Monitoring Of Reimbursement Significant Expenses

MORSE

Semi-annual Report (semester 1 - 2011)

data 2010

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 2010.

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 February 2011).

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 2011: not enough validated data are available about the expenditures (Farmanet February 2011, IMS May 2011) to draw up a reliable estimation or forecast of their 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 2011).

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

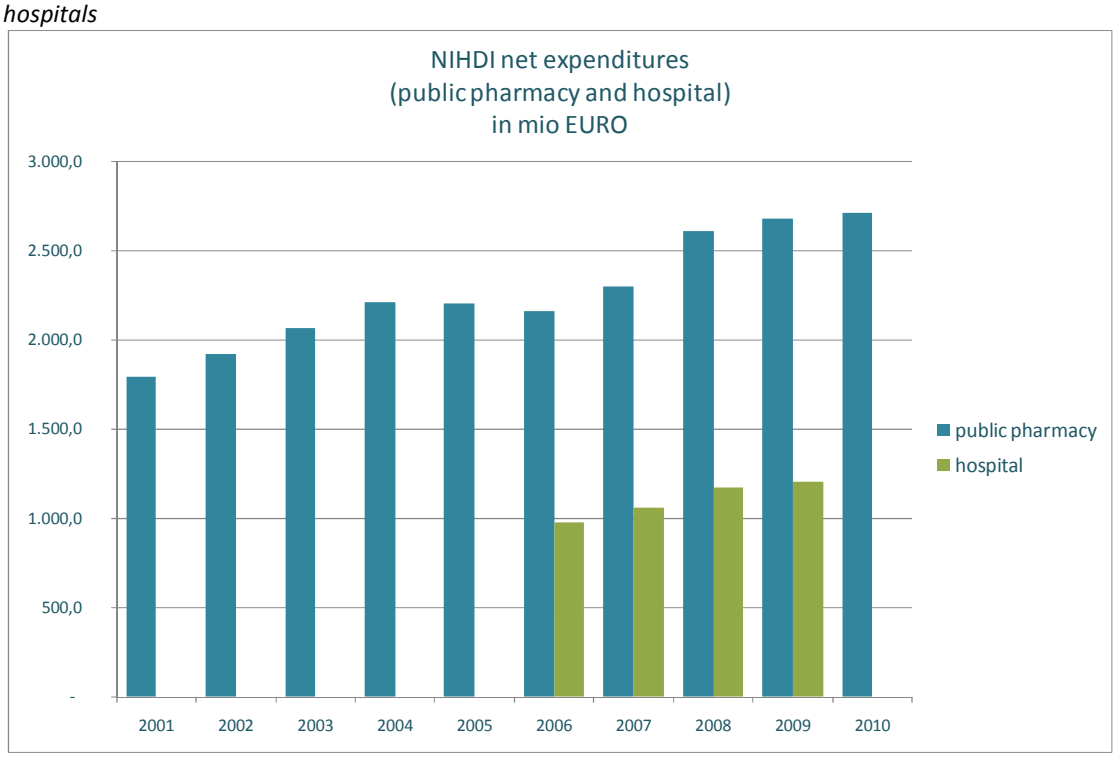
OVERVIEW OF THE GLOBAL EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES
BROKEN DOWN BY PUBLIC PHARMACIES AND HOSPITALS

General

Table 1: MORSE dataset: net annual expenditures NIHDI for drugs 2003 – 2010

Net expenditures NIHDI x 1,000,000 €								
	2003	2004	2005	2006	2007	2008	2009	2010
Public pharmacies	**2.063,3**	**2.213,0**	**2.203,6**	**2.161,1**	**2.297,9**	**2.611,1**	**2.680,8**	**2.711,4**
Hospitals				**975,5**	**1.057,8**	**1.171,4**	**1.205,9**	
Total				**3.136,6**	**3.355,7**	**3.782,5**	**3.886,7**	
Growth %								
	'02- '03	'03- '04	'04- '05	'05- '06	'06- '07	'07- '08	'08- '09	'09- '10
Public pharmacies	**7,4**	**7,3**	**min 0,4**	**min 1.9**	**6,3**	**13,6**	**2,6**	**1,1**
Hospitals					**8,4**	**10,7**	**2,9**	
Total					**7**	**12,7**	**2,7**	

Figure 1: NIHDI net expenditures for reimbursable pharmaceutical specialities in public pharmacies and hospitals



Net expenditures NIHDI for public pharmacies calculated on the basis of the available data to and including December 2010 (Farmanet)

Net expenditures NIHDI based on doc PH data 2006 to and including the 2nd semester 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.

A significant change in the trend appears to occur in the evolution of the expenditures – that is to say, the important growth to and including 2008 – for the reimbursement of pharmaceutical specialities in public pharmacies (*cave* extrapolation of the data for 2008 – not corrected for the effect of the changes related to 'small risks' for the self-employed). In 2009, the growth was only 2.6 %; in 2010 1.1 %.

Also in hospitals, one records a levelling off of growth, resulting in a total increase in expenditures for pharmaceutical specialities by 2.7 %.

