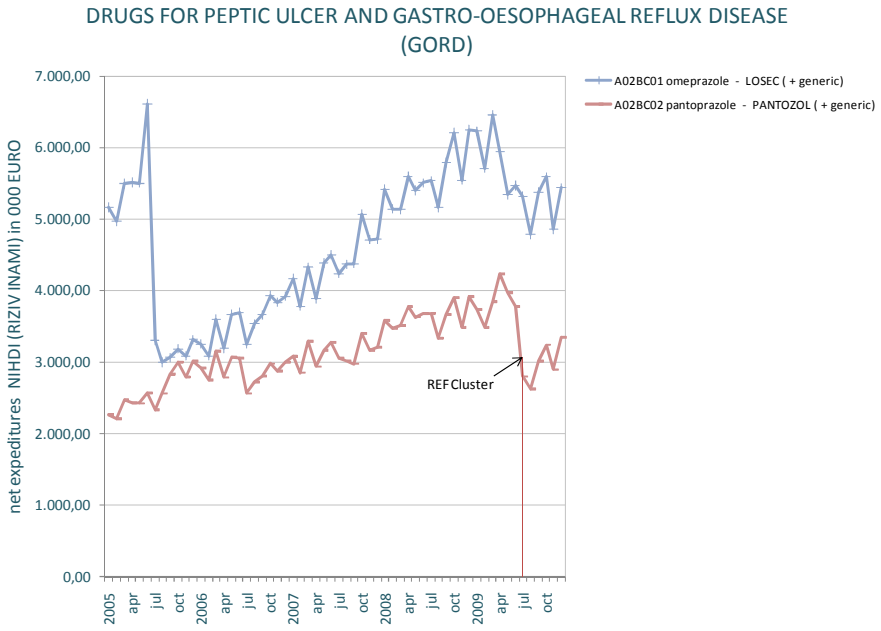


Figure 3: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class A02B Drugs Peptic Ulcer and Gastro-Oesophageal Reflux disease



The observed expenditures for the class A02B (proton pump inhibitors (PPI)), on the rise since 2006, have dropped slightly in 2009. In contrast, the number of patients for this class keeps on growing during the same period. This contrary trend is largely due to the introduction of the reference price system for

pantoprazol in July 2009, with simultaneous application to this molecule of the measure towards price reduction for the drugs that have been reimbursable for already more than 12 years (-15%). Further, the generic drugs with a pantoprazol base have been entered under Chapter II, while the original specialities are entered into Chapter IV. As was the case for the generic drugs with an omeprazol and lansoprazol base, this registration in Chapter II was linked to a reduction of the reimbursement base of 40%, this in addition to their initial decrease of 30%.

The extent of the reduction of the expenditures in 2009 was slowed by the significant increase in the number of patients treated with pantoprazol: 195.000 patients **+** 120 %, in other words, an addition of some 235.000 patients. A small number of these new patients were most likely treated previously with another PPI, in which case, in most instances, a slight drop in the number of patients is noticeable. At the same time, we note in 2009 a stabilisation of the number of patients treated with omeprazol, at the time the only inexpensive molecule under the PPI. In spite of the fact that numerous PPI and their generic drugs in Chapter II have been on the market already for a long time, the 'reservoir' of new patients for this group of proton pump inhibitors has clearly not been exhausted yet.

Table 8: Evolution of the number of patients with PPI treatment in 2005 – 2009

	Number of patients 2006	Number of patients 2007	Number of patients 2008	Number of patients 2009
A02BC01 – OMEPRAZOL	500.148	612.449	786.918	788.154
A02BC02 – PANTOPRAZOL	176.992	177.759	195.280	428.755
A02BC03 – LANSOPRAZOL	45.862	54.477	59.606	49.773
A02BC04 – RABEPRAZOL	52.977	42.634	35.693	23.595
A02BC05 – ESOMEPRAZOL	90.605	94.949	102.993	87.157
TOTAL number of patients (*)	781.539	893.462	1.079.033	1.220.188

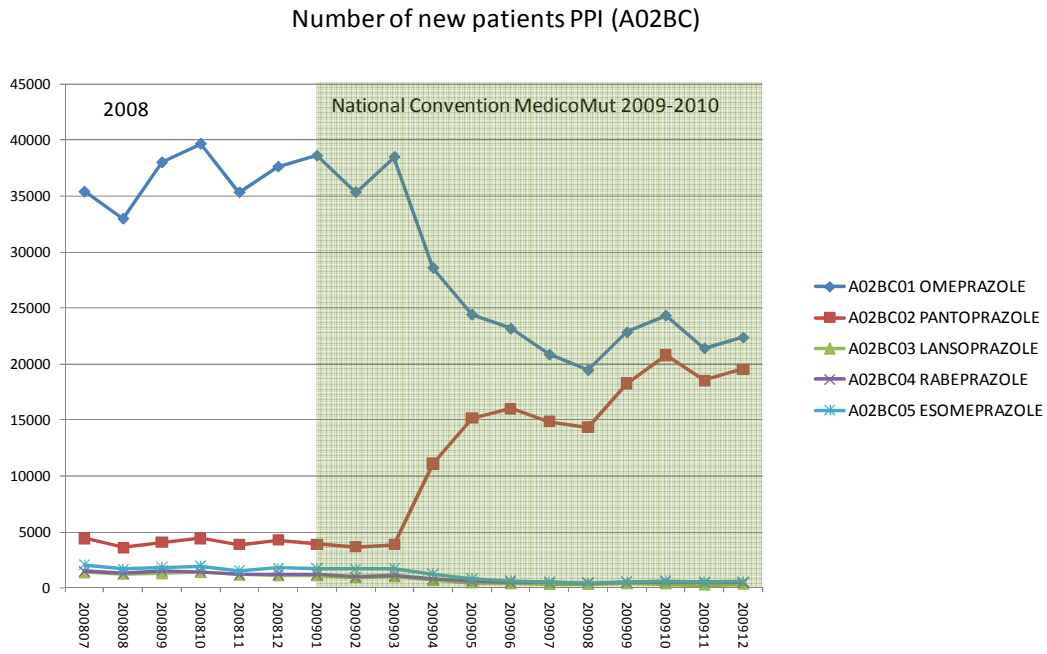
(*) The total number of patients under PPI is smaller than the sum of the molecules separately, since certain patients take various PPI per year.

One of the concrete prescription objectives entered into the National Accord between Physicians – Health Insurance Funds for 2009-2010 is to promote the prescription of the « least expensive » molecules at the start of a treatment.
Without prejudice to the quality of the treatment or to the therapeutic needs, the National Commission of Physicians – Health Insurance Funds (NCGZ) proposes to primarily concentrate on initial treatments, whether or not these are being initiated by a family doctor or a specialist. In this manner, one may avoid that existing treatments will eventually have to be changed.

The proton pump inhibitors (A02BC) is one of the groups for which physicians are engaging themselves to start, in principle and in at least 8 out of 10 cases, with one of the most inexpensive molecules of a group for so far as there does not exist a counter-indication for it and provided that the therapeutic objectives be realized.

Within the class of the proton pump inhibitors (A02BC), at the end of 2008, new patients did in 82% of the instances receive a treatment that started with the most inexpensive molecule omeprazol (Expenditures NIHDI/DDD).

Figure 4: Evolution of the number of new patients per PPI (A02BC) for 2008-2009



On evaluation of this measure, it was noted in 2009 that the percentage of new patients undergoing treatment started with omeprazol, the least expensive molecule, gradually declined from 83% in January 2009 to 52% end of 2009.
In contrast, we note a striking increase in the start-up treatment with pantoprazol (from 9% in January 2009 to 45% of new patients in December 2009). While for 2009, within the class of the PPI (A02BC) only omeprazol was noted as the least expensive molecule, as of January 2010, also pantoprazol and lansoprazol are added as inexpensive molecules.
Irrespective of the determination of a strongly increased volume for PPI in 2009 (246 million DDD for 2009 versus 210 million DDD in 2008), and taking into account the evolution of the cost price of pantoprazol (in the reference price system in July 2009) and the real dosages used, the agreed objective for the class of the PPI was achieved in 2009.

Table 9 allows us to deduce from the applied volume per patient that the omeprazols are used in the largest volume per patient, namely 210 DDD per patient in 2009. Every patient treated with omeprazol receives this treatment on the average during 5 to 6 months, at a dosage of 1 DDD per day.

Table 9: The used volume of PPI per patient (expressed in number DDD/patient)

	A02BC01 - OMEPRAZOL	A02BC02 - PANTOPRAZOL	A02BC03 - LANSOPRAZOL	A02BC04 - RABEPRAZOL	A02BC05 - ESOMEPRAZOL
2006	172,4	133,8	155,8	53,6	146,7
2007	179,0	145,2	161,1	56,7	151,2
2008	193,1	151,9	175,1	59,7	155,1
2009	209,6	131,8	197,5	64,8	156,6

Figure 5: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class A10A Insulins and Analogues

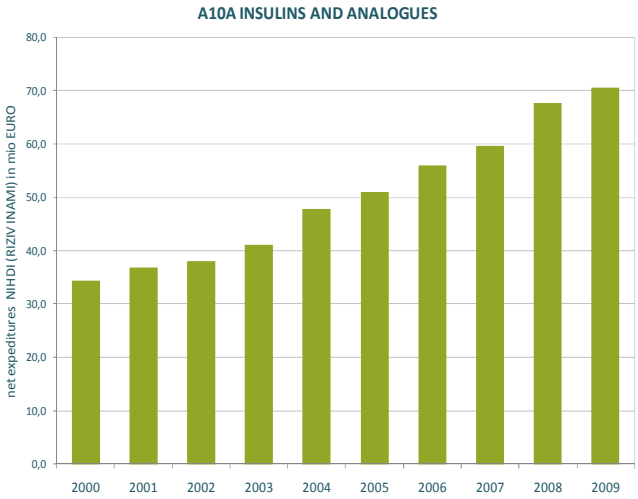
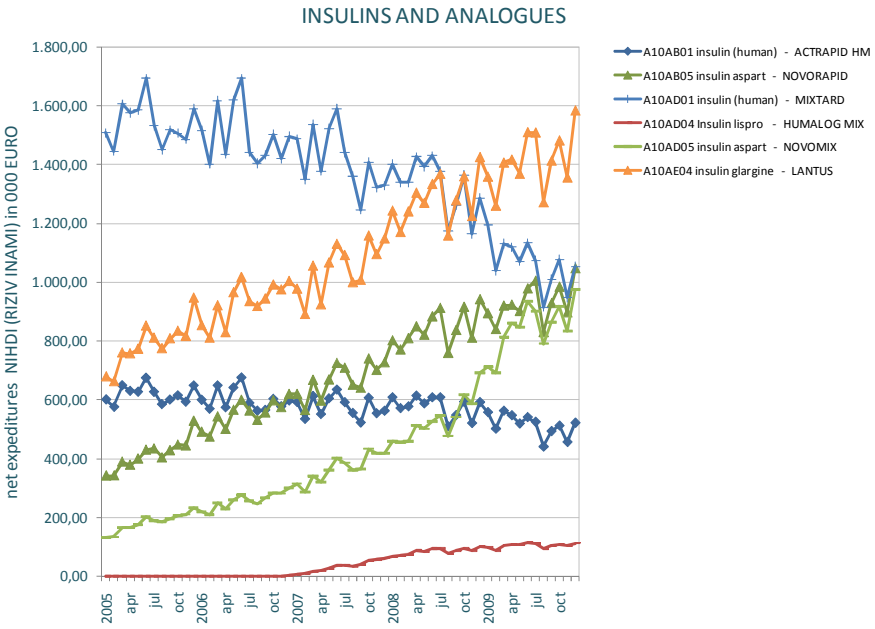


Figure 6: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class A10A Insulins and Analogues

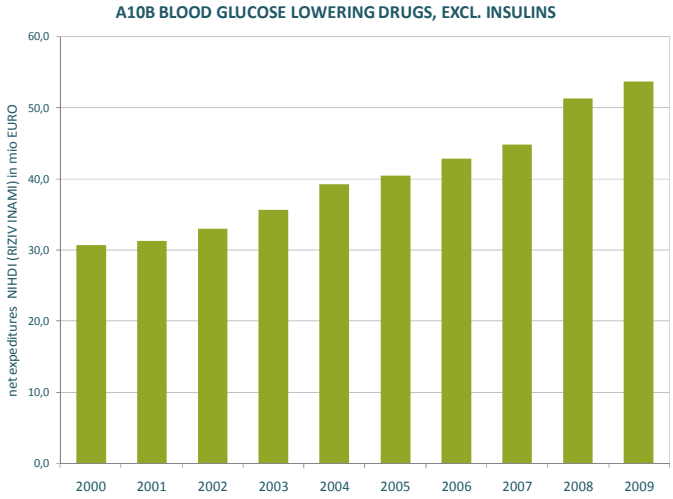


The increase in expenditures for this class is less pronounced than in the previous year, but a progressive switch from the human insulins (e.g., Mixtard®, Actrapid®) to insulin-analogues (e.g., Novorapid®, Lantus® and Humalog®Mix), which are more expensive, is still noted. Striking is the increase in the expenditures

for Novomix®, still more pronounced since July 2008, as a result of the expansion of the drug assortment with Novomix® 50 and Novomix® 70.

The current recommendations for treatment tend towards a more ready recourse to insulin. In 2008, amongst the 129.467 patients treated with insulin or an analogue, 62.000 patients suffered from type 2 diabetes. In 2009, 132.838 patients were treated with insulin or an analogue, being more than 1% of the Belgian population.

Figure 7: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class A10B Blood Glucose Lowering drugs, with the exclusion of insulins



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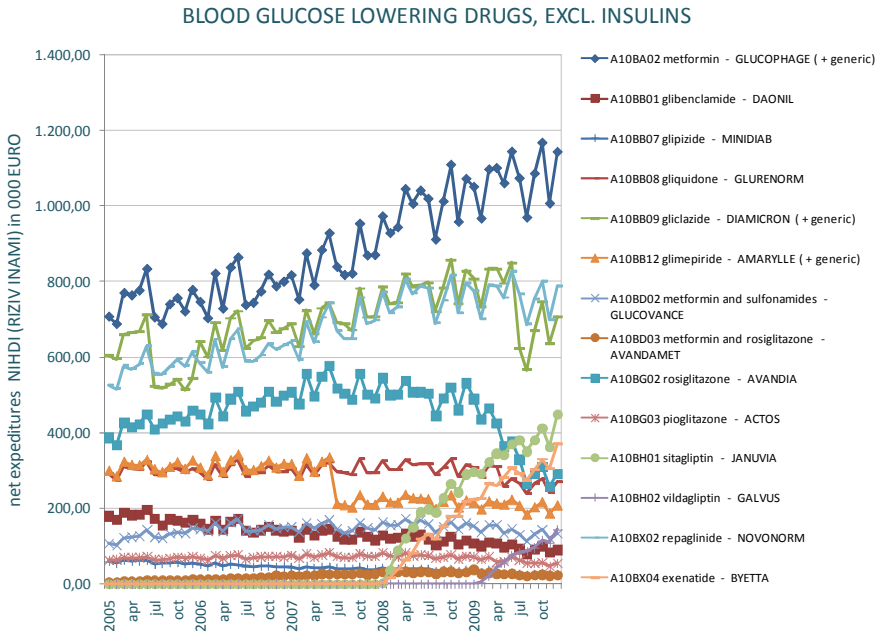


Aside from the remarkable increase in the use of new antidiabetics, as already stated in the previous MORSE report, we also note a pronounced rise in the use of metformin, a first-choice preparation when treatment with medications is necessary in dealing with type 2-diabetes, certainly in the case of obese persons.

The increasing expenditures since 2008 for metformin are attributable, on the one hand, to the rising number of new diabetes type 2-patients and, on the other, to the reimbursability of the novel specialities

Januvia® and Byetta® since 01/01/2008, which require a preliminary and simultaneous treatment with, respectively, metformin and metformin plus one sulphonamides. In 2008, the hypoglycaemic sulphonamides record for the first time in years a renewed rise in the number of applied DDDs.

The class of the glitazones (A10BG) has recorded a slight drop in expenditures since 2008. This decline, which is actually rising in 2009, can be explained practically wholly by the reduced use of rosiglitazone (Avandia®).

The American Food and Drug Administration (FDA) did on 21 May 2007 issue a warning concerning the heightened risk of cardiovascular accidents involving rosiglitazone (Avandia ®), as a result of which the FDA rescinded the drug's registration in 2010.

The firm GlaxoSmithKline (GSK), holder of the licence to market (VHB) of Avandia® and Avandamet® has decided to withdraw these drugs from the Belgian market upon the recommendation of the CHMP (Committee for Medical Products for Human Use) of the European Drug Agency (EMA) to suspend the VHB because of a heightened cardiovascular risk associated with the use of these drugs (implemented on 23 September 2010).

The decision by the European Commission, based on this judgment, is expected sometime in the coming weeks, whereby a procedure for the abolition of the marketing licence at the European level is being considered *(info December 2010).*

Given the fast evolution of their use and the extent of the expenditures, this class of drugs will be monitored in the future reports.

ANTITHROMBOTIC AGENTS

Figure 9: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class B01A Antithrombotic agents

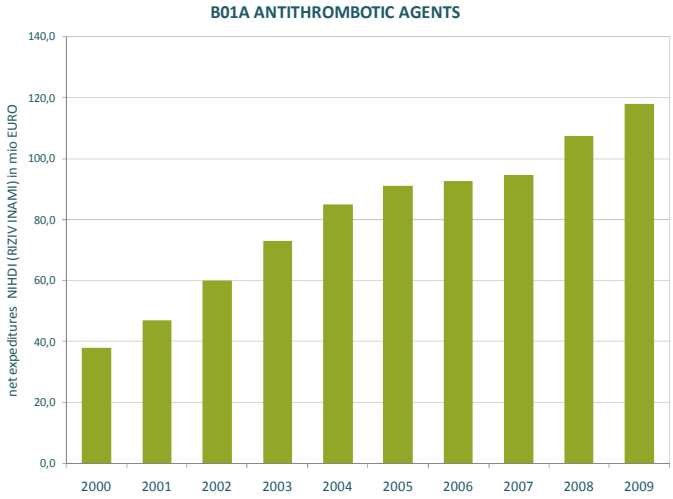
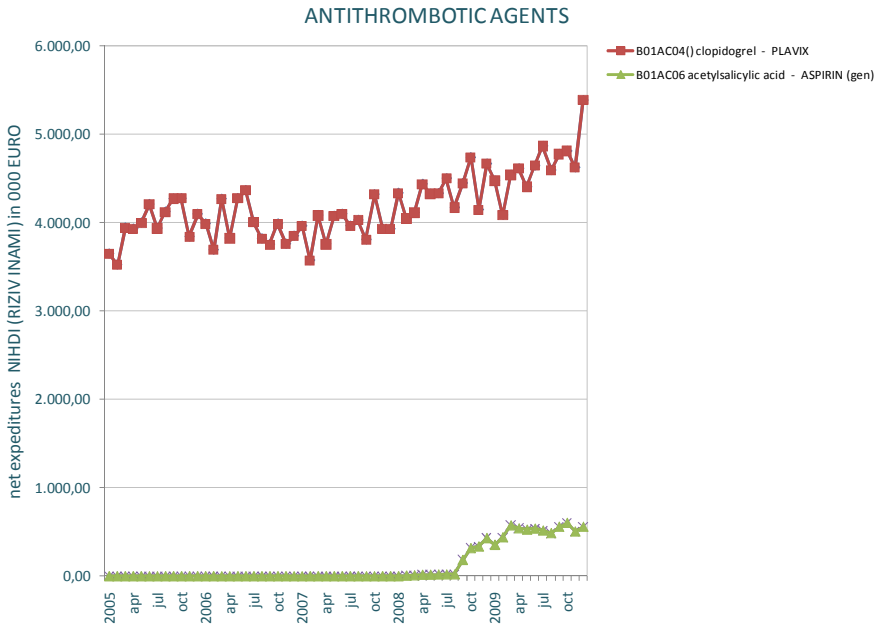


Figure 10: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class B01A Antithrombotic agents



In the analysis of the expenditures for clopidogrel and acetylsalicylic acid, the predicted switch in the use of clopidogrel (for which the reimbursement conditions were changed in 2009) to acetylsalicylic acid is not noticeable.

The effect of the availability of generics *(since mid- 2010)* on the evolution of the expenditures for this class of drugs will be monitored in future reports.

ACE INHIBITORS

Figure 11: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class C09A ACE inhibitors

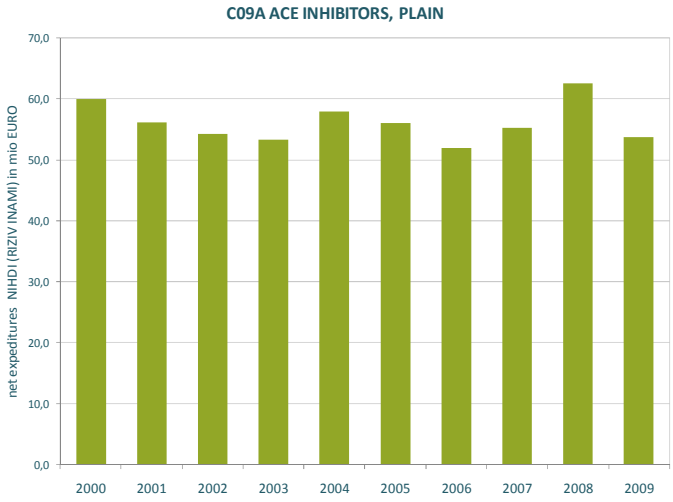
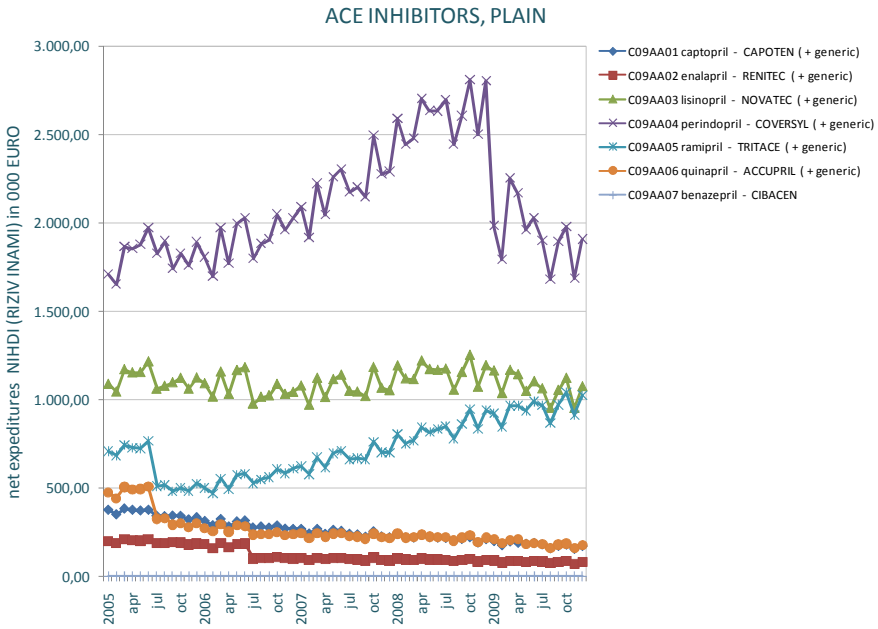


Figure 12: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class C09A ACE inhibitors



The expenditures for ACE inhibitors in 2009 have dropped by 14%, which is largely attributable to the entry into force of the reference cluster for perindopril in January 2009. Only the expenditures for ramipril, which becomes the second most important molecule, register a linear rise.

Figure 13: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class C09C Antagonists, plain

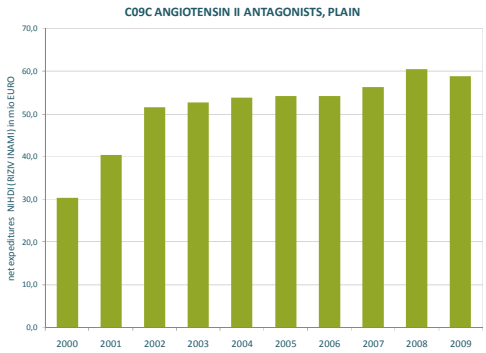


Figure 14: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class C09D Antagonists – combination preparations

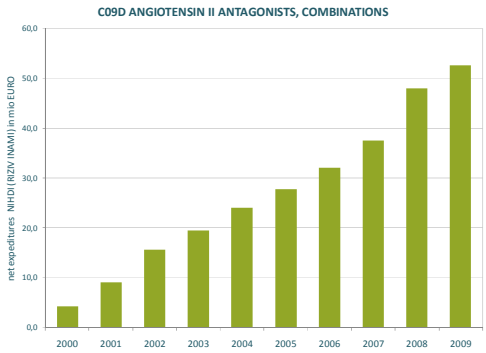
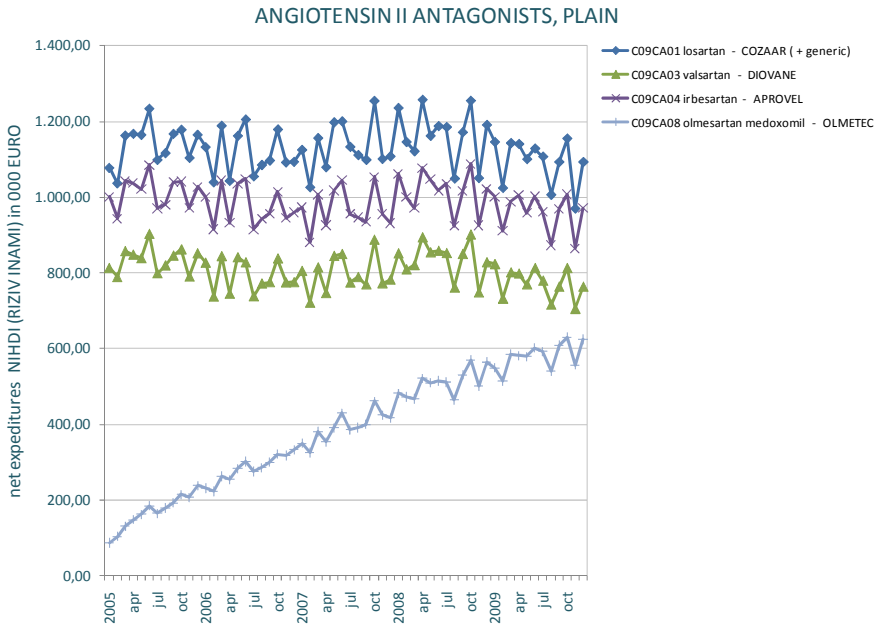


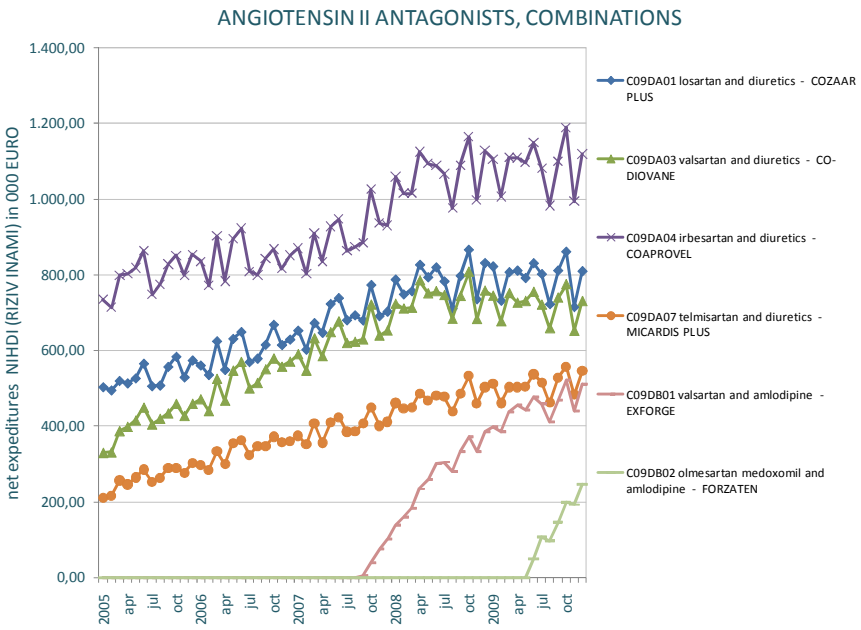
Figure 15: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class C09C Antagonists, plain



Within the class of the antagonists in monopreparations (C09C), it is primarily the molecule olmesartan (Olmetec®) that is showing an increase in expenditures. The expenditures of the molecules that are responsible for the major expenditures (losartan, valsartan, and irbesartan) each drop by 6 to 7% in 2009.

In addition, within the class of the antagonists in monopreparations for de molecule losartan, the reference reimbursement has become effective in July 2010, while for the molecule valsartan the reference cluster is expected during the course of 2011. The realized savings of these reference clusters need certainly to be monitored, given that they will be coupled to the registration of the generics based on losartan and valsartan in Chapter I, in contrast to the reference specialities Loortan®, Cozaar®, and Diovane® that are being reimbursed under Chapter IV with an *a priori* control.

Figure 16: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class C09D Antagonists – combination preparations



Contrary to the declining expenditures in 2009 of antagonists in monopreparations, we note a rise of 10% for the expenditures of the antagonists in combination preparations. The switch from monopreparations to fixed association preparations is also noted for the ACE-inhibitors.
The use of the new combinations with calcium antagonists registers a strong rise, aside from the growing use of the combinations with a thiazide diuretic.

It is important to note that aside from a declining number of patients for antagonists in mono-preparations, there is the tendency to administer treatment with ever higher dosages of antagonists.

Table 10: Evolution of the number of patients treated with ACE-inhibitors and Antagonists in mono- and combination preparations.

ATC	Name	Number patients 2006	Number patients 2007	Number patients 2008	Number patients 2009
C09	***AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM***	***940.294***	***1.010.138***	***1.140.756***	***1.195.284***
C09A	**ACE-INHIBITORS, MONOPREPARATIONS**	**515.311**	**549.849**	**609.439**	**625.547**
C09B	**ACE-INHIBITORS, COMBINATION PREPARATIONS**	**118.238**	**139.655**	**175.442**	**203.859**
C09BA	ACE-INHIBITORS WITH DIURETICS	118.238	135.075	162.650	168.293
C09BB	ACE-INHIBITORS WITH CALCIUM-ANTAGONISTS	0	4.933	13.642	38.557
C09C	**ANTAGONISTS, PLAIN**	**247.933**	**252.156**	**267.259**	**263.168**
C09D	**ANTAGONISTS, COMBINATION PREPARATIONS**	**136.940**	**157.394**	**193.968**	**213.040**
C09DA	ANTAGONISTS WITH DIURETICS	136.940	155.603	181.615	188.889
C09DB	ANTAGONISTS WITH CALCIUM-ANTAGONISTS	0	2.190	13.965	27.204

There is growing evidence that, for most of the indications, the effectiveness of the antagonists is identical to the one of the ACE-inhibitors (C09A), but antagonists are rather more expensive[5].
The least expensive molecule within the class of the products acting on the renin-angiotensin system (C09) comprises, in effect, the inhibitors of the conversion-enzyme (C09A), for which the expenditures in 2009 dropped by 14% but for which the number of patients rose.

The physicians that joined into the National Accord of Physicians – National Health Insurance Funds 2009-2010, engage themselves also for the pharmaceutical group of ACE-inhibitors and Antagonists (C09), as of 1 January 2009, to use at the start of a treatment in at least 8 out of 10 cases one of the least expensive molecules of this group, being the inhibitors of the conversion-enzyme in monopreparations (C09A) and in combination preparations (C09B), if there exists no counter-indication to this and with proviso that the therapeutic objectives be achieved.
From the evaluation of the 2009 data, we may deduce that the predetermined objective was achieved and that between 86% and 90 % of the new patients in 2009 were treated with an inexpensive ACE-inhibitor (C09A +C09B).

Table 11: Number of new patients treated with ACE-inhibitors in monopreparations (C09A) and combination preparations (C09B) in 2009.

	New patients C09A ACE-inhibitors MONO	New patients C09B ACE inhibitors COMB	Total New patients - CO9	% inexpensive GM (C09A + C09B)
2009/01	12.119	3.094	17.649	86,2%
2009/02	11.438	2.947	16.549	86,9%
2009/03	12.998	3.371	18.570	88,2%
2009/04	11.757	3.372	17.194	88,0%
2009/05	10.844	3.261	15.849	89,0%
2009/06	10.679	3.177	15.619	88,7%
2009/07	9.027	2.618	13.276	87,7%
2009/08	7.888	2.291	11.522	88,3%
2009/09	9.253	2.906	13.527	89,9%
2009/10	11.031	3.564	16.083	90,8%
2009/11	9.746	3.281	14.517	89,7%
2009/12	10.257	3.676	15.482	90,0%

[5] **after the** Annotated Drug Repertory 2010 (BCFI, 2010)

LIPID MODIFYING AGENTS

Figure 17: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class C10A Lipid modifying agents, plain

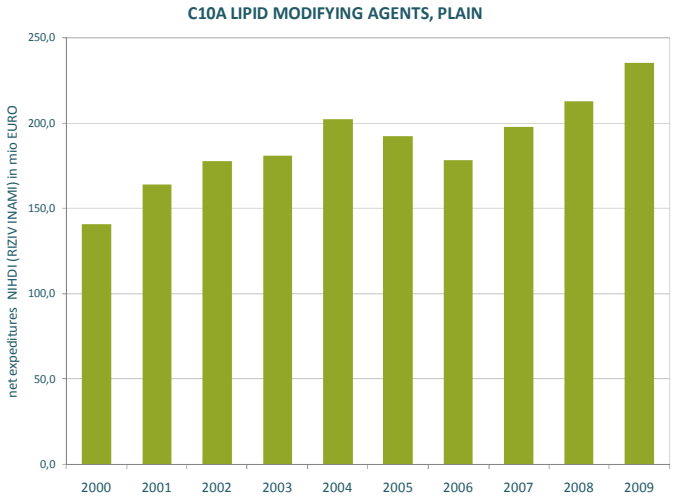
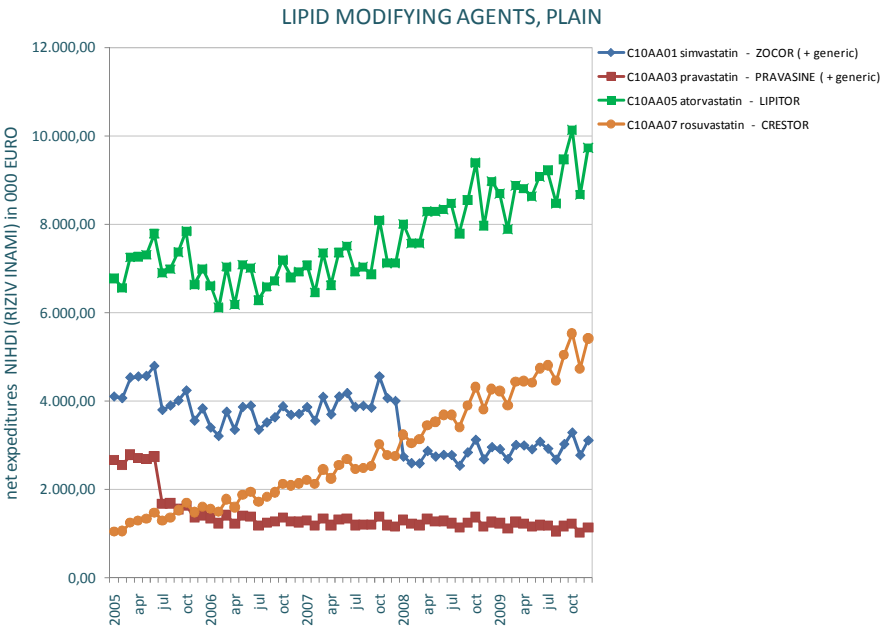


Figure 18: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class B01A Lipid modifying agents, plain



The physicians that join into the National Accord of Physicians – National Health Insurance Funds 2009-2010, engage themselves as of 1 January 2009, to use at the start of a treatment with a statin (C10AA), in principle and in at least 8 out of 10 cases, one of the least expensive molecules of this group, in so far as there exists no counter-indication to this and with proviso that the therapeutic objectives be achieved.

Pravastatin (following modification of the DDD- see ***Table 14***) and simvastatin were identified as the least expensive molecules of the group.

Figure 18 does, however, demonstrate a continuous rise in expenditures for the molecules atorvastatin and rosuvastatin, while the expenditures of the least expensive molecules remain stagnant. The above-described measure, taken within a context of a feasible savings of 42.5 Euro, appears to have no direct effect on the prescription trend for statins. It is notable that the annual number of new patients pertains to a very small percentage of the total population that was treated with statins, namely 228.300 new patients out of a total population of 1.272.600 patients treated with statins in 2009.

Table 12: Distribution of the treatments with a statin (C10AA - Inhibitors of the HMG-CoA reductase) with new patients end of 2008, prior to the National Accord between Physicians and National Health Insurance Funds 2009-2010.

ATC-code	Name of the molecule	Name of the most prescribed speciality	% of the volume of new patients
C10AA01	SIMVASTATIN	ZOCOR 20 mg	59%
C10AA03	PRAVASTATIN	PRAREDUCT 40 mg	9%
C10AA04	FLUVASTATIN	LESCOL EXEL 80	1%
C10AA05	ATORVASTATIN	LIPITOR 20	20%
C10AA07	ROSUVASTATIN	CRESTOR 10 mg	11%

Table 13: Distribution of the treatments with a statin (C10AA - Inhibitors of the HMG-CoA reductase) with new patients and all treated patients end 2009.

ATC-code	Name of the molecule	% of the volume of new patients	% of the volume of treated patients
C10AA01	SIMVASTATIN	**61%**	**51%**
C10AA03	PRAVASTATIN	8%	10%
C10AA04	FLUVASTATIN	0.5%	1%
C10AA05	ATORVASTATIN	**14%**	**23%**
C10AA07	ROSUVASTATIN	17%	19%

We may deduce from the above *Table 13* that the percentage of patients treated with simvastatin has declined from 61% at the start of the treatment to 51% as chronic therapy, while the percentage of patients ultimately treated with atorvastatin registers a notable rise from 14% at the start of the treatment to 23 % as chronic therapy.
The measure for the start-up of a treatment with an inexpensive statin in at least 8 out of 10 cases was in this case not achieved in 2009.

The National Commission of Physicians and National Health Insurance Funds (NCGZ) is therefore of the opinion that a number of additional measures need to be seriously entertained, pertaining, amongst others, to the further promotion of prescribing the least expensive molecules within the statins class.
In 2009, the CRM [Commission for the Teimbursement of Medicines] (at the suggestion of the tri-part work group), in that regard and taking into account the conclusions of the consensus conference of May 2009, made recommendations for the prescription of statins for what concerns the start-up and continuation of an intensified statin treatment and the use of the more expensive statins.

Table 14: Modification of the value for the DDD statins 2008 – 2009

Name of the molecule	DDD 2008	DDD 2009
SIMVASTATIN	15 mg	30 mg
PRAVASTATIN	20 mg	30 mg
FLUVASTATIN	40 mg	60 mg
ATORVASTATIN	10 mg	20 mg
ROSUVASTATIN	-	10 mg

The comparison of the DDD with the NIHDI cost per molecule manifests the great differences between the most and the least expensive statins. For instance, in 2009, the NIHDI expenditures for the specialities based on simvastatin amounted to 35 million Euro, corresponding to 160 million DDD simvastatin, while the NIHDI expenditures for the specialities based on atorvastatin amount to 108 million Euro, with a number of 97 million DDD atorvastatin.

Table 15: NIHDI cost price per DDD for the various statins in 2009.

Name of the molecule	DDD 2009	Net cost 2009 (Euro)	Cost price per DDD (Euro)
SIMVASTATIN	160.333.488	35.393.550	0,22
PRAVASTATIN	37.692.735	14.044.850	0,37
FLUVASTATIN	6.082.942	3.308.494	0,54
ATORVASTATIN	97.078.720	107.778.525	1,11
ROSUVASTATIN	81.869.027	56.255.235	0,69

Figure 19: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class J05A Direct Acting Antiviral Agents

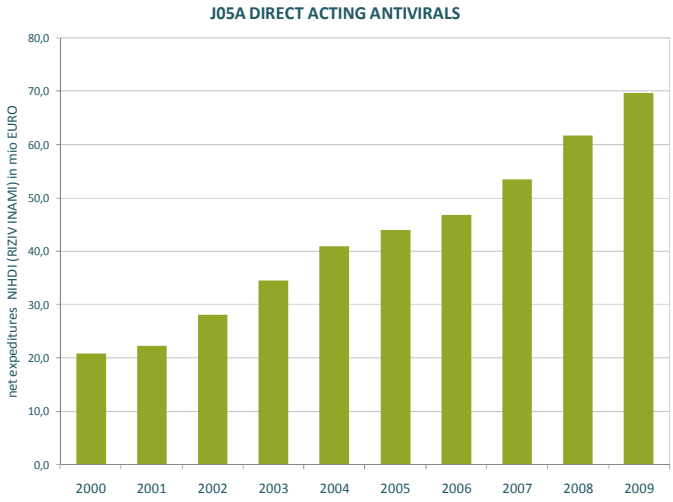
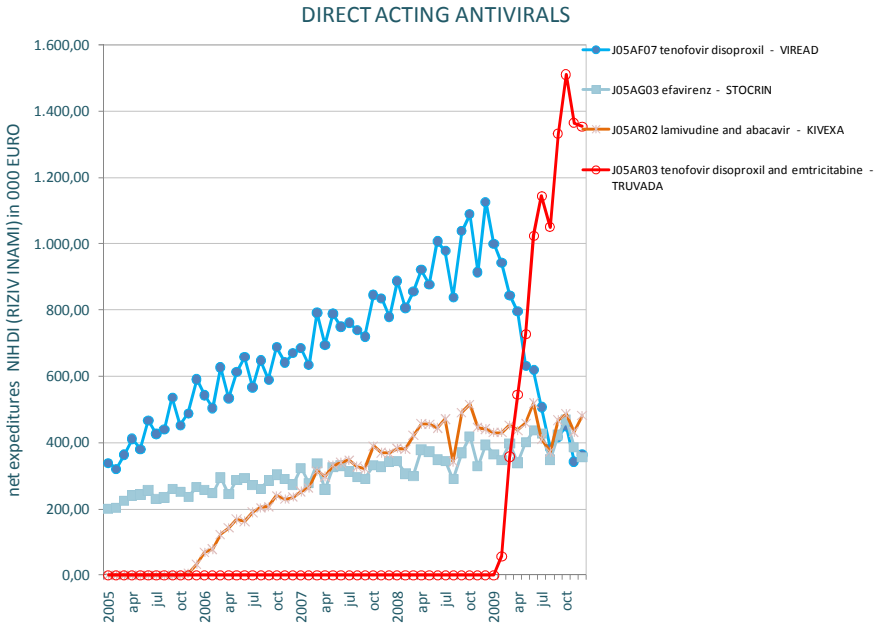


Figure 20: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class J05A Direct Acting Antiviral Agents



The registration of Truvada® (fixed combination of the active ingredients of Viread® and Emtriva®) on the list of the reimbursable specialities would, in theory, imply a savings, given that the combination is less expensive than the two molecules separately taken. In order to estimate the budgetary impact, one needs to take into account, however, an array of other possible scenarios, amongst which the switch of one of both molecules to the combination, or the switch between combinations amongst themselves (with Kivexa®, for instance).

As observed on the graph, the registration of Truvada® corresponds with a significant drop in the expenditures for Viread®. One may thus conclude that a massive shift away from Viread® to Truvada® is happening. The expenditures for Viread® in December 2009 (381.603€) are in fact only at 30% of those of one year earlier (1.275.928€). Given the difference in day cost (13,81€ for Viread®, 19,06€ for Truvada®), this switch has resulted in unfavourable budgetary consequences that need to be followed up and the extent of which depends on the evolution of the expenditures for Emtriva®. Following a significant rise in 2008, the expenditures in 2009 for this speciality drug have fallen back to the level of 2007, or to circa 730.000 Euro.

The expenditures of the ATC-group J05A are largely due to the application of antiviral agents against HIV. This concerns a therapeutic domain where recourse to poly-therapy is current, with recommendation to use an increasing number of antiretroviral agents (2 before, 3 at present), but where also the molecules of the latest generations are replacing the older ones or are being added very rapidly (greater resistance, more significant user comfort, better functionality, etc.).
As a result, the introduction of the reference price system for the specialities used against HIV will not have a marked impact on the expenditures, in any event not during the next coming years.

On the other hand, the expenditures for Viread®, which in 2008 represented nearly triple the initially estimated budget, need to be further monitored, given the addition of the indication for the treatment of hepatitis B in November 2009.

In fine, it is still too early to estimate at the end of 2009 the budgetary impact of the reimbursement of Atripla®, which combines the active ingredients of Stocrin®, Emtriva® and Viread®.

IMMUNOSUPPRESSANTS

Figure 21: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class L04A Immunosuppressants

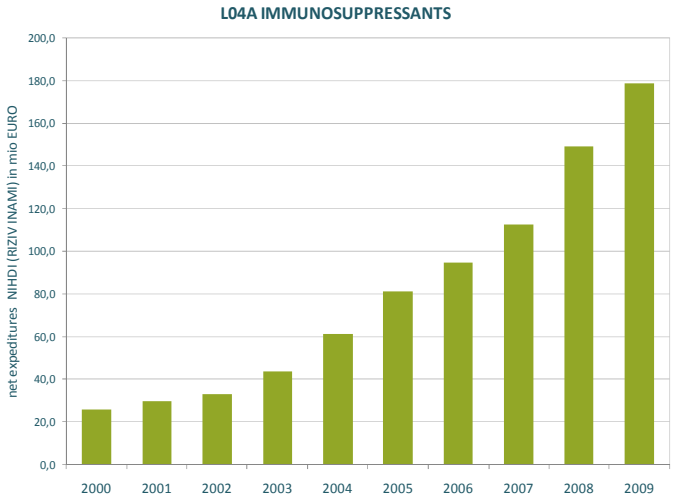
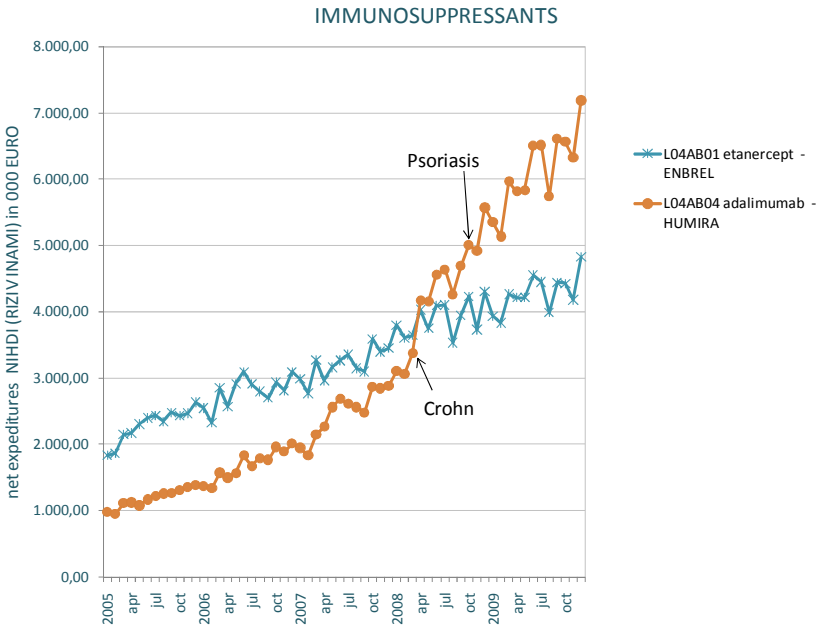


Figure 22: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class L04A Immunosuppressants



The ATC-3 class with the most notable rise in expenditures for 2009 in public pharmacies is unquestionably the class of the Immunosuppressants (L04A). The expenditures in public pharmacies rise in 2009 by 20%.
The TNF-inhibitors Humira® and Enbrel® remain responsible for the most significant increases of the expenditures in public pharmacies.

The most remarkable molecule within this class is adalimumab (Humira® - L04AB04), for which the monthly expenditures over a five-year period rose from 1 million Euro per month to 7 million Euro per month. The reimbursement conditions for this molecule were in 2008 expanded by 2 new indications (Crohn's Disease in March 2008 and psoriasis in October 2008), aside from the already existing reimbursement for rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. Seeing that Humira® is the third anti-TNF-α on the market for the treatment of psoriasis, the applicant did not predict any market expansion. The report of the Drug Reimbursement Commission estimated the number of patients treated for "psoriasis" via a market shift at 400, corresponding with a treatment cost of circa 15.000 Euro per patient per annum. This cost is lower than for the treatment with Remicade® in hospitals (circa 16.000 Euro/patient per annum), but higher than the treatment with Enbrel® (circa 11.500 Euro /patient per annum). At that time, the reimbursement modalities for Enbrel® foresaw for the indication "psoriasis" an interruption of the treatment after 24 weeks for at least 8 weeks, whereas Humira® was reimbursed during continuous treatment of psoriasis.

Table 16: Number of treated patients per year with Humira and Enbrel

		2006	2007	2008	2009
HUMIRA L04AB04		1.945	2.875	5.372	7.206
growth patients			47,8%	86,9%	34,1%
ENBREL L04AB01		3.479	3.980	4.721	5.117
growth patients			14,4%	18,6%	8,4%

Table 17: Growth of the net expenditures for Humira and Enbrel in 2005-2009.

	2005	2006	2007	2008	2009
Enbrel L04AB01	27.500.133	33.538.207	38.442.386	46.743.844	51.313.037
Humira L04AB04	14.180.450	20.249.119	29.680.197	51.495.493	73.543.021
growth Enbrel		22,0%	14,6%	21,6%	9,8%
growth Humira		42,8%	46,6%	73,5%	42,8%

The forecast positive budgetary impact for the other reimbursable indications of Humira® (being rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and Crohn's Disease), resulting from the accepted price drop of 4 % for the indication "psoriasis", was more than neutralized by the strong rise in the number of patients treated with Humira® in 2008 and 2009.
The maximum budgetary impact for Humira® in the indication "Crohn's Disease" was for the first year in the evaluation report of the Drug Reimbursement Commission estimated at 8.6 million Euro and would according to the previous MORSE report at least be realized.
An observed rise in the expenditures for Humira for 2009 by 22 million Euro largely exceeds the expectations.

Furthermore, it needs to be noted that also within the hospital environment, this class ranks within the top 3 of drug expenditures and that there is an increase of the expenditures for 2009 of 18.6%.

Figure 23: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class M05B Drugs affecting bone structure and mineralization

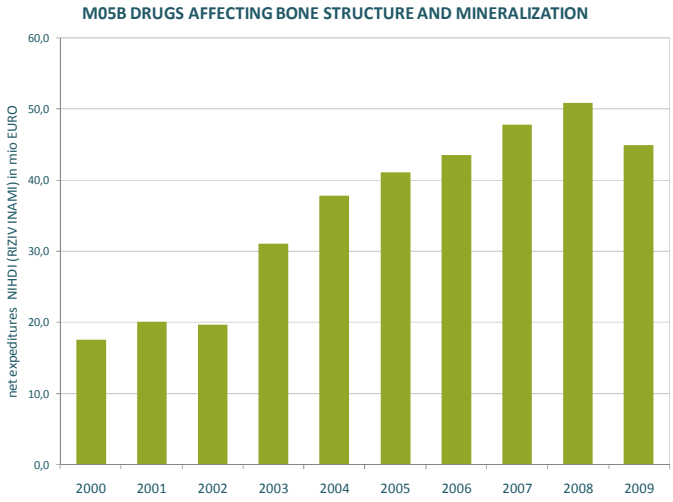
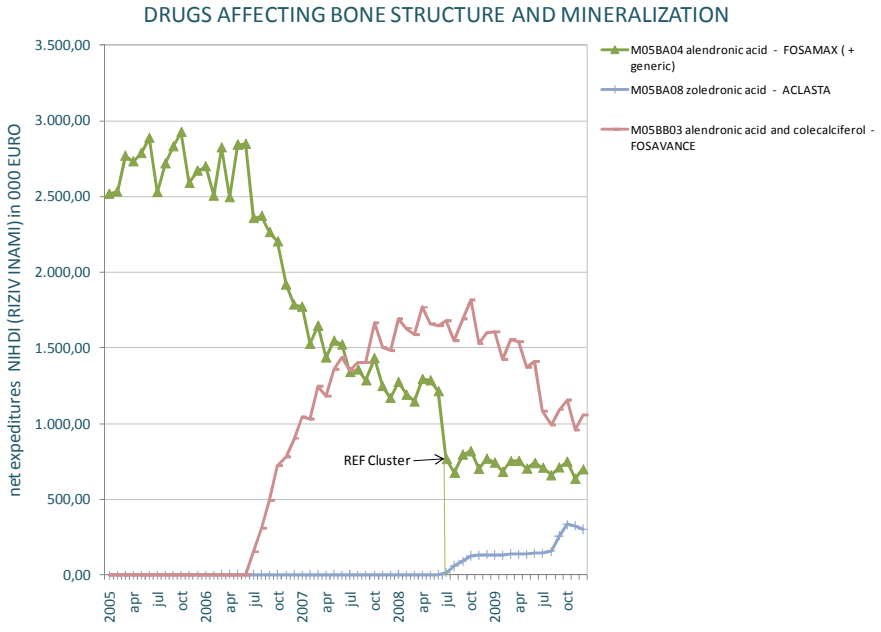


Figure 24: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class M05B Drugs affecting bone structure and mineralization



The anticipated stabilisation of the expenditures for this ATC-class in the previous report is in 2009 even translated into a significant decrease in expenditures by 12 %. This stabilisation was slowed by the delay in the price decrease for Fosavance® (1 May 2009), which had been foreseen for the moment that Fosamax® was introduced into the reference price system (1 July 2008).

The foreseen price increase for Aclasta® as of 1 August 2009, as a result of the addition of the indication osteoporosis for men and the elimination of the previous conditions of contra-indication in alendronates, is clearly noticeable, but to a larger degree than forecast in the estimates: for the last 5 months of 2009 versus the previous 5 months, the added cost is 679.603 Euro, which, for one year, corresponds to some additional expenditures of 1.631.000 Euro.
In contrast, the foreseen annual cost increase for both the indications together was in the application dossier estimated at some 530.000 Euro only, part of which would be offset by a simultaneously implemented price reduction of 3.6 %.

ANTIEPILEPTICS

Figure 25: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class N03A Antiepileptics

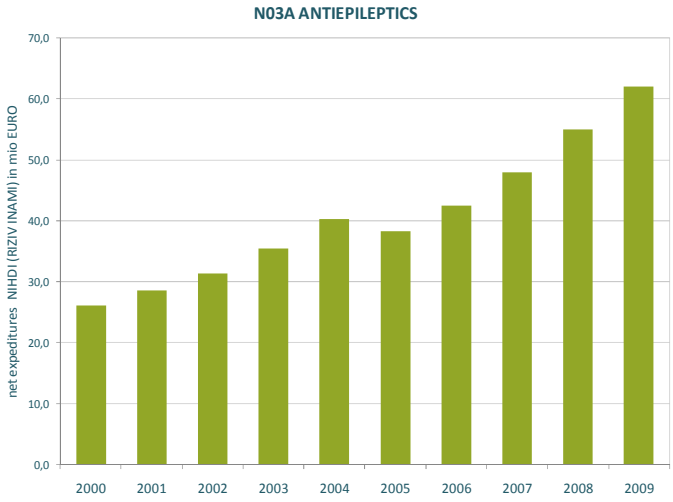
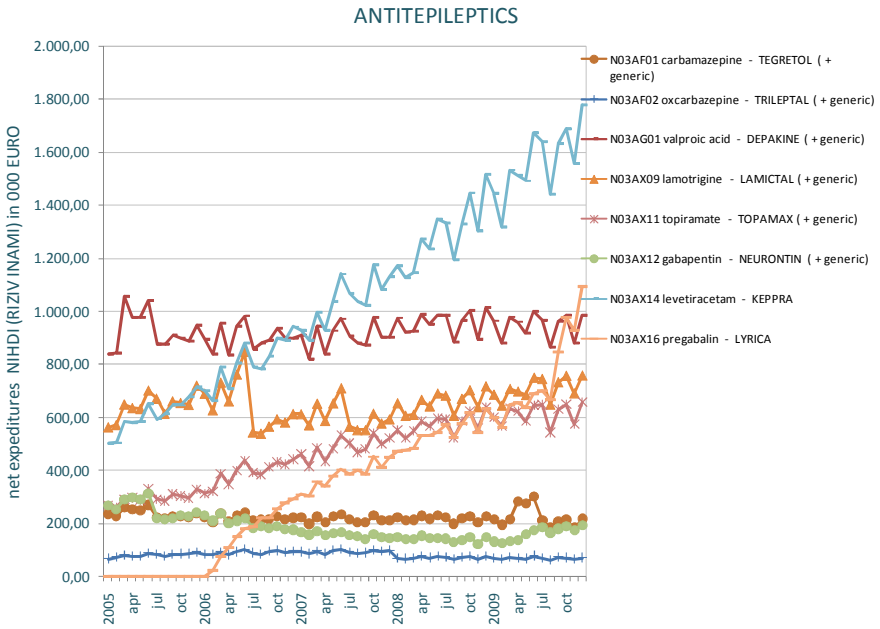


Figure 26: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class N03A Antiepileptics



Within this class of drugs, it is especially the evolution of the expenditures for levetiracetam and for pregabalin that need future monitoring. The notable rise in the expenditures for pregabalin is presumable wholly due to the expansion of the reimbursement modalities with the indication 'neuropathic pains'.

Figure 27: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class N05A Antipsychotics

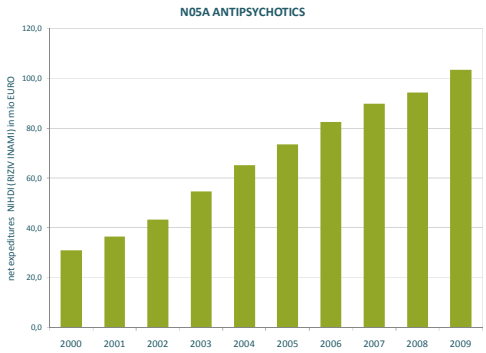


Figure 28: evolution of the net expenditures NIHDI (public pharmacies 2000 - 2009) for ATC class N06A Antidepressants

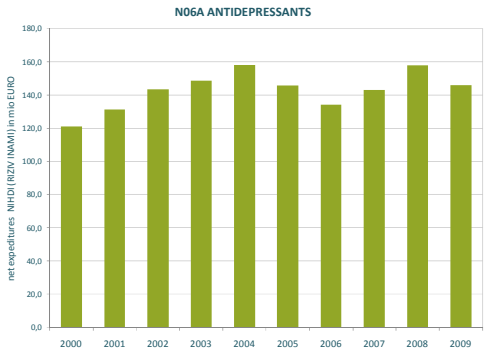
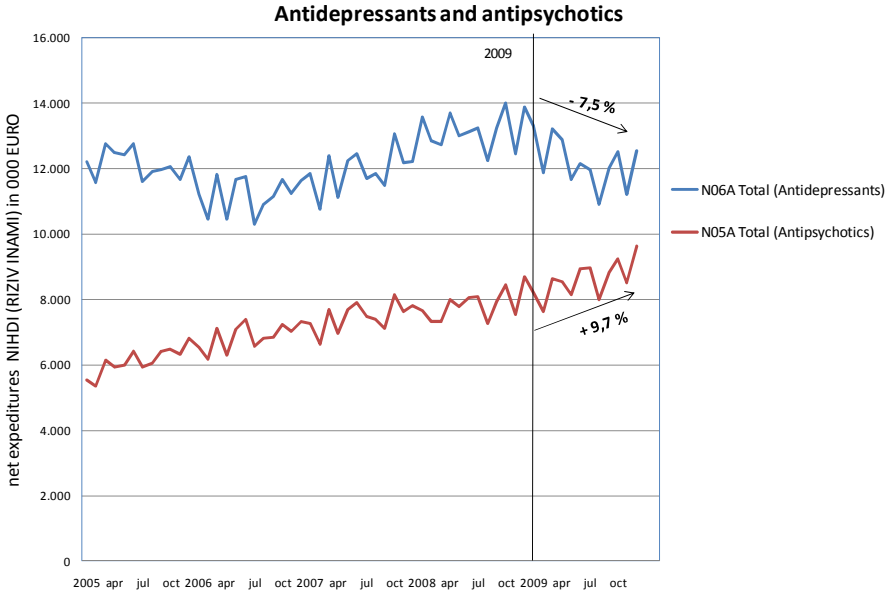


Figure 29: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class N06A Antidepressants and N05A Antipsychotics



When the evolution of the antidepressants and the antipsychotics are scrutinized together, it may be concluded that the savings in the expenditures of the antidepressants (N06A) for 2009 are largely neutralized by the rising expenditures in the class of the antipsychotics (N05A).

In spite of the entry into force of various reference clusters (Sertraline in 01/01/2006, Risperidone in 01/01/2008, and Venlafaxine in 01/05/2009), no noticeable drop in expenditures during the past few years is observed.

At the end of 2008, the new patients within the class of the SSRI (N06AB) received treatments divided as follows (division on the basis of the volume in DDD):

Table 18: Divisions of the new treatments with an SSRI in 2008

ATC-code	Name of the molecule	Name of the most prescribed speciality	% of the volume of new patients
N06AB03	FLUOXETINE	FLUOXETINE EG	8%
N06AB04	CITALOPRAM	CITALOPRAM EG	15%
N06AB05	PAROXETINE	SEROXAT	21%
N06AB06	SERTRALINE	SERLAIN	21%
N06AB08	FLUVOXAMINE	FLOXYFRAL	0%
N06AB10	ESCITALOPRAM	SIPRALEXA 10 mg	**34%**

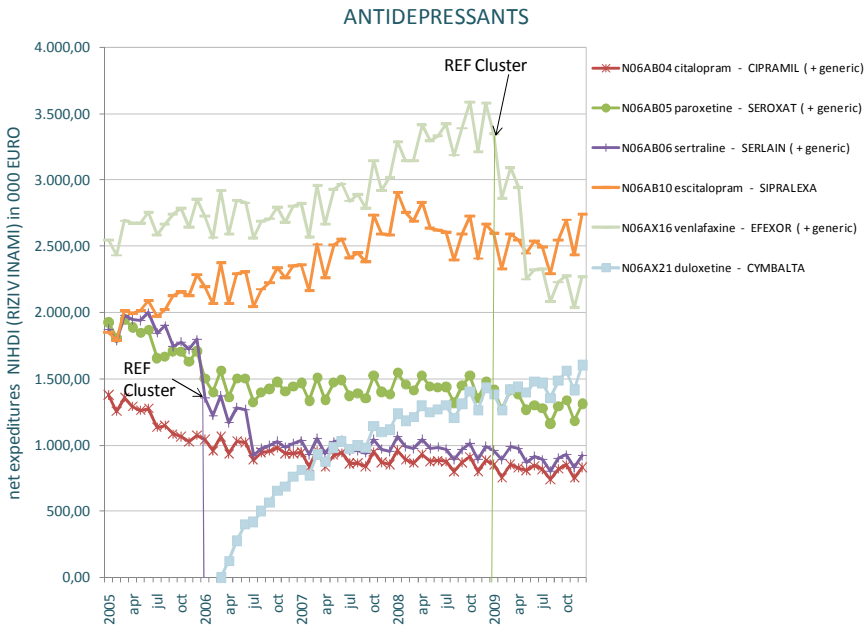
From the division of the newly treated patients with an SSRI and of all patients treated with an SSRI, it may be concluded for 2009 (***Table 19***) that in the case of more than one-third of the patients, the treatment once started is being continued with the expensive escitalopram (Sipralexa®). This speciality received an exemption from the application of the reference price system (for citalopram).

Table 19: Division of the new treatments and all treatments with an SSRI in 2009

ATC-code	Name of the molecule	% of the volume new patients (n= 220.208)	% of the volume of patients treated (n= 673.781)
N06AB03	FLUOXETINE	7,1%	9,3%
N06AB04	CITALOPRAM	14,8%	16,3%
N06AB05	PAROXETINE	17,6%	23,0%
N06AB06	SERTRALINE	18,5%	19,3%
N06AB08	FLUVOXAMINE	0,5%	0,9%
N06AB10	ESCITALOPRAM	41,6%	37,2%

The measure adopted into the National Accord between Physicians and Health Insurance Funds 2009-2010 for this class (SSRI- N06AB) to use the least expensive molecules in 8 out of 10 instances when starting a new treatment, including all of the above-mentioned molecules (with here also the exception being escitalopram), was abandoned mid-2009 following the argumentation proffered by the medical community.

Figure 30: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class N06A Antidepressants



From the graph showing the evolution of the expenditures for the antidepressants (N06A) it may likewise be deduced that the most recent and most expensive molecules (duloxetine as Cymbalta® and escitalopram as Sipralexa®), together with venlafaxine, form the top 3 molecules responsible for the highest expenditures.

The expenditures for Cymbalta®, reimbursable since April 2006, keep increasing. Cymbalta® is reimbursable under Chapter I and has, aside from the indication "major depression", also the registered and reimbursable indication "peripheral diabetic neuropathy".

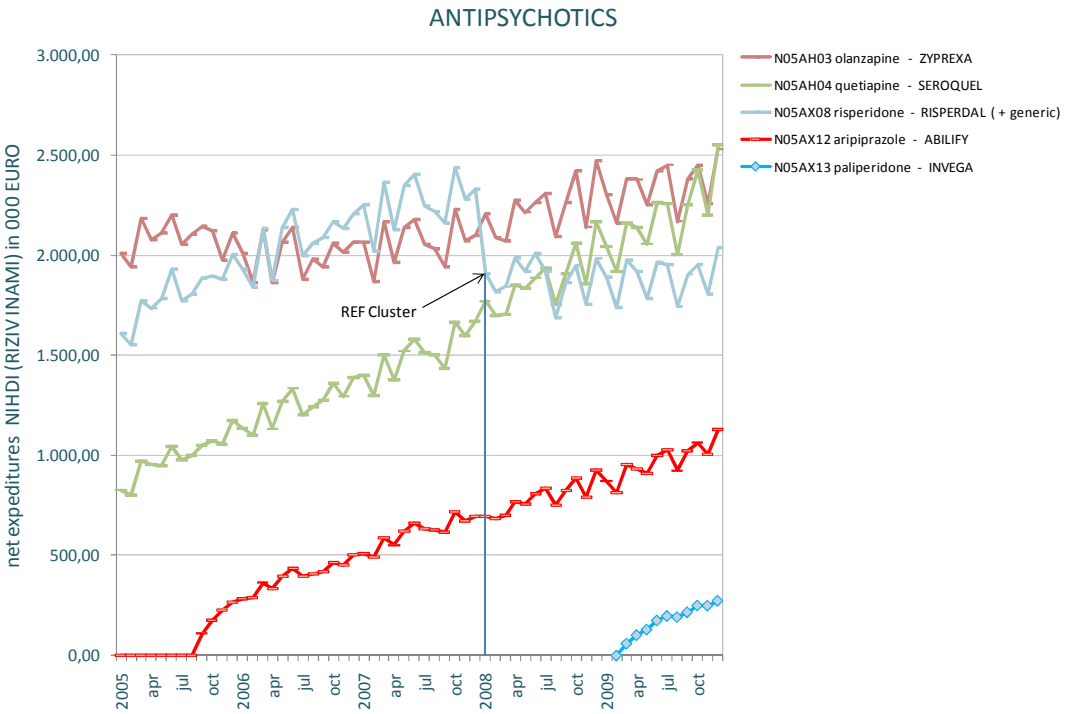
Table 20: Evolution of the number of patients treated with Cymbalta®

Name	Number patients in 2006	Number patients in 2007	Number patients in 2008	Number patients in 2009	% growth patients 2008-2009
Duloxetine (N06AX21) - Cymbalta	42.017	71.682	79.839	80.759	1,15%

Aside from an increasing number of patients, possibly an increased daily dosage (120 mg/ day instead of 60 mg/day) may be held responsible for the rise of the expenditures. In the report of the Drug Reimbursement Commission, the applicant estimated the number of patients taking 120 mg/day for "major depression" at 2.5 % and for "peripheral diabetic neuropathy" at 5 %. The recommended dose in the insert with the product is 60 mg duloxetine per diem.

In the National Accord of Physicians – Health Insurance Funds, these classes are likewise involved in an approach to promote the further optimisation of a rational drug consumption. The classes N05/N06 (psycholeptics/psychoanaleptics) belong to the drugs for which attempts are made to suppress an unrealistic elevated volume of prescribed drugs amongst certain care providers. To this end, the prescription profiles of the physicians will be monitored.

Figure 31: evolution of the net expenditures NIHDI per month (public pharmacies 2005 - 2009) for ATC class N05A Antipsychotics



Within the class of the antipsychotics (N05A), it is especially the expenditures of the molecules quetiapine and aripiprazol that show a strong increase. The expenditures for Risperdal® and generics have remained well nigh constant since the entry into force of the reference cluster in January 2008. The rise in expenditures within this class has for years already been attributed to the further evolution and the increasing use of the atypical antipsychotics versus the use of the traditional antipsychotics.

Furthermore, the new molecule paliperidone as Invega® has become reimbursable since March 2009. Paliperidone is an active metabolite of risperidone and its effective mechanism is largely comparable. One dose a day is possible and dosage titration is really superfluous (as it is for certain other antipsychotics). From the studies on hand it may only be concluded that it is unclear what dosage to use in practice. The optimal dose of paliperidone is – according to the insert with the drug - 6 mg. These expenditures can be further followed up in a coming report.

Quetiapine (Seroquel®) remains strongly on the rise in 2009 and, together with olanzapine (Zyprexa®), accounts for expenditures that at the end of 2009 reach 2.5 million Euro per month. Seroquel® has since 1 August 2009 also been reimbursable in lozenges with extended provision (Seroquel XR®) at the same cost for treatment.

Table 21: Evolution of the number of patients treated with various antipsychotics

Name	Number patients in 2006	Number patients in 2007	Number patients in 2008	Number patients in 2009	% growth patients 2008-2009
Quetiapine (N05AH04)- Seroquel	26.213	31.630	38.744	46.865	**20,96** %
Olanzapine (N05AH03) - Zyprexa	41.349	42.588	43.972	44.000	0,06 %

Aripiprazol (N05AX12) - Abilify	8.106	11.379	14.276	17.240	**20,76** %
Risperidone (N05AX08) Risperdal + generics	78.707	80.024	83.491	80.560	- 3,51 %

From the evolution in the number of patients, it may be concluded that this new form with extended effect for seroquel® is contributing to a further market expansion.
Likewise for Abilify®, reimbursable since September 2005, the number of patients remains on the rise for 2009 by 20%.

The number of patients that received a reimbursement in 2009 for an antipsychotic drug largely exceeds the epidemiological estimates for patients suffering from the most serious indications (schizophrenia and bipolar disorders). In 2009, 368.500 patients received reimbursement for a treatment with antipsychotics versus an epidemiological estimated number of patients with schizophrenia and bipolar disorders ranging from 70.000 to 197.000.

EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES IN HOSPITALS

General

Table 22: net annual expenditures NIHDI for drugs 2006 - 2009 (doc PH)

Net expenditures NIHDI x 1,000,000 EUR

	2006	2007	2008	2009
Hospital	**979,4**	**1.062,3**	**1.178,5**	**1.216,1***

Growth %

		2006-2007	2007-2008	2008-2009
Hospital		8,5	10,9	3,2

* extrapolation of doc PH data semester 1 - 2009 to the complete year 2009

Table 23: top 80% for drugs in hospitals

Rank	Rank	Forfait	ATC 3		growth (%)	growth (%)	growth (%)	total in million EURO
2009	**2008**				**07-06**	**08-07**	**09-08**	**2009 (*)**
1	1	No	L01X	OTHER CYTOSTATICS	41,9	21,7	11,6	191,1
2	3	No	L04A	IMMUNOSUPPRESSANTS	21,7	37,3	18,6	98,3
3	2	No	B03X	OTHER AGENTS WITH ANEMIA	-3,7	-2,4	-3,5	89,0
4	4	Yes	B05B	INTRAVENOUS SOLUTIONS	-3,1	3,7	-0,6	62,2
5	5	No	J06B	IMMUNOGLOBULINS	6,8	7,1	9,5	45,1
6	6	Yes	V08A	X-RAY CONTRAST MEDIA, IODINATED	-1,2	1,0	-0,3	41,1
7	8	No	L01C	ALKALOIDS AND OTHER NATURAL PRODUCTS	-1,9	4,8	6,4	40,3
8	9	Yes	N01A	GENERAL ANAESTHETICS	-1,5	5,6	2,3	37,0
9	7	Mix	B01A	ANTITHROMBOTICS	-2,2	-0,4	-4,4	36,4
10	11	Yes	J01C	BETALACTAM-ANTIBIOTICS, PENICILLINS	0,6	5,9	3,9	35,8
11	10	No	B02B	VITAMIN K AND OTHER HAEMOSTATICS	15,7	7,9	-8,3	32,9
12	14	No	L03A	CYTOKINES AND IMMUNO-MODULATING AGENTS	8,8	10,0	10,4	32,3
13	12	Mix	J01D	OTHER BETA-LACTAM-ANTIBACTERIALS	-0,8	4,2	-0,4	32,0
14	13	Yes	N05A	ANTIPSYCHOTICS (NEUROLEPTICS)	3,9	15,7	2,2	30,4
15	16	Mix	A16A	OTHER PREPARATIONS re GASTROINTESTINAL TRACT AND METABOLISM	43,3	30,8	18,1	29,3
16	15	No	L01B	ANTIMETABOLITES	31,5	25,9	0,7	28,4
17	18	yes	M05B	AGENTS AFFECTING BONE STRUCTURE AND MINERALIZATION	-14,2	3,2	9,8	21,7
18	17	Mix	V03A	ALL OTHER THERAPEUTIC AGENTS	0,1	22,6	-4,8	20,3
19	22	No	S01L	OSCULAR VASCULAR DISORDER AGENTS	1,5	269,5	32,8	19,6
20	19	mix	J02A	ANTIMYCOTICS FOR SYSTEMIC USE	-1,1	11,8	7,2	19,4
21	20	No	B05A	BLOOD PRODUCTS AND RELATED PRODUCTS	-6,9	1,2	1,7	16,2
(25)	21	No	L01D	CYTOTOXIC ANTIBIOTICS AND RELATED SUBSTANCES	6,6	-1,6	-19,8	12,7

(*) expenditures calculated on the basis of :

- The available doc PH data: 1st semester 2006 to and including the 1st semester 2009 (NIHDI data), whereby total expenditures= expenditures ambulant + expenditures outside of the forfait + 4 x expenditures within the forfait
- linear extrapolation (at the level ATC 3) for 2009, taking the date of the 1st semester 2009, whereby total expenditures= expenditures ambulant + expenditures outside of the forfait + 4 x expenditures within the forfait

The overview of the (virtual) expenditures and the *expected growth* per ATC3-class shows that **21 of the 172 classes** are responsible for **80% of the expenditures in hospitals.**

Further in this report, the evolution of the expenditures for the oncolytics will be commented upon.

Expenditures for drugs in hospitals: the 'drug forfait'

General

Since 1 July 2006, a fixed amount for drug reimbursement, the **drug forfait,** has been introduced into the acute hospitals for hospitalized patients. For these patients, the rule is that, in principle, all drugs fall under this fixed reimbursement scheme.

There exists, nonetheless, a list of exclusions (based on the ATC5 code).
Drugs are excluded statutorily (such as the orphan drugs, cytostatics, … cf. art 95 §3 b) 3rd paragraph of the RD 21.12.2001) or by proposal of the "permanent working group on drug forfait specialities" (if, on the one hand, the active ingredient is of great importance in the medical practice and, on the other, the cost price of it might severely limit their administration in the event of a fixed reimbursement).

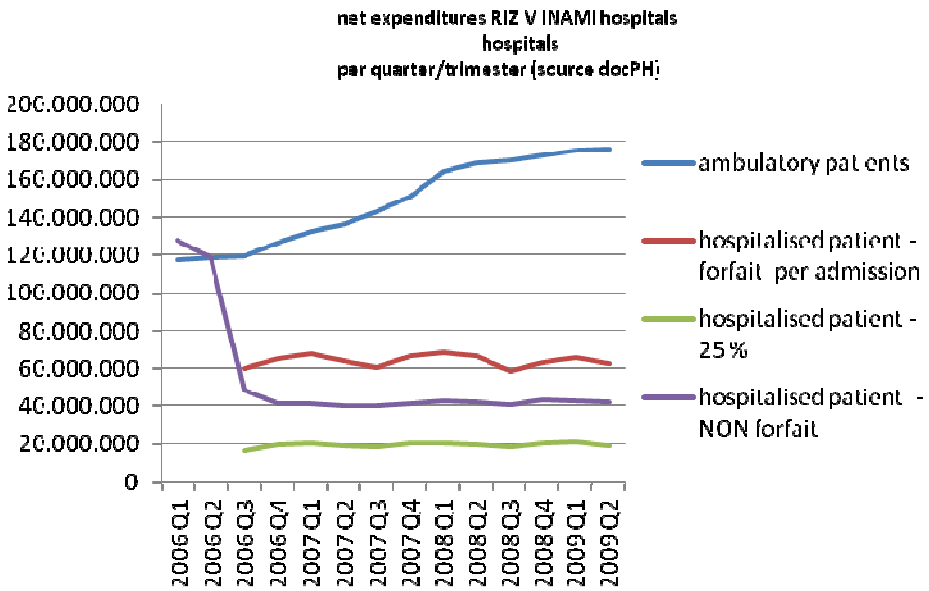
The regulation provides that for the specialities that fall under the forfait, 25% of the reimbursement basis is still being billed per speciality. The remainder is covered by a forfait per admission.

Because of the partial reimbursement (25% of the reimbursement base is still being billed according to the conventional method, namely billing by unit used), it is possible to monitor the real drug use without its being absorbed by a drug reimbursement total based on APRDRG (All Patients Refined Diagnosis Related Groups).

Basis

We are using doc PH data : consolidated billing data (net expenditures NIHDI), with differentiation per speciality packaging and per type patient (hospitalized (either under the forfait scheme or not) – ambulatory).
In contrast to docN data – consolidated billing data (net expenditures NIHDI), without differentiation per speciality packaging – the use of doc PH data allows us to conduct detailed analyses.

Figure 32: net expenditures NIHDI period 2006-2009 semester 1 (source doc PH)



Accounting of the **quarterly figures** per type of patient gives us the above graph.
The expenditures for hospitalized patients, both for the drugs under the forfait regime and for those outside of it, remain stable.

The expenditures for the ambulatory patients, however, remain on the increase. The stronger growth of the expenditures for ambulatory patients that we note as of the 4th quarter 2006 and that was maintained until the 1st quarter in 2008 has, nonetheless, declined as of the 2nd quarter in 2008.

It is the rise of the expenditures for the ambulatory patients that is responsible for the increase in hospital expenditures.

The forfait per admission shows a slightly declining trend.
The national budget for the forfait reimbursement system (billing via amount per admission) is being established annually by the General Council. This concerns open envelopes. The individual hospital receives, depending on the reported casemix (on the basis of MCD), a fixed amount per admission.

Table 24: fixed amounts national budget for forfait per admission for the period July 2006 to July 2009

Period	Fixed national budget (in million Euro)
1/7/2006 - 30/6/2007	258,863
1/7/2007 - 30/6/2008	260,846
1/7/2008 - 30/6/2009	247,989

On an **annual basis,** we arrive at the following amounts (***Table 25***) for the various types of expenditures.

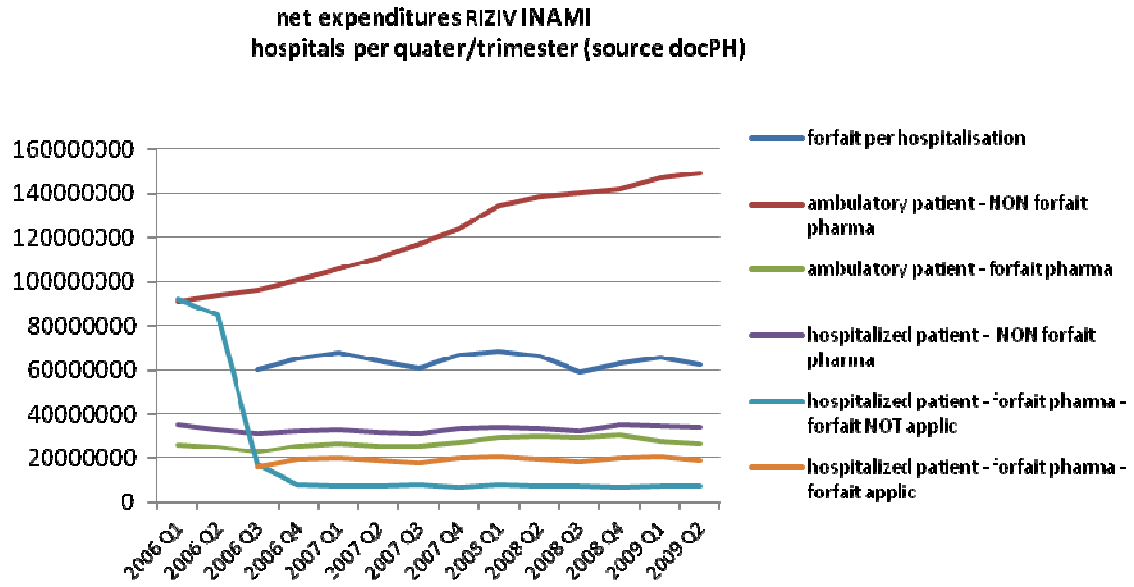
Table 25: net expenditures NIHDI period 2006-2009 (source doc PH – in Mil EURO) – break-down expenditures hospitals

	2006	2007	2008	2009 extrapol
Ambulatory patients [1]	482,0	563,6	675,7	711,8
Hospitalized patients total	497,4	498,8	502,8	504,3
- hospitalized patients – NON forfait [2]	336,9	162,7	168,0	170,6
- hospitalized patients – forfait [3]	35,6	77,2	78,2	78,0
- forfait per admission [4]	124,8	258,9	256,5	255,8
Total hospital	**979,4**	**1.062,3**	**1.178,5**	**1.216,1**

[1]*Ambulatory patients*	*Given to ambulatory patients in the hospitals, always outside of the fixed reimbursement (reimbursement base rate 100%, according to the reimbursement category)*
[2]*Hospitalized patients – NON forfait*	*Given to hospitalised patients whereby the reimbursement falls outside of the fixed reimbursement scheme, as* - *it pertains to a drug outside of the fixed reimbursement (included in the list of exclusions)* - *it pertains to a drug that was provided to a patient:* *- admitted prior to 1.07.2006 (effective date of the drug forfait)* *- admitted to a non-acute hospital* *(basis for reimbursement 100%, contribution according to the reimbursement category)*
[3]*Hospitalized patients – forfait 25 %*	*Given to hospitalised patients in an acute hospital (admission date after 1.07.2006) of a drug that falls under the forfait* *(contribution = 25% of the reimbursement base rate; abolition of the contribution according to the reimbursement category)*
[4]*Forfait per admission*	*Fixed amount that the hospital receives per admission.* *This amount is reviewed annually and depends on the casemix reported by the hospital* (MKG).

Seeing that the data are available for the specialities level, the net expenditures by hospitals as shown in ***Figure 33*** can be broken down depending on whether or not it concerns expenditures for forfait drugs, e.g., drugs that fall under the forfait regime if they are being provided within the forfait context.

Figure 33: net expenditures hospitals – break-down of the expenditures depending on whether or not it pertains to forfait drugs



Explanation of the concepts:

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

Figure 33 demonstrates, as already shown in ***Figure 32***, that the expenditures for hospitalized patients, both for patients falling under the forfait regime and for those that are outside of it, on the whole remain steady during the period July 2006 to and inclusive of July 2009.
If these expenditures are broken down depending on whether or not it pertains to forfait drugs, one notes that for the first 3 years after the introduction of the forfait regime, there are no significant shifts in the expenditures for both types of drugs (forfait and NON forfait).
The expenditures for forfait drugs for patients falling under the forfait system remain more or less steady. Likewise, the expenditures for the drugs that fall outside of the forfait, and thus are reimbursed for 100%, remain stable.

Under the same breakdown of the expenditures for ambulatory patients in hospitals, we note that these expenditures for the forfait drugs remain likewise more or less at the status quo (This is, of course, merely a theoretical exercise, as the forfait does in any case not apply to ambulatory patients). The rise of the

expenditures for the ambulatory patients is due to a rapid increase – slowed as of the 2nd quarter 2008 – in the expenditures for drugs outside of the forfait regime (here again this is a theoretical exercise). Consequently, it is this group of non-forfait drugs that is responsible for the rise in expenditures for drugs in hospitals.

The data currently at our disposal do not alter the position taken in the second-semester MORSE report 2008 concerning shifts:
A global analysis of the available data does not show any indication that would make us assume that, within hospitals, the use of forfait drugs is shifting from the hospital setting to the ambulant setting, or towards non-forfait drugs.

Forecasting of the expenditures for drugs in hospitals - testing

Based on the available data, it is possible, for an estimation of the evolution of the expenditures in hospitals (for which no doc PH data are available as yet), to apply an analogous approach system to the one that was used in the previous reports for the estimation of the evolution of the expenditures in public pharmacies and hospitals.

To this effect, we try to determine the correlation between doc PH data and the more recent IMS data. In case the correlation is deemed adequate ($r^2 \geq 0,75$), the IMS-data are then converted; if not, the doc PH data are being extrapolated in linear fashion. For the period Q4 2008 to the end of 2009, the data arrived at in the previous report were extrapolated in this linear manner.

To check the correlation IMS – doc PH, for the doc PH data the expenditures for ambulatory patients in hospitals, the expenditures for hospitalized patients under the forfait regime, and the expenditures for hospitalized patients outside of the forfait are being tallied. Seeing that the expenditures under the forfait are reimbursed at the rate of 25% of the reimbursement base, this amount is being multiplied by 4, so that the total expenditures hospitalized patients = expenditures ambulatory + 4 expenditures within the forfait + expenditures outside of the forfait.

The result is only an approximation of the real expenditures (virtual total) and the amounts should not be taken as absolutes.

Table 26: forecast evolution of the expenditures for drugs in hospitals 2006 – 2009 (previous report)

	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 doc PH data : first semester 2006 to and including the 2nd semester 2007 (NIHDI data), whereby total expenditures = expenditures ambulant + expenditures outside of the forfait + 4 x expenditures within the forfait
- conversion of IMS-data (data to and including the 3rd quarter 2008) for the classes (ATC3 level) with a correlation IMS-doc PH $r^2 > 0,75$ for the first three quarters 2008
- linear extrapolation for 2008 and 2009 for other data

Herein it was held that it pertained to an underestimate (global: this is not of application for ATC3 class where all specialities fall outside of the forfait) seeing that the expenditures for forfait drugs for hospitalized patients were extrapolated from 25% to 100%, and hence no account is taken of the amount foreseen for the real forfait per admission.

The comparison between the forecast in the previous report (***Table 26***) and the real data (***Table 22***) illustrates that this approach can prove meaningful in the forecasting of expenditures in hospitals.

Nonetheless, because of the absence of sufficient additional doc PH data, such a prediction was not made for this report.

DOSSIER – ONCOLYTICS IN HOSPITALS

An overview of all new oncolytic drugs, registered in the list of reimbursable specialities, and of all oncolytics for which the reimbursement modalities were changed in the course of 2009, has been appended to this report in attachment.

In the analysis of the top 80% of the expenditures for pharmaceutical specialities in hospitals (***Table 23***) it is noted that the ATC class L01 denomination is responsible for a very large percentage of these expenditures (***Table 27***).

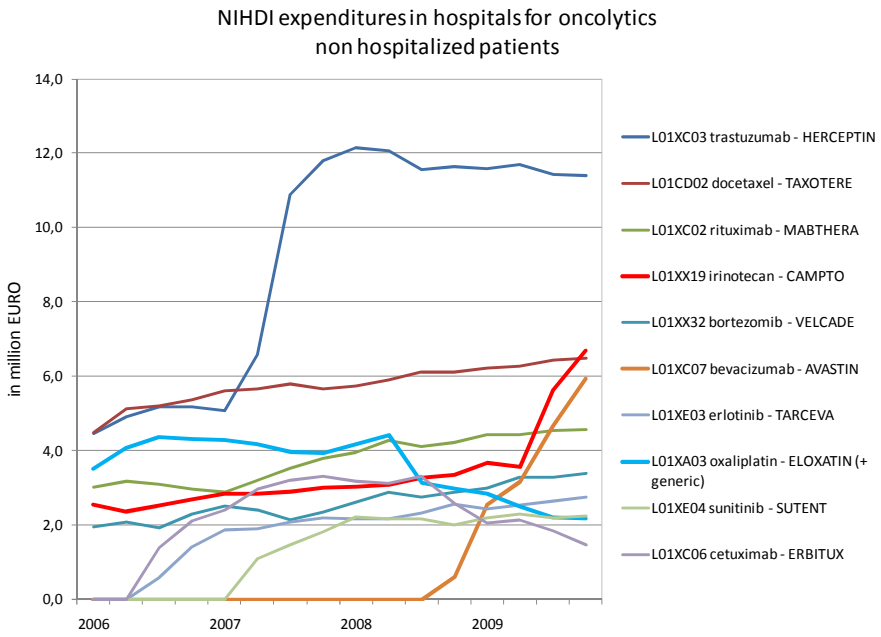
Furthermore, it pertains to ATC classes for which the expenditures have registered, or are registering, rapid growth.

Table 27: expenditures for oncolytics in hospitals

ATC-3		growth (%) 07-06	growth (%) 08-07	total 2009 In million EURO	growth (%) 09-08
L01X	OTHER CYTOSTATICS	41,9	21,7	191,1	11,6
L01C	ALKALOIDS AND OTHER NATURAL PRODUCTS	-1,9	4,8	40,3	6,4
L01B	ANTIMETABOLITES	31,5	25,9	28,4	0,7
L01D	CYTOTOXIC ANTIBIOTICS AND RELATED DRUGS	6,6	-1,6	12,8	-19,8

A detailed analysis shows us that the growth of the expenditures is to a large degree attributable to a limited number of molecules (19 molecules represent 90% of the expenditures).

Figure 34: evolution of the expenditures for oncolytics in hospitals (ambulatory patients) - in Mil EURO



For what concerns the L01 class, the expenditures are attributable primarily to the non-hospitalized patients (89% of the expenditures versus 11% for the hospitalized patients).

The molecule representing the highest cost is trastuzumab (HERCEPTIN®) (17 % of the expenditures of the L01 class).

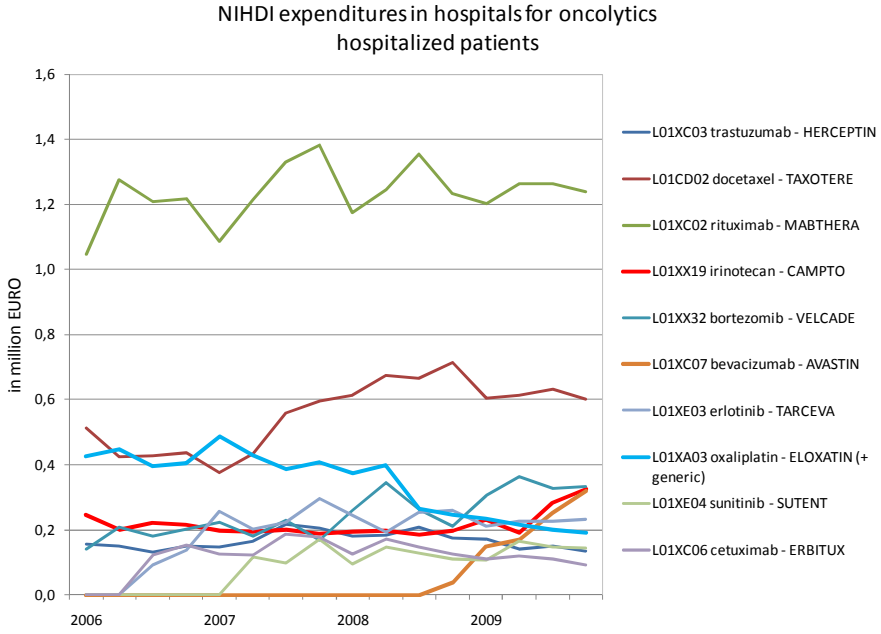
Other important molecules are docetaxel (TAXOTERE®) and rituximab (MABTHERA®).
For both these molecules, a further rise of expenditures as of 2010 may be expected:

- for rituximab, since in the course of 2009 (on 1 June 2009 and on 1 September 2009) the reimbursement conditions were twice expanded (each time with an estimated budget impact of 1.2 million Euro),
- for docetaxel, since as of 1 January 2010, the reimbursement conditions are being expanded (with an estimated budget impact of 1.87 million Euro).

Two other molecules with a strong growth pattern are irinoctecan (CAMPTO®) and bevacizumab (AVASTIN®). Also for Avastin® a strong rise of expenditures is expected as of 2010 since, on 1 January 2010, an expansion of the reimbursement conditions entered into force for which the budget impact is estimated to be 0.5 million Euro for 2010.
In contrast, for irinotecan it may be expected that the growth will be (partially) neutralized by the introduction of the drug in the reference price system (as of 1 January 2010).

For oxaliplatin (ELOXATIN®**)** we note as of mid-2008 a strong drop in the expenditures. This is due to the introduction of this molecule into the reference price system on 1 July 2008.

Figure 35: evolution of the expenditures for oncolytics in hospitals (hospitalized patients) - in Mil EURO



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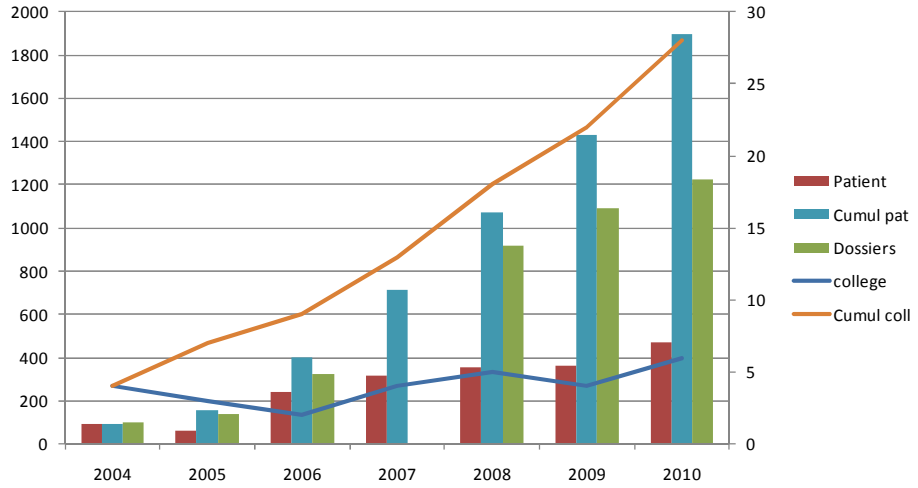
DOSSIER – ORPHAN DRUGS

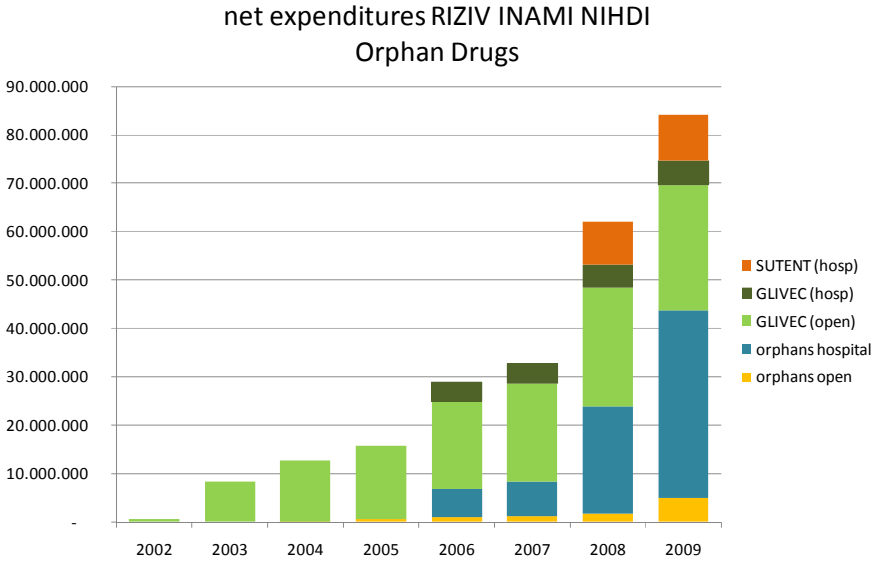
Given the ongoing special attention to orphan drugs in various specific forums, this report refers for all detailed information to the annual activities reports of the Colleges for Orphan Drugs and the Rare Diseases and Orphan Drugs Fund (Koning Boudewijn Foundation) and a summary account thereof.
At the end of 2009, 48 orphan drugs were reimbursable in Belgium. At the end of October 2010, 28 Orphan Colleges were active in this area, processing dossiers for 1899 individual patient dossiers (cumulative – 469 new patients in 2010, 360 in 2009).

Figure 36: Overview working Colleges for Orphan drugs – numbers of individual patient dossiers



An analysis of the evolution of the NIHDI expenditures for orphan drugs shows a rise during 2009 to 84.16 million EURO (expenditures for GLIVEC – officially not of an orphan drug status – and SUTENT, for which the orphan drug status was abandoned/lifted

Figure 37: Evolution of the expenditures for orphan drugs in Belgium



Noteworthy is a recent article[6] published in the 'Journal of Medical Economics' (2010, 13(2): 295-301) wherein an attempt was made to forecast the impact of orphan drugs on the budget for the drugs in Belgium for the period 2008 – 2013.

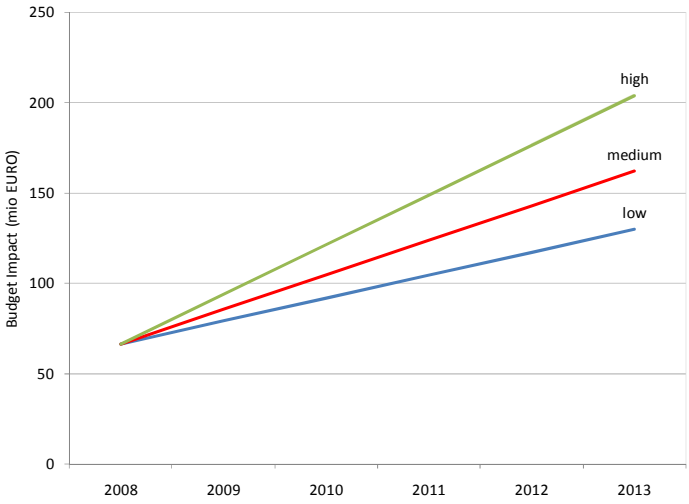
The predictions in the articles are based on:

- a forecast of the number of orphan drugs for which a European permit is issued towards its introduction into the commercial market
- the (relative – 90%) number of drugs that in Belgium is registered in the list of reimbursable specialities
- the average cost of an orphan drug in Belgium (2,135 million EURO – partially based on analyses of the budget impact by the Drug Reimbursement Commission)

The authors of this article acknowledge that there are a number of debatable assumptions included in their argumentations:

- no (change of the) non-drug-costs
- no alternative mechanisms for the organisation of the reimbursement of orphan drugs (such as contracts)
- no account has been taken of the compensation of orphan drugs via the Special Solidarity Fund
- no account has been taken with an (expensive) orphan drug for which no analysis of the budget impact was available
- no account has been taken of future (possibly very) expensive orphan drugs

Figuur 38: Budget Impact estimation for orphan drugs in Belgium 2008 - 2013 (after Budget Impact Analysis of Orphan Drugs in Belgium **(Alain Denis, Lut Mergaert, Christel Fostier, Irina Cleemput, Steven Simoens, 2010)***)*



On the basis of a medium-high growth scenario, the expenditures in 2013 will, according to the authors, amount to 162 million EURO, or 4% of the expenditures for drugs in general and more than 10% of the expenditures for drugs in hospitals.

Low and high growth scenarios predict expenditures in 2013 of, respectively, 130 million EURO to 204 million EURO.

[6] Budget Impact Analysis of orphan drugs in Belgium: estimates from 2008 to 2013 (Alain Denis, Lut Mergaert, Christel Fostier, Irina Cleemput, Steven Simoens, 2010)

THE DRUG REIMBURSEMENT COMMISSION

General

This analysis evaluates two of the objectively quantifiable variables that are co-determinant of the access to new, either or not innovative, drugs in Belgium: **numbers of submitted claims for reimbursement (dossiers)** and **proposals by the Commission and decisions by the Minister** for new drugs for which an application was submitted.
In the evaluation and the interpretation of the data, an 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 claims for reimbursement by pharmaceutical companies. This is absolutely determinant for the packet 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 claims, the claim may already be submitted as of the moment that the applicant has been given favourable advice 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 databank** that is used by the Secretariat of the Drug Reimbursement Commission in the ongoing monitoring of procedures and of the processing time delays. For the analysis of the numbers of dossiers, the data of the dossiers submitted between 1 January 2003 and 1 January 2010 were incorporated.
- for this analysis, only **unique dossiers** are taken into account. That means that in the event of simultaneous claims for different doses /packaging for specialities, dossiers are being pooled when the contracting party, type of dossier, day 0, active ingredient, proposal by the Commission, and the 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 claims of dossiers following a negative decision by the Minister and renewed claims 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 being processed **administratively** (RD 15 February 2007), which means without the intervention of the Commission, and for which the procedure is limited to 60 days.

Number of claims (dossiers)

The number of dossiers submitted via the CRM-procedure (RD 21.12.2001) in 2009 is slightly higher than the fairly constant number noted for the previous years, nonetheless with important differences depending on the type of claim
(see ***Figure 39***):

It is to be noted that:

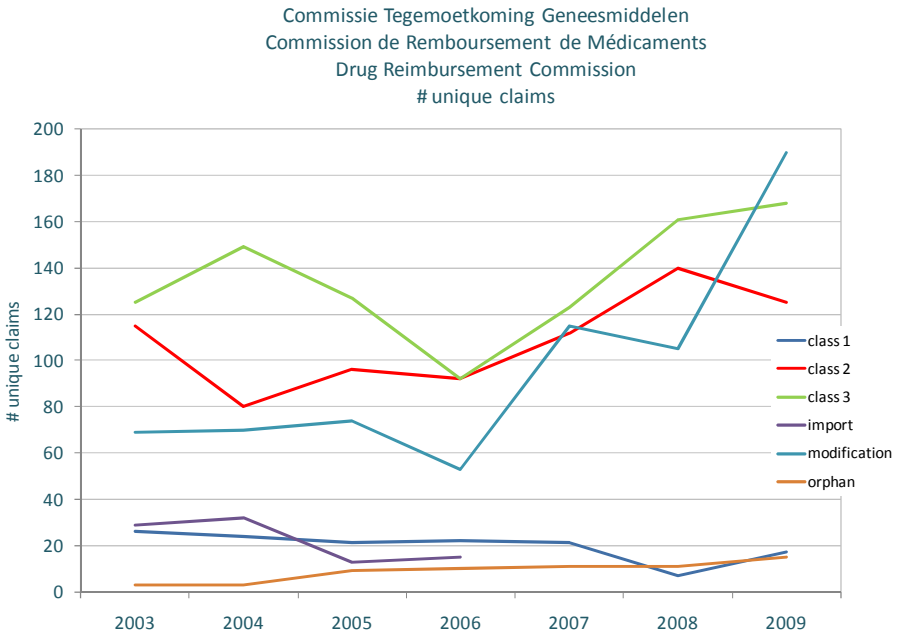
- The number of class 1 claims (on the average some 25 per annum up to 2006) appears to be declining slightly since the first semester of 2006 and in 2008 attained the lowest number – 7 (seven) - ever. In 2009, this negative trend did recover (somewhat) – 16 (sixteen).

- The number of claims for orphan drugs was 15 (fifteen) in the year 2009. 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 for class 2 and 3 claims came to a stop in 2006 and, in effect, ever since that time, an increase has been noted (to be monitored further for Class 2 drugs).

- The recent increase in claims for modifications to the reimbursement modalities is striking; however, it is to be noted that this pertains to both an expansion of indication 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. This is also pertinent to 2009, where for a large number of dossiers it was a question of modifications of the tariff rules (contrast means), administrative simplifications (transfers to Chapter I for Antagonists and ACE-inhibitors – reformulation of the reimbursement modalities with a view to enhancing their coherence for EPOs).

Figure 39: number of claims per year (unique dossiers – including completed procedures, withdrawn claims, current procedures)



Proposals of the Commission and Decisions by the Minister

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 made known to the applicants within a delay of **180 calendar days following the submission of the claim**, and this without account taken of possible suspensions of the procedures.

The Minister takes this decision following the proposal by the Drug Reimbursement Commission, which is required to formulate this proposal within 150 days following the application.
The Minister cannot depart from the Commission's proposal, unless for budgetary or social reasons, and can only himself make a decision if the Commission fails to formulate a proposal within the foreseen 150 days delay (the company can request a suspension of the procedure during the two different stages: evaluation and proposal).

Proposals of the Commission (both positive and negative) are adopted by a 2/3 majority – abstaining votes are discounted. In other words: in case the voting members that do NOT abstain from casting a vote do not reach a 2/3 majority, neither on a proposal to register a (new) drug in the list nor to NOT register it, it shall be recorded that the Commission FAILED to formulate a proposal.

Table 28 shows for the period 2005-2009 to what extent a positive or negative proposal was formulated by the Commission for the different types of claims, and in how far no 2/3 majority was reached to formulate such a proposal. Detailed data for the various years are entered into the attachments to this report.

It is notable that for the 'difficult'/ 'expensive ' dossiers, class 1 drugs and orphan drugs, trying to reach a 2/3 majority for the formulation of a proposal poses greater problems (29% and 20 % no proposal), and that for these same drugs it is more common to propose that they not be reimbursed (26% and 18%).

Table 28: number of unique claims for registration in the list of reimbursable specialities versus proposal of the Drug Reimbursement Commission (2005-2009)

2005 - 2009							
	positive		negative		no proposal		total
	number	%	number	%	number	%	number
class 1	35	45%	20	26%	23	29%	78
class 2	354	75%	48	10%	71	15%	473
class 3	558	97%	13	2%	5	1%	576
modification	379	83%	43	9%	32	7%	454
orphan	30	61%	9	18%	10	20%	49
total	1356	83%	133	8%	141	9%	1630

Table 29 shows for the period 2005-2009 to what degree a positive or negative proposal formulated by the Commission for the various types of applications was adopted by the Minister. For de dossiers where the Commission did not formulate a proposal, it was checked out to what degree the Minister decided either positively or negatively. Detailed data for the various years have also been entered into the attachments to this report.

Table 29: decisions by the Minister in function of the proposal by the CRM (unique dossiers 2005 - 2009)

2005 – 2009											
	positive decision Min		negative decision Min		no decision Min (pos)		no data (in procedure, suspended,…)		withdrawn (company)		total
CTG CRM proposal	number	%	number	%	number	%	number	%	number	%	**number**
class 1	47	60,3%	21	26,9%	3	3,8%	6	7,7%	1	1,3%	78
positive prop	34	97,1%	1	2,9%		0,0%		0,0%		0,0%	35
negative prop	1	5,0%	13	65,0%	2	10,0%	3	15,0%	1	5,0%	20
no prop	12	52,2%	7	30,4%	1	4,3%	3	13,0%		0,0%	23
class 2	387	81,8%	68	14,4%	3	0,6%	6	1,3%	9	1,9%	473
positive prop	339	95,8%	8	2,3%	1	0,3%	3	0,8%	3	0,8%	354
negative prop	5	10,4%	37	77,1%		0,0%	1	2,1%	5	10,4%	48
no prop	43	60,6%	23	32,4%	2	2,8%	2	2,8%	1	1,4%	71
class 3	551	95,7%	15	2,6%		0,0%	6	1,0%	4	0,7%	576
positive prop	543	97,3%	5	0,9%		0,0%	6	1,1%	4	0,7%	558
negative prop	5	38,5%	8	61,5%		0,0%		0,0%		0,0%	13
no prop	3	60,0%	2	40,0%		0,0%		0,0%		0,0%	5
modification	394	86,8%	46	10,1%	4	0,9%	7	1,5%	3	0,7%	454
positive prop	365	96,3%	1	0,3%	4	1,1%	6	1,6%	3	0,8%	379
negative prop	5	11,6%	38	88,4%		0,0%		0,0%		0,0%	43
no prop	24	75,0%	7	21,9%		0,0%	1	3,1%		0,0%	32
orphan	40	81,6%	6	12,2%		0,0%	1	2,0%	2	4,1%	49
positive prop	29	96,7%	1	3,3%		0,0%		0,0%		0,0%	30
negative prop	3	33,3%	3	33,3%		0,0%	1	11,1%	2	22,2%	9
no prop	8	80,0%	2	20,0%		0,0%		0,0%		0,0%	10
total	1419	87,1%	156	9,6%	10	0,6%	26	1,6%	19	1,2%	1630

It is notable herewith that, in most instances, the Minister adopts the proposals of the Commission.

Where the Commission fails to formulate a proposal, the Minister takes a positive decision in somewhat more than half of the cases, with exception of orphan drugs (80%)

DOSSIER - THERAPEUTIC ADDED VALUE

Within the context of the Belgian Presidency of the EU, a Ministerial Conference was organized on 23-24 September by NIHDI, FAGG (Federal Agency for Medicines and Health Products), and the FPS Public Health and Social Affairs around the theme 'Innovation and Solidarity'.

During this conference, a background report was presented *(' A call to make valuable innovative medicines accessible in the European Union – Recommendations for a coordinated action to stimulate, measure, and valorise pharmaceutical innovation')*, realized by the NIHDI in collaboration with university specialists, FAGG, KCE… In support of this report, a study was conducted by NIHDI, with the collaboration of IMS, KCE and university specialists for the purpose of constructing an up-to-date picture of the access to innovative drugs within Europe.

This Chapter probes more deeply into the results of the study towards the first objective of this research: the formation of a picture of the 'recognition' of innovation/therapeutic added value.

The study compared the findings of the assessment in Belgium and in France of a set (n=84) of drugs that could be considered worthy of the label 'therapeutic added value'.
This set was composed from all unique Class 1 claims in Belgium (n=69) and unique claims for orphan drugs (n=44) during the period 2005-2009 + claims (n=2) that in France were submitted during the identical period and received an ASMR *('Amélioration de Service Médical Rendu' [Improvement in actual benefit])* qualification I-II and in Belgium had been entered as Class 2.
The dossiers for which the procedure was still running in Belgium or for which the procedure had been halted by the company were removed from the set (n=20), plus the dossiers for which in France no corresponding claim had been submitted (n=9), as were also the double dossiers (n=2). All data originate with NIHDI and HAS ('*Haute Autorité de Santé*' [*French National Authority for Health*]).

'Therapeutic Added Value'/ 'Innovation' was defined as 'Orphan drug' of Class 1' recognition in Belgium and ASMR I and II in France.

Table 30: comparison of the assessment and decision regarding claims for reimbursement of drugs with a 'claimed' therapeutic added value in Belgium and France (2005-2009)

Claim		**Assessment**			**Reimbursement Decision**		
Belgium Orphan (n=35) Class 1 (n=47) Class 2 (n=2)	Belgium						
		Orphan	35		31	yes	
					4	no	
		Class 1	29		28	yes	
					1	no	
		Class 2	19		11	yes	
					8	no	
		-	1		1	no	
	France						
		ASMR I	5		81	yes	*with SMR major/important*
		ASMR II	28				
		ASMR III	20		2	yes	*with SMR moderate*
		ASMR IV	18				*with SMR weak*
		ASMR V	11		1	no	*with SMR insufficient*
		-	2				

From the results of the study (see ***Table 30***), it appeared that the 'recognition' of 'innovation' or 'therapeutic added value' differs to a large extent amongst various nations, even when these nations may reasonably be deemed similar in terms of their health care systems and their organisation.
In Belgium, 76% of the claims for 'therapeutic added value (for the definition, see supra) were recognized as such; in France, this figure was only 38%. It has to be noted herewith that in/for Belgium, orphan drugs are anyhow labelled as 'innovative'. At the same time, it deserves notice that with an expansion of the reimbursable indications, a Class 1-labelling is no longer possible.

For what concerns the reimbursement of these same drugs, the study presents us with an entirely different picture: in France, only for 1 of the studied drugs was reimbursement rejected; in Belgium, 14 (17 %) of these same drugs were not registered in the list. *(note: it needs to be remarked that, in the meantime, new claims are being evaluated for a number of these drugs or have already been fully processed, with or without favourable results).*

Notable is the fact that the 'recognition' of a 'therapeutic added value' is substantially higher for orphan drugs.

The same analysis – seen from a different perspective (***Table 31***) – displays only a limited overlap for what concerns the recognition of a 'therapeutic added value' between the two countries.

Table 31: analysis of the 'overlap' on recognition of therapeutic added values in Belgium and France

recognition 'added value'	number	percentage
both in Belgium and in France	24	29
only in Belgium	34	42
only in France	9	11
neither in Belgium nor in France	15	18

REFERENCES

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ADDITIONAL USEFUL INFORMATION SOURCES

Report “Permanent Audit”:
Actuarial Department

Report “Infospot”
Objective : Every three months, a current subject about drugs is elucidated on the basis of the Farmanet-data.
Link : http://inami.fgov.be/drug/nl/statistics-scientific-information/Farmanet/info-spot/index.htm

QUOTED SOURCES

Alain Denis, Lut Mergaert, Christel Fostier, Irina Cleemput, Steven Simoens. (2010). Budget Impact Analysis of orphan drugs in Belgium: *Journal of Medical Economics* , 13(2): 295-301.

NIHDI. (2010 May). *Gestandaardiseerd verslag in toepassing van artikel 51, § 4 van de GVU Wet - Sector 3: Farmaceutische Verstrekkingen - Geboekte Uitgaven 200912.*

NIHDI. (2010 September). *note CGV 2010/303 Evolutie van de maandelijkse uitgaven van de verzekering voor geneeskundige verzorging. MAY 2010, p 7.*

ATTACHMENT 1

ONCOLYTICS
Overview of the changes to the list of reimbursable specialities
in attachment to the RD of 21.12.2001
- new registrations
- changes in the reimbursement modalities (new reimbursable indications)

SPECIALITY		
HYCAMTIN (topotecan)	*10 hard capsules 0,25 mg* *10 hard capsules 1 mg*	*Claim 2B*
effective as of : 01-01-2009 *hospital: * and ***	Second-line treatment of a **recurrent small-cell lung cancer**	BI : 500.000 € - 1.000.000 €.
YONDELIS (trabectedine)	*0,25 mg injection flask powder for concentrate for infusion 0,05 mg/ml* *1 mg injection flask powder for concentrate for infusion 1 flask 0,05 mg/ml*	*orphan drug*
effective as of : 01-02-2009 *hospital: * and ***	Treatment of an **advanced weak parts sarcoma**, - following unsuccessful treatments on the basis and anthracyclines and ifosfamide Or - with patients unable to get these drugs on the basis of co-morbidity	BI: 242.798 € - 353.161 €.
MABCAMPATH (alemtuzumab)	*30 mg/ml concentrate for solutions for intravenous infusions, Injection flasks 3 x 1 ml*	*Modification*
effective as of : 01-02-2009 *hospital: * and ***	Treatment of a patient with **chronic lymphatic leukemia** (CLL), who is treated with at least one standard therapy with an alkylating agent and for whom during a treatment with fludarabine phosphate no complete or partial response or only a brief remission (shorter than 6 months) was obtained.	BI: per 100 patients: 1.717.827 € for the first year , 1.112.107 € for the second year , 806.834 € for the third year.
HERCEPTIN (trastuzumab)	*150 mg 1 injection flask powder solution for infusion*	*Modification*
effective as of : 01-02-2009 *hospital: * and ***	**Adjuvant treatment of breast cancer** with a tumoral over-expression of the Human Epidermal growth factor Receptor-2 (HER2 or Human Epidermal growth factor Receptor-2), and the treatment with HERCEPTIN is administered within the context of therapy scheme containing a classic adjuvant chemotherapy that is provided with a prosology of proven functionality	BI: -
CAMPTO (Irinotecan)	*20mg/ml 1 injection flask concentrate for solution for infusion, 1 flask 15 ml*	*Claim 2A*
effective as of : 01-03-2009 *hospital: * and ***	- Treatment of **metastatic colon rectal cancer** in association with 5-fluorouracil and calciumleucovorin, amongst entitled parties that previously have had no or, at the most, an adjuvant chemotherapy treatment - **Second-line treatment of a metastatic colon rectal cancer**, following prior chemotherapy with 5-fluorouracil, in the event of failure of recurrence within 6 months.	BI: Savings of 256.000 € /year
FLUDARABINE TEVA (fludarabine phosphate)	*25 mg/ml concentrate for solution for injection of infusion flask of 50 mg/2 ml, 1 flask 2 ml*	*Modification*
effective as of : 01-03-2009 *hospital: * and ***	First-line treatment of advanced **chronic lymphatic leukemia (CLL)** of the B-cells (Rai-stage I/II or III/IV with disease related symptoms Or, if no reaction to the treatment with at least one standard therapy with an alkylating agent or if the disease has spread further after that treatment	BI: 1.5 million €

EPOSIN (etoposide)	*20 mg/ml concentrate for solution for intravenous infusion, injection flask 1 x 25 ml*	*Claim 2A*	
effective as of : 01-03-2009 *hospital: * and ***	**Treatment of small-cell lung cancer**; **Testicular cancer; Acute monoblastic and myelomonoblastic leukemia; Malignant lymphoma** (non-Hodgkin)	BI:	14.000 €
VELCADE (bortezomib)	*3,5 mg powder for solution for injection, 1 injection flask*	*Modification: extra indication*	
effective as of: 01-04-2009 *hospital: * and ***	**1st line** in combination with melfalan and prednison for the treatment of patients with **multiple myeloma** not eligible for a high-dosage chemotherapy with bone marrow transplantation.	BI:	2009: 536.500 € 2010: 1.671.000 € 2011: 2.827.000 €
ALIMTA (pemextrexed)	*500 mg solution for intravenous infusion*	*Modification: extra indication*	
effective as of : 01-05-2009 *hospital: * and ***	- Treatment of chemotherapy-naive patients with **inoperable malignant mesothelioma of the pleura of the epithelial type,** in **association with cisplatin**. - Treatment of a **locally advanced or metastatic not small-cell bronchus carcinoma** in monotherapy, with a histology that is not predominantly of the spinocellular type, and in the past treated already with chemotherapy.	BI:	7.700.000 €
MABTHERA (rituximab)	*100 mg/10 ml, 20 ml solution of intravenous infusion, 2 injections flask* *500 mg/50 ml, 50 ml solution of intravenous infusion, 1 injection flask*	*Modification*	
effective as of : 01-06-2009 *hospital: * and ***	- in association with chemotherapy consisting of minimum two cytostatics for the treatment of patients of **follicular lymphoma stage III-IV**, and that were not in the past treated by means of chemotherapy. - in association with chemotherapy consisting of minimum two cytostatics for the treatment of patients with a **recurrent or refractory follicular lymphoma stage III-IV**	BI:	1.2 million € / year
ERBITUX (cetuximab)	*2 mg/ml solution for infusion, flask of 50 ml*	*claim 2B*	
effective as of : 01-06-2009 *hospital: * and ***	Treatment of **metastatic colon rectal cancer with a non-mutated** K-RAS gen (= wild-type K-RAS gene): - in 1st line if with the combination FOLFIRI or FOLFOX - in 2nd line if the speciality is administered together with irinotecan after failure of a treatment with the combination FOLFOX. - as monotherapy with patients who already in the past were treated with oxaliplatin and irinotecan and that can no longer be treated with irinotecan	BI:	2009: 7.700.000 € 2010: 16.100.000 € 2011: 17.255.000 €
OXALIPLATINE TEVA (oxaliplatin)	*5 mg/ml concentrate for solution for infusion, flask 50 mg/10 ml; flask 100 mg/20 ml; flask 200 mg/40 ml*	*Modification*	
effective as of : 01-09-2009 *hospital: * and ***	- **1st line treatment of a metastatic colon rectal cancer**, ~~in association with 5-fluorouracil and folic acid;~~ - **adjuvant treatment of stage III (Duke's C) colon cancer**, following a complete resection of the primary tumour~~, in association with 5-fluorouracil and folic acid;.~~	BI:	-

ELOXATIN(oxaliplatin)	*5 mg/ml Concentrate for solution for infusion, Injection flask 1 x 10 ml, 1 x 20 ml, 1 x 40 ml*	*Modification*
effective as of : 01-09-2009 *hospital: * and ***	- **1st line treatment of a metastatic colon rectal cancer**, ~~in association with 5-fluorouracil and folic acid;;~~ - **adjuvant treatment of** stage **III (Duke's C) colon cancer**, following a complete resection of the primary tumour~~, in association with 5-fluorouracil and folic acid;~~	BI: -
OXALIPLATINE MEDAC (oxaliplatin)	*5 mg/ml* *50 mg powder for solution for injection* *100 mg powder for solution for injection* *150 mg powder for solution for injection*	*Modification*
effective as of : 01-09-2009 *hospital: * and ***	- **1st line treatment of a metastatic colon rectal cancer**, ~~in association with 5-fluorouracil and folic acid;;~~ - **adjuvant treatment of** stage **III (Duke's C) colon cancer**, following a complete resection of the primary tumour~~, in association with 5-fluorouracil and folic acid;~~	BI: -
OXALIPLATINE EG (oxaliplatin)	*5 mg/ml powder for solution for infusion, flask 50 mg and 100 mg*	*Modification*
effective as of : 01-09-2009 *hospital: * and ***	- **1st line treatment of a metastatic colon rectal cancer**, ~~in association with 5-fluorouracil and folic acid;;~~ - **adjuvant treatment of** stage **III (Duke's C) colon cancer**, following a complete resection of the primary tumour~~, in association with 5-fluorouracil and folic acid;~~	BI: -
OXALIPLATIN MAYNE (oxaliplatin)	*5 mg/ml solution for infusion,* *1 flask 10 ml and 20 ml*	*Modification*
effective as of : 01-09-2009 *hospital: * and ***	- **1st line treatment of a metastatic colon rectal cancer**, ~~in association with 5-fluorouracil and folic acid;;~~ - **adjuvant treatment of** stage **III (Duke's C) colon cancer**, following a complete resection of the primary tumour ~~in association with 5-fluorouracil and folic acid;~~	BI: -
TYVERB (lapatinib)	*250 mg 140 coated tablets*	*Claim 2B*
effective as of : 01-09-2009 *hospital: * and ***	Treatment of a patient with **metastatic breast cancer** with a tumoral over-expression of the Epidermal Growth Factor Receptor 2 (HER2 of Human Epidermal Growth Factor Receptor-2)	BI: added cost of 2.398.006 €
MABTHERA (rituximab)	*100 mg/10 ml, 20 ml solution for intravenous infusion, 2 injections flask* *500 mg/50 ml, 50 ml solution for intravenous infusion, 1 injection flask*	*Modification: extra indication*
effective as of : 01-10-2009 *hospital: * and ***	**1st line treatment of B-cell chronic lymphatic leukemia, i**n combination with chemotherapy that fludarabin contains	BI: 1.240.236 €
GLIOLAN (aminolevulinic acid)	*30 mg/ml powder for drink, flask 1 x 1,5 g*	*orphan drug*
effective as of : 01-11-2009	**Visualisation of the tumoral tissue** with the	BI: 407.980 €

*hospital: * and ***	removal of a malignant glioma (WHO grade III or IV)		
VIDAZA (Azacitidine)	*100mg powder for suspension for injection, 1 injection flask*	*orphan drug*	
effective as of : 01-12-2009 *hospital: * and **	- Treatment of **myelodysplastic syndrome**, - Treatment of **chronic myelomonocytic leukemia** with 10-29 % bone marrow blasts without myeloproliferate syndrome, - Treatment of **acute myeloblastic leukemia** met 20-30 % blastic cells and dysplasia of several cell lines according to the classification of the WHO	BI:	9.481.900 €
OXALIPLATIN SANDOZ (oxaliplatin)	*5 mg/ml powder for solution for infusion, flask 10ml (50 mg) and 20ml (100 mg)*	*Modification*	
effective as of : 01-12-2009 *hospital: * and **	- in the context of the **1st line treatment of metastatic colon rectal cancer**, ~~in association with 5-fluorouracil and folic acid;~~ in the context of the **adjuvant treatment of stage III (Duke's C) colon cancer** , following a complete resection of the primary tumour~~, in association with 5-fluorouracil and folic acid;~~	BI:	-
AVASTIN (Bevacizumab)	*25 mg/ml concentrate for solution for infusion, 100 mg/4 ml and 400 mg/16 ml*	*Modification*	
effective as of : 01-01-2010 *hospital: * and **	- 1st line treatment of patients with **metastatic colon or rectal cancer** - halt to the treatment by progression - in combination with intravenous 5-fluorouracil/folinic acid and irinotecan or 5-fluorouracil/folinic acid **and oxaliplatin** AVASTIN + FOLFOX	BI : 	2010 : 500.000 € 2011 : 600.000 € 2012 : 772.000 €
TAXOTERE (docetaxel)	*20 mg concentrate for solution for infusion 1 flask 10 mg/1 ml* *80 mg concentrate for solution for infusion 1 flask 10 mg/1 ml*	*Modification: extra indication*	
effective as of : 01-01-2010 *hospital: * and **	Adjuvant treatment of an operable breast cancer on patients that are lymph-node positive, either in association with an anthracyclin and cyclophosphamide, or in association with only cyclophosphamide with those patients that cannot be considered for treatment with an anthracycline	BI :	1.870.000 €
AVASTIN (Bevacizumab)	*25 mg/ml concentrate for solution for infusion, 100 mg/4 ml and 400 mg/16 ml*	*Modification*	
effective as of : 01-02-2010 *hospital: * and **	1st line treatment of patients **metastatic triple negative breast cancer (**ER-negative, PR-negative and Her-2 negative) in combination with paclitaxel.	BI :	2010: 500.000 €, 2011: 900.000 € 2012: 1.300.000 €
SPRYCEL (Dasatanib)	*100 mg 30 coated tablets*	*Claim 2A*	
effective as of : 01-01-2010 *hospital: * and **	- Treatment of **chronic myeloid leukemia** with presence of the Philadelphia chromosome in case of resistance to a prior treatment with inclusion of imatinib mesilate or in case of intolerancy that would justify the halting of a treatment with imatinib mesilate, with patients 18 years or older and amongst whom the **chronic myeloid leukemia is found in** the **chronic stage** - treatment of chronic myeloid leukemia with presence of the Philadelphia chromosome in case of resistance to a prior treatment with inclusion of	BI:	-

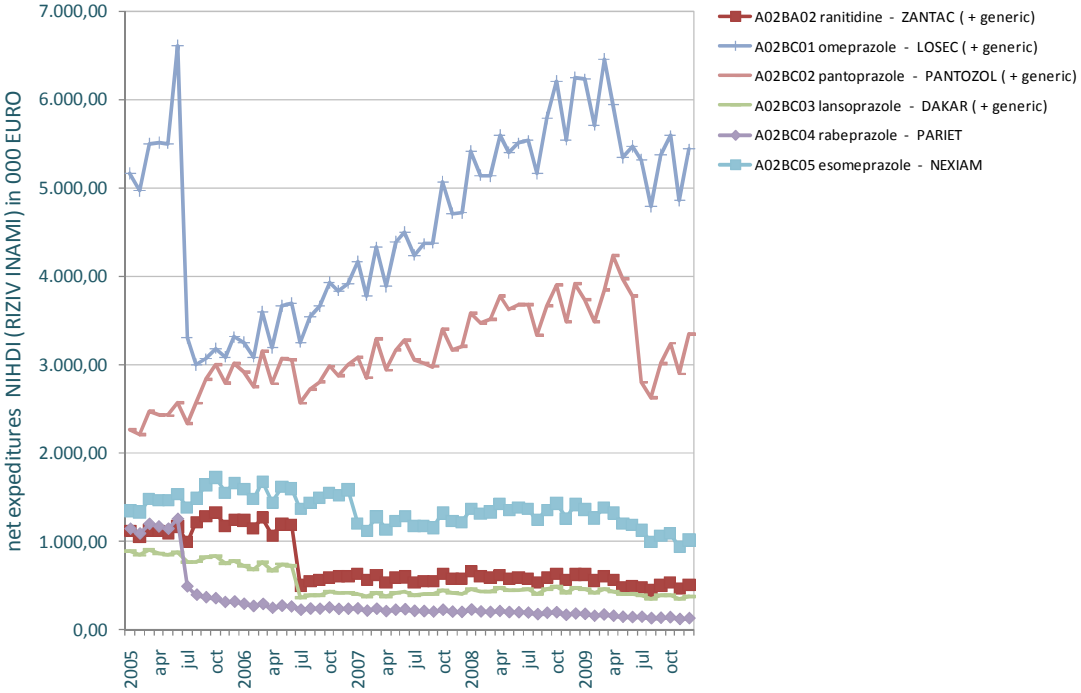
	imatinib mesilate or in case of intolerancy that would justify the halting of a treatment with imatinib mesilate, with patients 18 years or older and amongst whom the **chronic myeloid leukemia is found in an accelerated stage or a blastic crisis**. - treatment of **acute lymphoblastic leukemia** with presence of the Philadelphia chromosome in case of resistance to a prior treatment or in case of intolerancy that would justify the halting of a prior treatment of a legally entitled individual of 18 years of age or older		
CAELYX (Doxorubicine, - hydrochloride)	*2 mg/ml injection flask concentrate for solution for infusion 1 x 25 ml ; 1 x 10 ml*	*Modification*	
effective as of : 01-01-2010 *hospital: * and ***	Administered in association with VELCADE to patients with **multiple myeloma**, that display a progression of the disease and that have undergone at least one previous treatment cycle containing at least a stem cell transplantation, except in cases where the patient is not eligible for this.	BI:	220.000 € - 370.000 €
ERBITUX (cetuximab)	*2 mg/ml solution for infusion, flask van 50 ml* *5mg/ml solution for infusion, 1 flask of 20 ml and 100 ml*	*Modification: extra indication*	
effective as of : 01-03-2010 *hospital: * and ***	Initial treatment cycle together with cisplatin as 1st line treatment of a recurrent and/or metastatic squamous cell carcinoma of the head – neck area.	BI:	3.595.623 €/year

ATTACHMENT 2

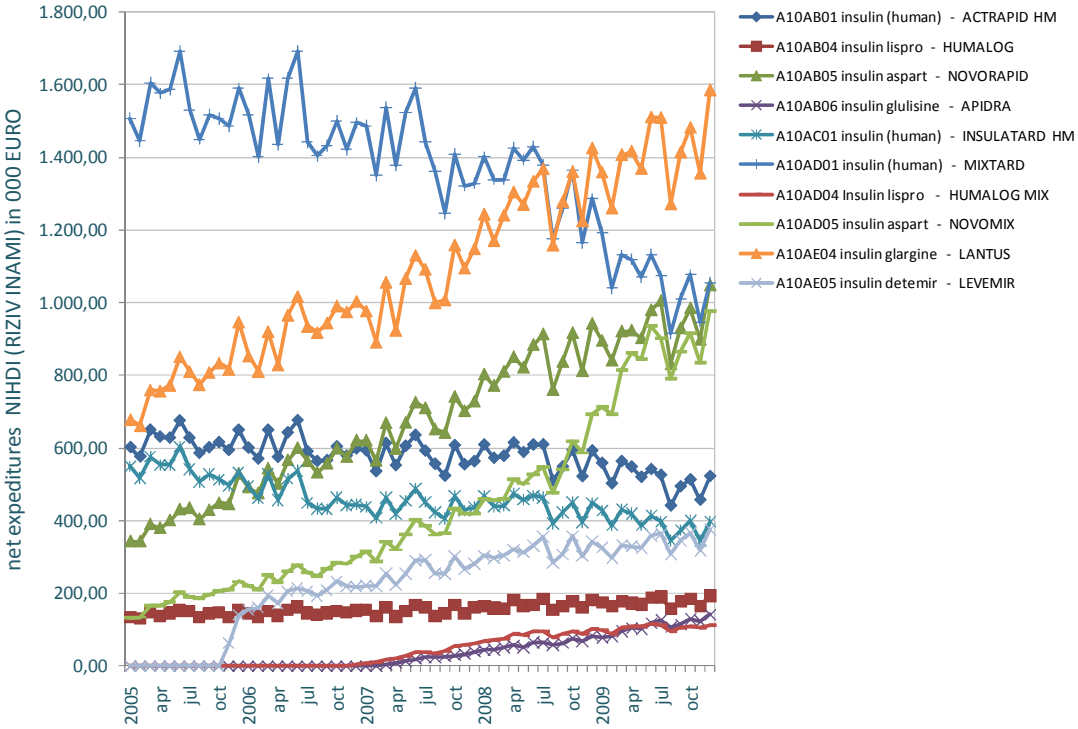
NET EXPENDITURES IN PUBLIC PHARMACIES for reimbursable specialities
overview of the expenditures per molecule
detailed graphics

Note: The following graphics show per ATC class (level 4) the evolution per month of the net expenditures NIHDI for all active ingredients, with the exception of those for which the expenditures have remained steady and for which these expenditures may be considered merely negligible (< 5 % of total)

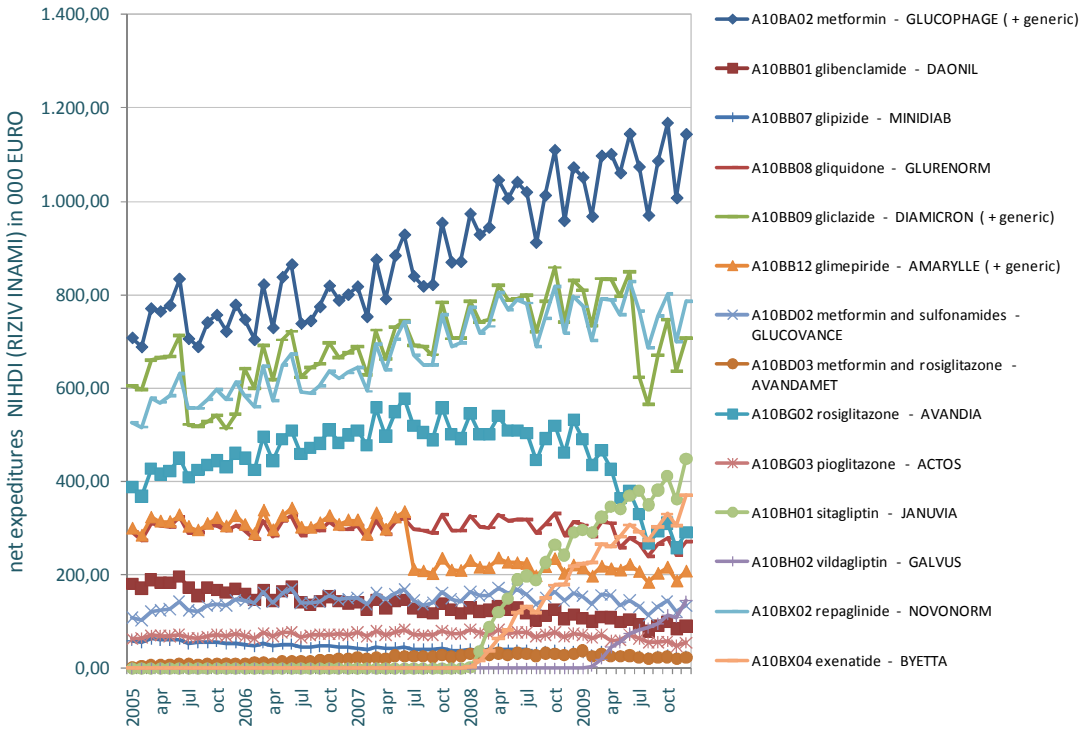
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)



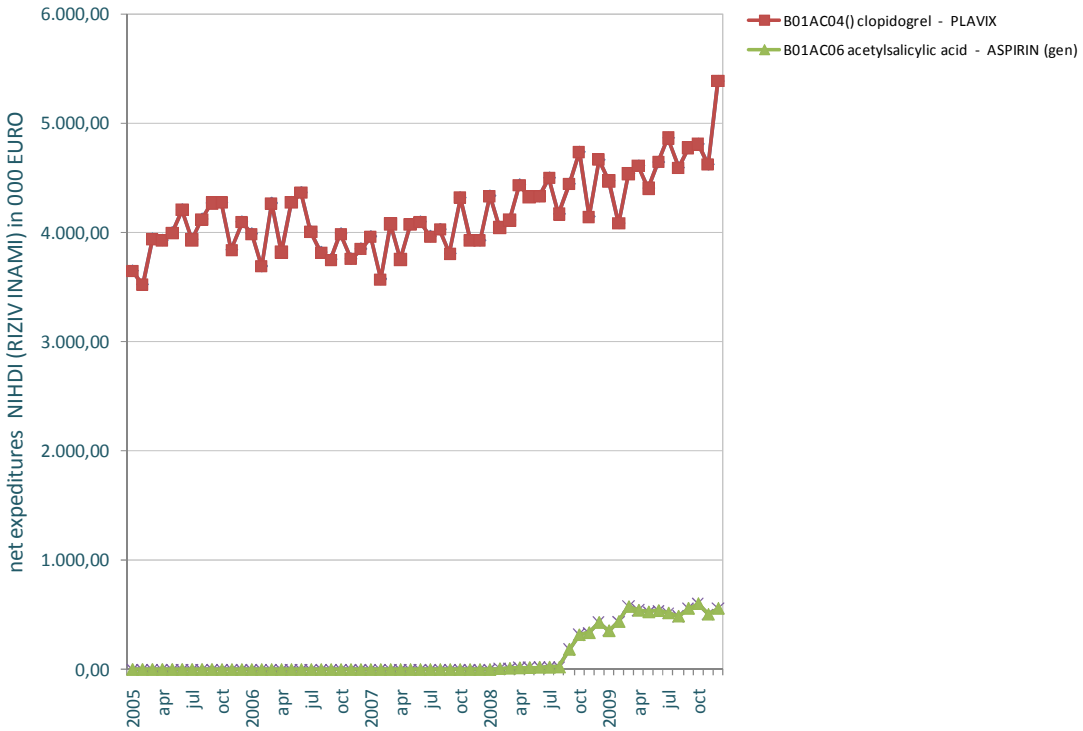
INSULINS AND ANALOGUES



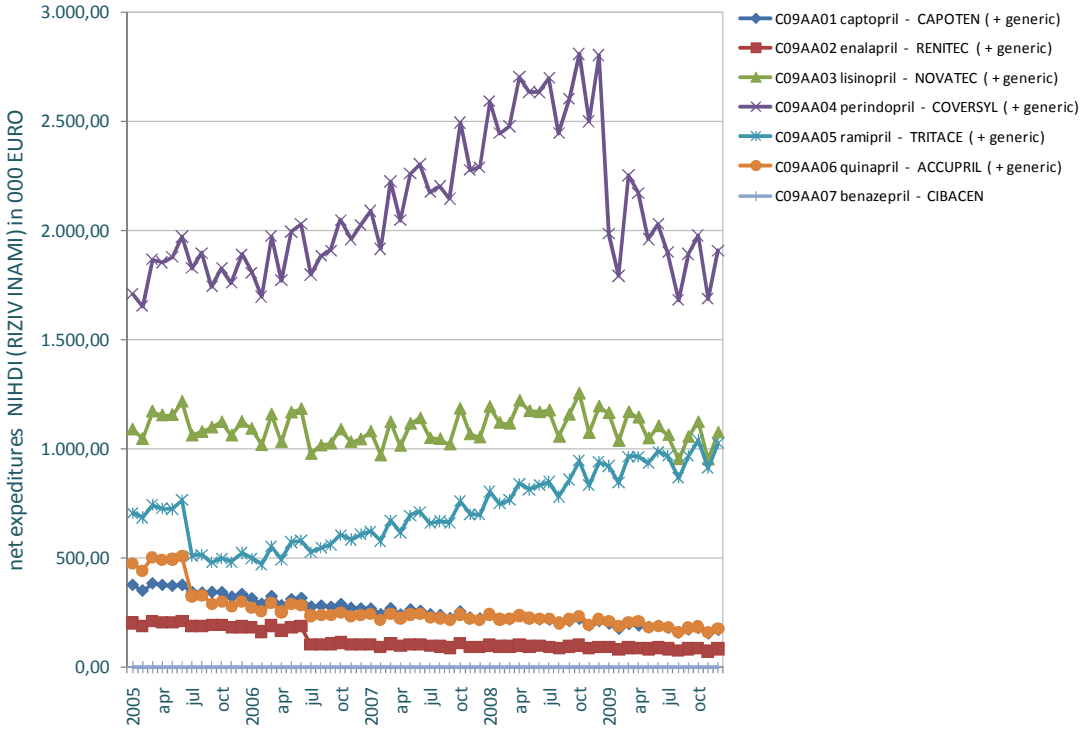
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS



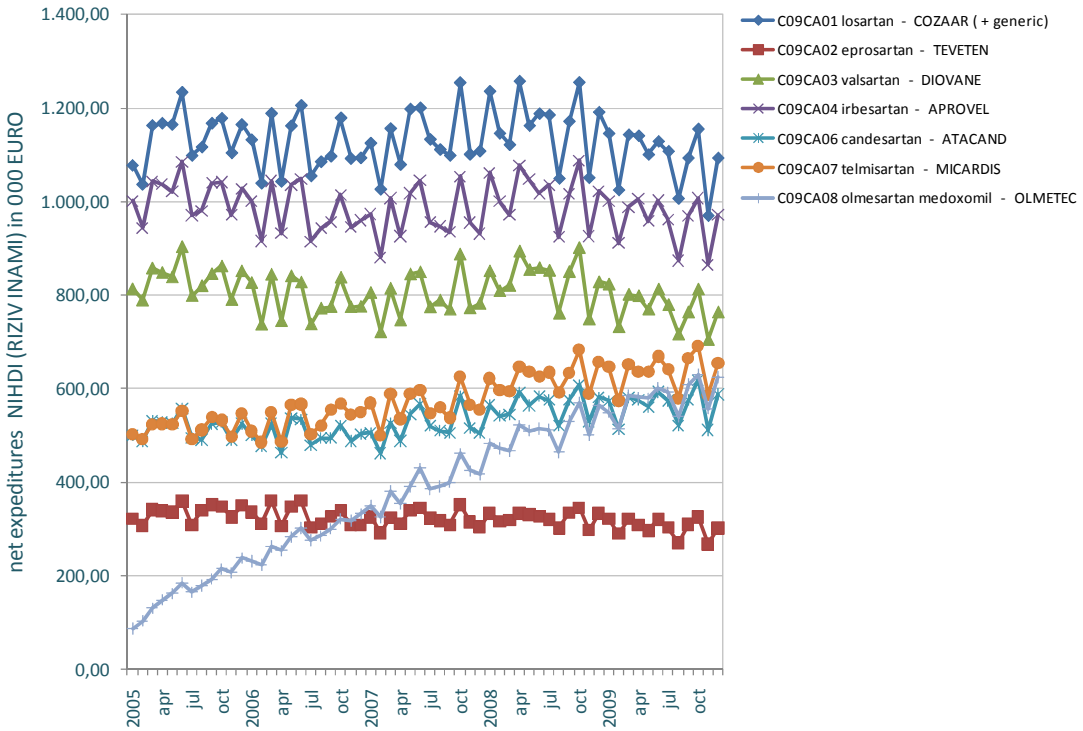
ANTITHROMBOTIC AGENTS



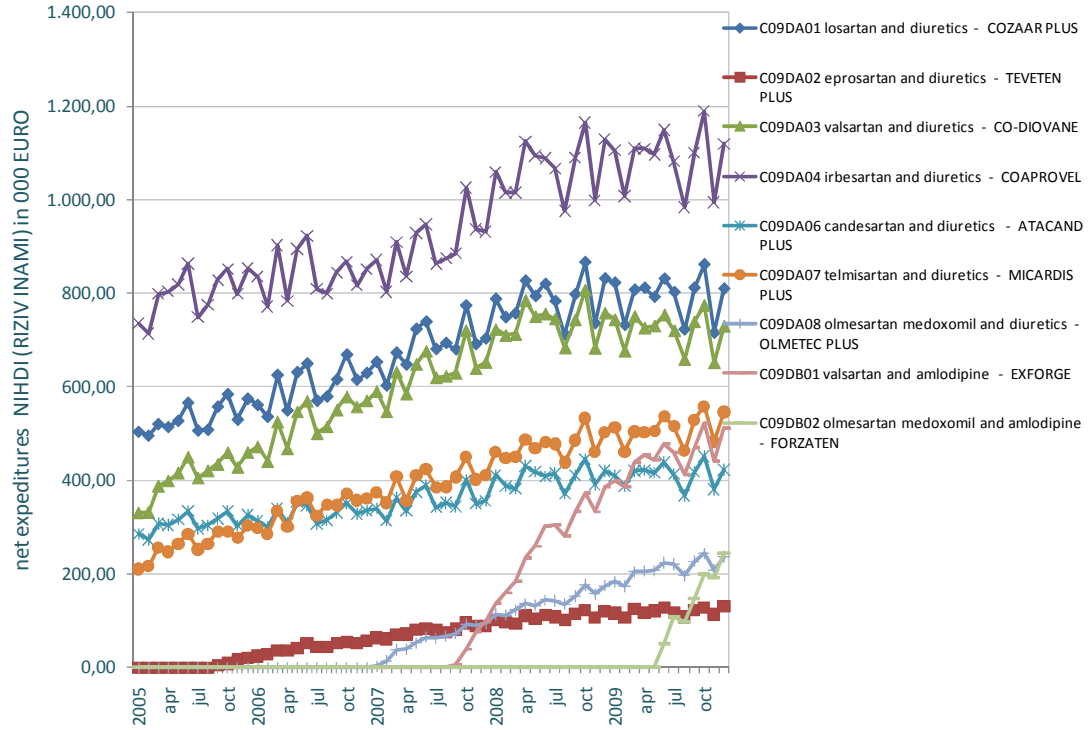
ACE INHIBITORS, PLAIN



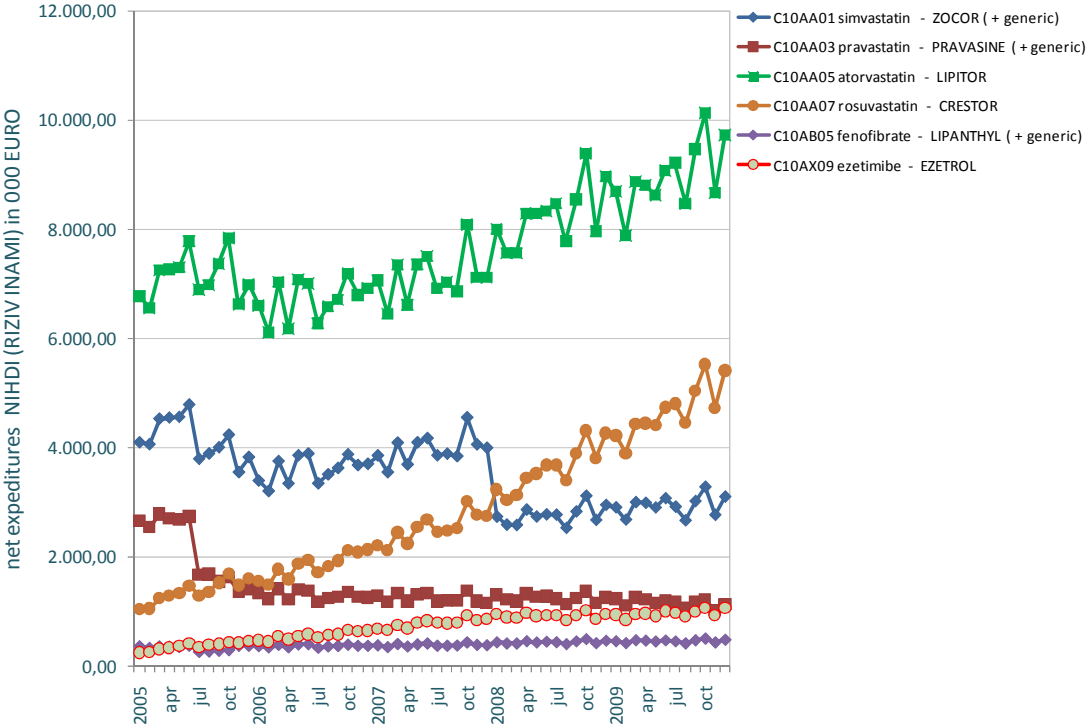
ANGIOTENSIN II ANTAGONISTS, PLAIN



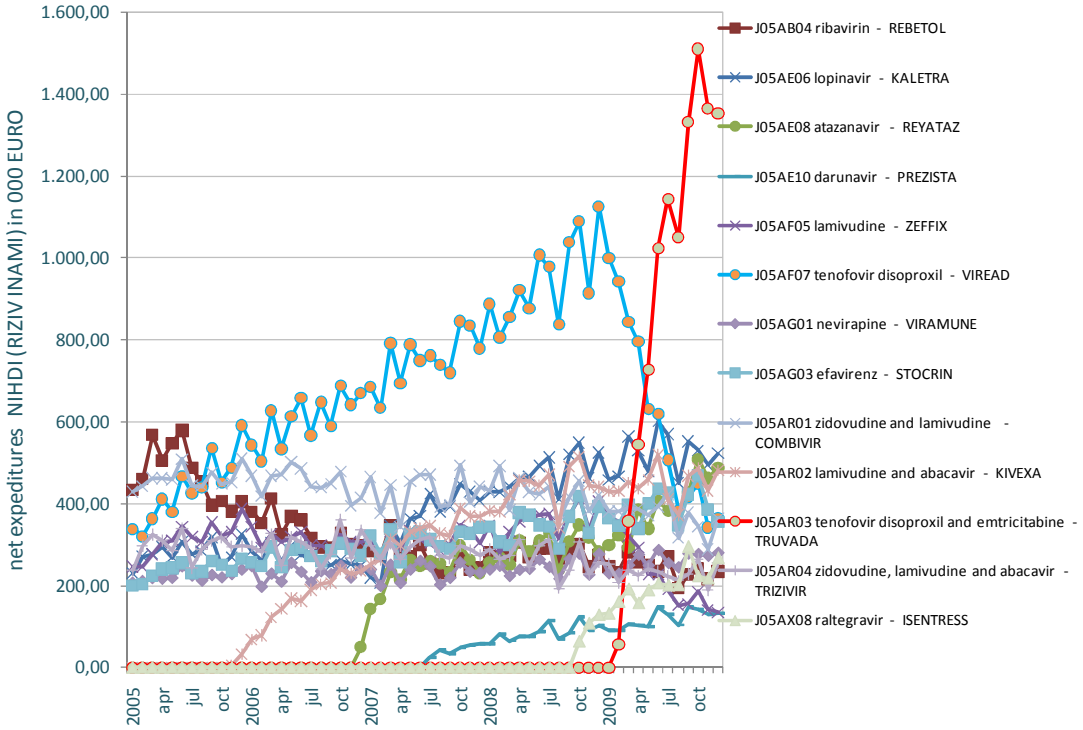
ANGIOTENSIN II ANTAGONISTS, COMBINATIONS



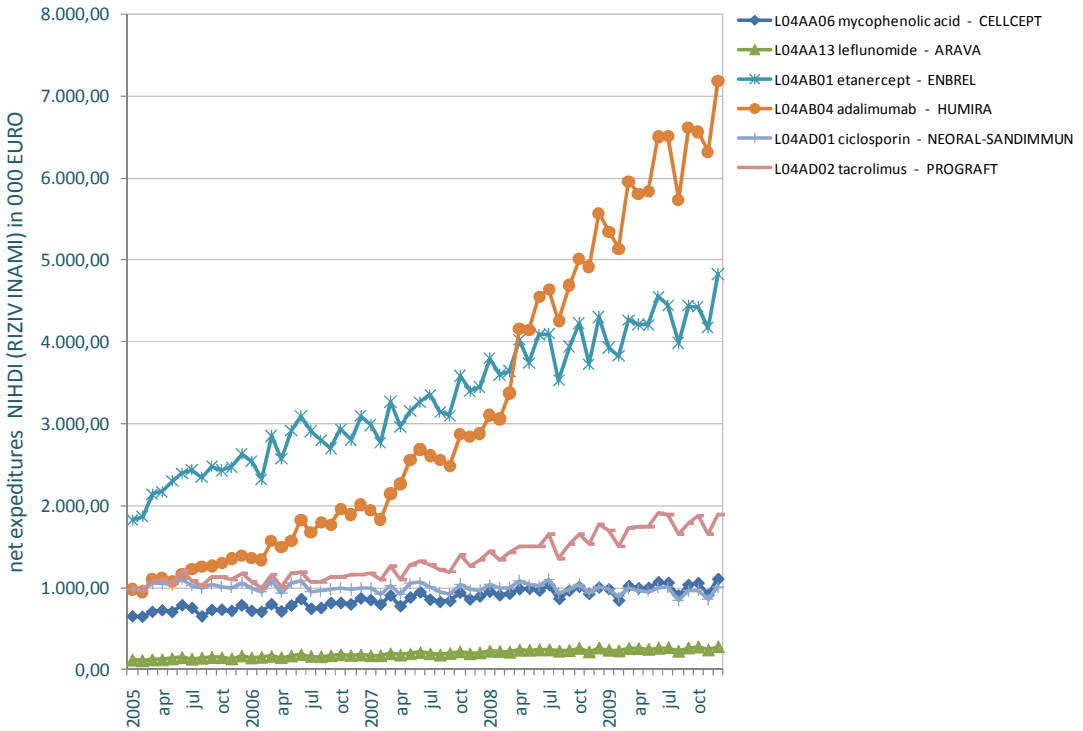
LIPID MODIFYING AGENTS, PLAIN



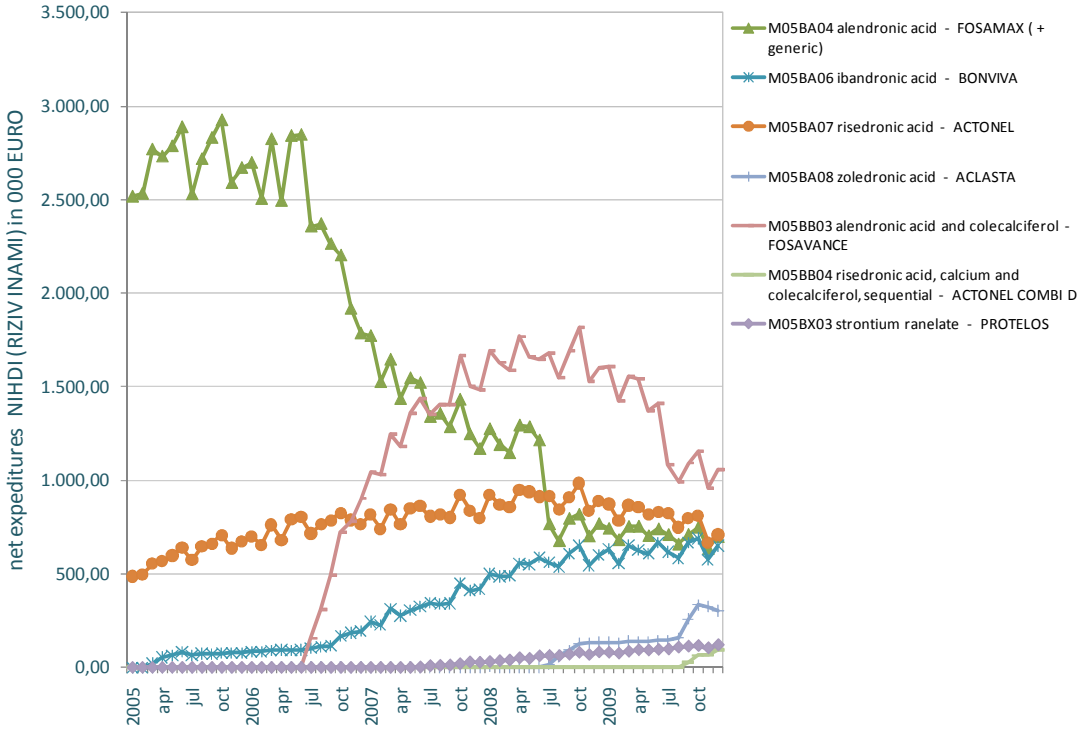
DIRECT ACTING ANTIVIRALS



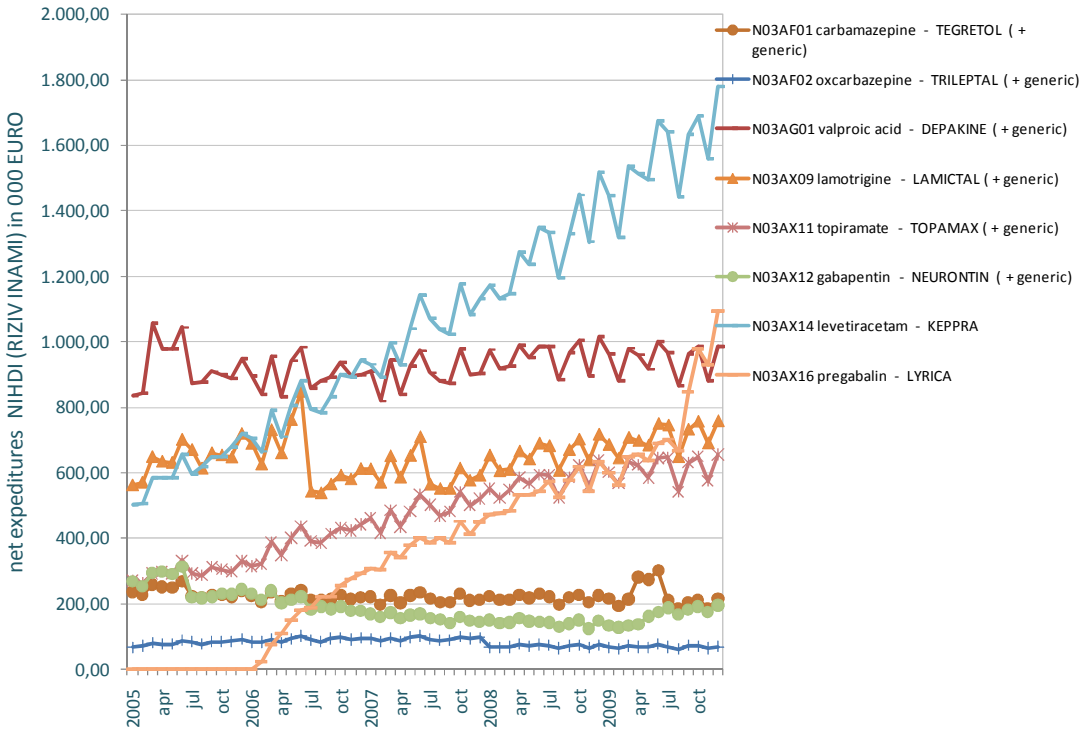
IMMUNOSUPPRESSANTS



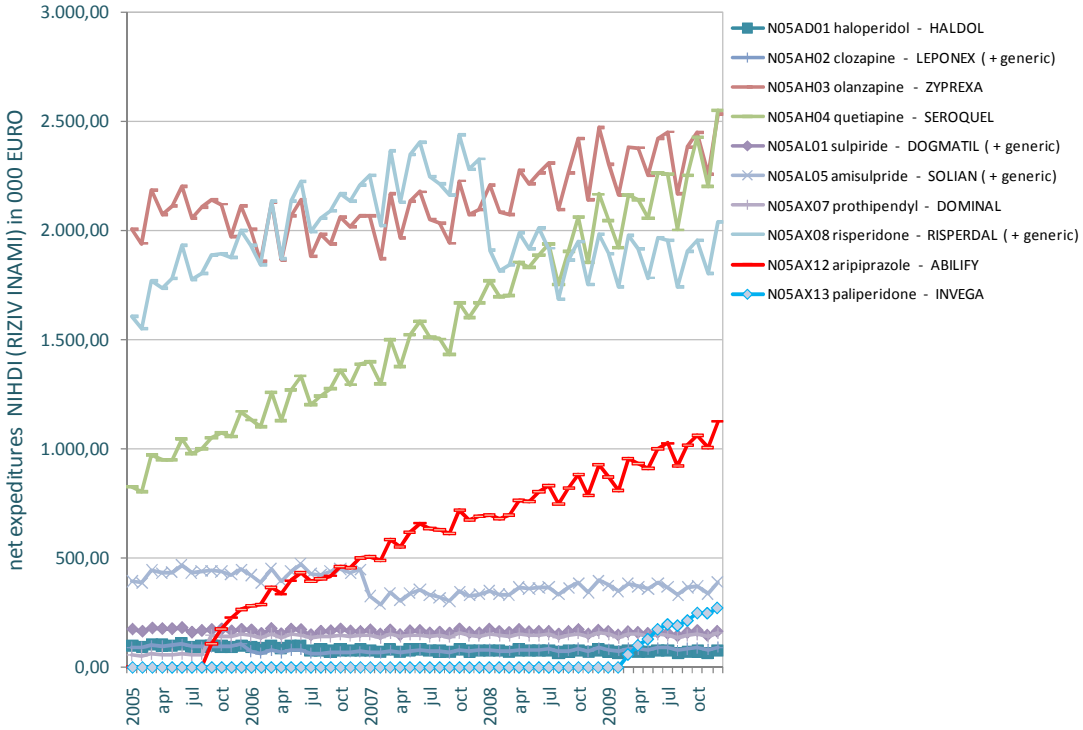
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION



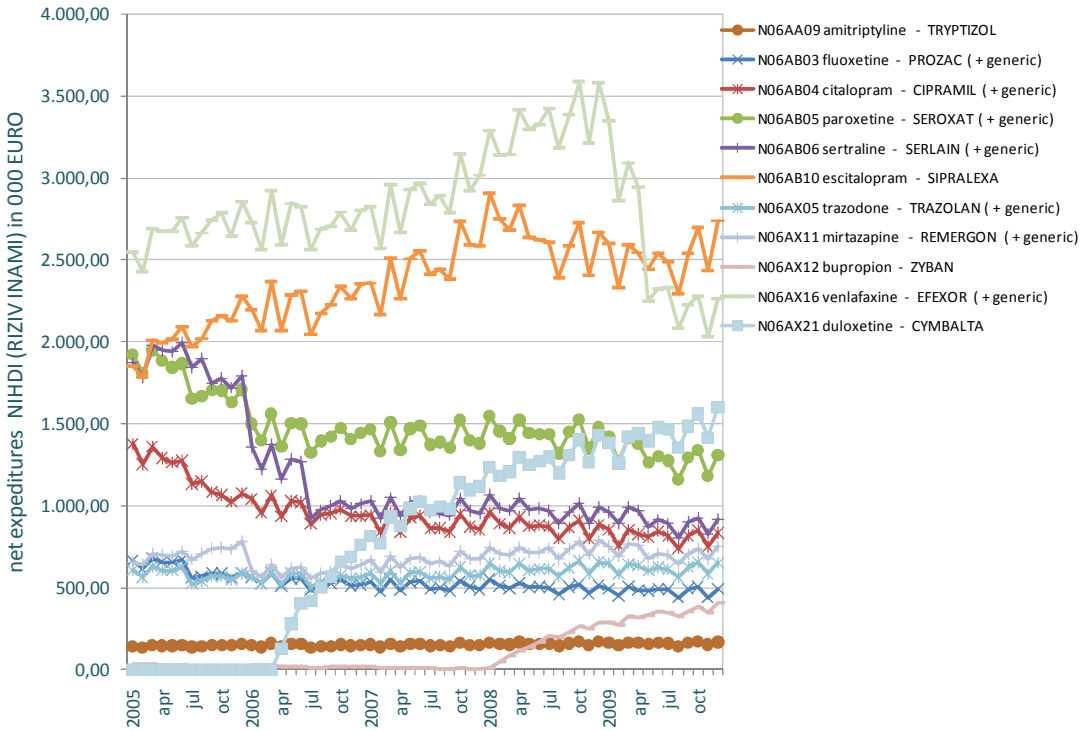
ANTITEPILEPTICS



ANTIPSYCHOTICS



ANTIDEPRESSANTS



ATTACHMENT 3

PROCEDURES OF THE CRM
overview of the results of the procedures (RD 21 12 2001)
for claims for modification to the list of reimbursable specialities
2007 – 2009

PROPOSALS OF THE CRM in function of the TYPE OF CLAIM

Table 32: number of unique claims for registration in the list of reimbursable specialities versus proposal of the Commission for the Reimbursement of Medicines (2009)

2009							
	positive		negative		no proposal		total
	number	%	number	%	number	%	number
class 1	6	38%	5	31%	5	31%	16
class 2	89	83%	6	6%	12	11%	107
class 3	150	99%	1	1%	1	1%	152
modification	145	90%	11	7%	6	4%	162
orphan	9	64%	2	14%	3	21%	14
total	399	88%	25	6%	27	6%	451

Table 33: number of unique claims for registration in the list of reimbursable specialities versus proposal of the Commission for the Reimbursement of Medicines (2008)

2008							
	positive		negative		no proposal		total
	number	%	number	%	number	%	number
class 1	4	67%	0	0%	2	33%	6
class 2	90	78%	14	12%	12	10%	116
class 3	130	96%	6	4%	0	0%	136
modification	79	82%	12	13%	5	5%	96
orphan	6	75%	1	13%	1	13%	8
total	309	85%	33	9%	20	6%	362

Table 34: number of unique claims for registration in the list of reimbursable specialities versus proposal of the Commission for the Reimbursement of Medicines (2007)

2007							
	positive		negative		no proposal		total
	number	%	number	%	number	%	number
class 1	10	59%	2	12%	5	29%	17
class 2	66	69%	12	13%	17	18%	95
class 3	95	95%	2	2%	3	3%	100
modification	87	88%	6	6%	6	6%	99
orphan	6	60%	2	20%	2	20%	10
total	264	82%	24	7%	33	10%	321

DECISIONS OF THE MINISTER in function of the PROPOSAL OF THE CRM

Table 35: decisions of the Minister in function of the proposal of the CRM (unique dossiers 2009)

2009											
	positive decision Min		negative decision Min		no decision Min (pos)		no data		withdrawn (company)		**total**
CTG CRM proposal	number	%	number	%	number	%	number	%	number	%	**number**
class 1	**7**	**43,8%**	**3**	**18,8%**			**5**	**31,3%**	**1**	**6,3%**	**16**
positive prop	6	100%									**6**
negative prop	1	20,0%					3	60,0%	1	20,0%	**5**
no prop			3	60,0%			2	40,0%			**5**
class 2	**90**	**84,1%**	**10**	**9,3%**	**1**	**0,9%**	**5**	**4,7%**	**1**	**0,9%**	**107**
positive prop	81	91,0%	4	4,5%	1	1,1%	2	2,2%	1	1,1%	**89**
negative prop	2	33,3%	3	50,0%			1	16,7%			**6**
no prop	7	58,3%	3	25,0%			2	16,7%			**12**
class 3	**144**	**94,7%**	**2**	**1,3%**			**3**	**2,0%**	**3**	**2,0%**	**152**
positive prop	144	96,0%					3	2,0%	3	2,0%	**150**
negative prop			1	100%							**1**
no prop			1	100%							**1**
modification	**146**	**90,1%**	**11**	**6,8%**			**5**	**3,1%**			**162**
positive prop	140	96,6%					5	3,4%			**145**
negative prop	1	9,1%	10	90,9%							**11**
no prop	5	83,3%	1	16,7%							**6**
orphan	**11**	**78,6%**	**2**	**14,3%**			**1**	**7,1%**			**14**
positive prop	8	88,9%	1	11,1%							**9**
negative prop	1	50,0%					1	50,0%			**2**
no prop	2	66,7%	1	33,3%							**3**
total	**398**	**88,2%**	**28**	**6,2%**	**1**	**0,2%**	**19**	**4,2%**	**5**	**1,1%**	**451**

Table 36: decisions of the Minister in function of the proposal of the CRM (unique dossiers 2008)

2008											
	positive decision Min		negative decision Min		no decision Min (pos)		no data		withdrawn (company)		**total**
CTG CRM proposal	number	%	number	%	number	%	number	%	number	%	**number**
class 1	**6**	**100%**									**6**
positive prop	4	100%									**4**
negative prop											
no prop	2	100%									**2**
class 2	**94**	**81,0%**	**15**	**12,9%**					**7**	**6,0%**	**116**
positive prop	87	96,7%	2	2,2%					1	1,1%	**90**
negative prop	2	14,3%	7	50,0%					5	35,7%	**14**
no prop	5	41,7%	6	50,0%					1	8,3%	**12**
class 3	**129**	**94,9%**	**4**	**2,9%**			**3**	**2,2%**			**136**
positive prop	127	97,7%					3	2,3%			**130**
negative prop	2	33,3%	4	66,7%							**6**
no prop											
modification	**84**	**87,5%**	**9**	**9,4%**	**2**	**2,1%**	**1**	**1,0%**			**96**
positive prop	75	94,9%	1	1,3%	2	2,5%	1	1,3%			**79**
negative prop	4	33,3%	8	66,7%							**12**
no prop	5	100%									**5**
orphan	**7**	**87,5%**	**1**	**12,5%**							**8**
positive prop	6	100%									**6**
negative prop	1	100%									**1**
no prop			1	100%							**1**
total	**320**	**88,4%**	**29**	**8,0%**	**2**	**0,6%**	**4**	**1,1%**	**7**	**1,9%**	**362**

Table 37: decisions of the Minister in function of the proposal of the CRM (unique dossiers 2007)

2007											
	positive decision Min		negative decision Min		no decision Min (pos)		no data		withdrawn (company)		**total**
CTG CRM proposal	number	%	number	%	number	%	number	%	number	%	**number**
class 1	12	70,6%	4	23,5%			1	5,9%			17
positive prop	10	100%									10
negative prop			2	100%							2
no prop	2	40,0%	2	40,0%			1	20,0%			5
class 2	78	82,1%	16	16,8%					1	1,1%	95
positive prop	64	97,0%	1	1,5%					1	1,5%	66
negative prop	1	8,3%	11	91,7%							12
no prop	13	76,5%	4	23,5%							17
class 3	96	96,0%	3	3,0%					1	1,0%	100
positive prop	93	97,9%	1	1,1%					1	1,1%	95
negative prop	1	50,0%	1	50,0%							2
no prop	2	66,7%	1	33,3%							3
modification	92	92,9%	6	6,1%			1	1,0%			99
positive prop	87	100%									87
negative prop			6	100%							6
no prop	5	83,3%					1	16,7%			6
orphan	9	90,0%							1	10,0%	10
positive prop	6	100%									6
negative prop	1	50,0%							1	50,0%	2
no prop	2	100%									2
total	287	89,4%	29	9,0%			2	0,6%	3	0,9%	321

ATTACHMENT 4

SUMMARY OF THE FIGURES

SUMMARY OF THE TABLES