An important portion of the growth of the expenditures in 2008 is to be attributed to the integration of the small risks coverage for the self-employed since 1 January 2008 (+ 6.2 %). The expenditures for drugs for the self-employed, however, are no longer rising faster than the expenditures within the general regime (see *Table 2*)[1].
For the 2008 and 2009 data, one has to take into account that the effect of new measures is not always immediately obvious, for instance, because of the fact that primarily 'posted' data are used and that there are 'delays' in the implementation in the daily practice (amongst others, because the measures are not adequately or fully 'known' amongst the parties involved, in casu, the self-employed).

Table 2: Evolution posted expenditures on annual basis per regulation: total specialities, in Mil EURO (source Permanent Audit May 2011)

	2005	2006	2007	2008	2009	2010
General regulation	3.042,1	3.005,3	3.215,2	3.444,6	3.569,2	3.668,8
Self-employed	128,2	130,5	146,0	306,3	334,6	343,9
Total	3.170,3	3.135,8	3.361,2	3.750,8	3.903,8	4.012,7

evolution in %

General regulation	2,3	-1,2	7,0	7,1	3,6	2,8
Self-employed	4,6	1,7	11,9	109,8	9,3	2,8
Total	**2,4**	**-1,1**	**7,2**	**11,6**	**4,1**	**2,8**

The most recent IMS data indicate an analogous evolution of the expenditures – with the exception of the year 2008, during which, for instance, the same effect of the contribution to the costs of drugs for the self-employed (integration of the 'small risks ') is not being capped. The self-employed were, in fact insured on a voluntary basis or they paid the cost of their drugs themselves.

Although this report is not meant to make a forecast of the evolution of the expenditures for reimbursable drugs for 2011, it may be noted from the available IMS data (see *Table 3*) that in 2011 no significant rise in these expenditures is to be expected.

Figure 2 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.

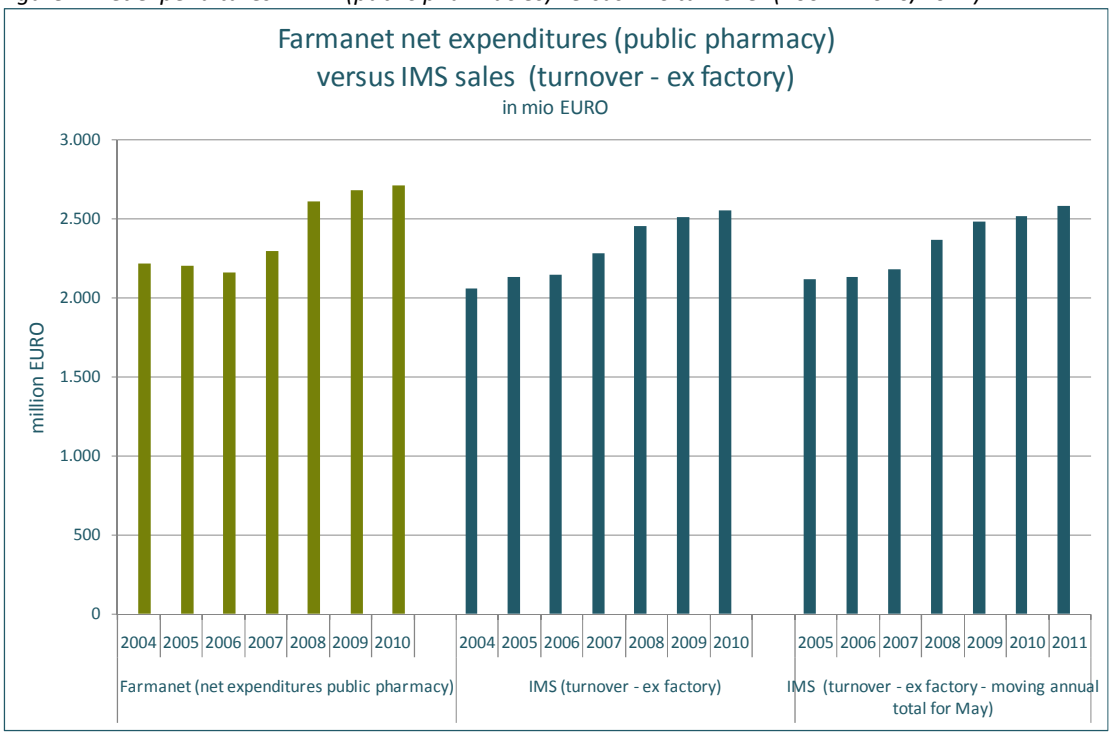
[1] Standardized report in application of article 51, § 4 of the GVU Law (mandatory health insurance) - Sector 3: Pharmaceutical Provisions – Posted expenditures 201012, p 3.3. table 3.1.2.2. (NIHDI, Standardized report in application of article 51, § 4 of the GVU Law – Sector 3 : Pharmaceutical Provisions – Posted Expenditures 201012, 2011 May)

Table 3: IMS dataset: evolution of the gross turnover reimbursable drugs and 'moving annual total'[2] 2006 – 2010/2011 (in Mil EURO)

	2006	**2007**	**2008**	**2009**	**2010**
total	2.143,0	2.280,5	2.454,8	2.511,0	2.549,6
% increase versus the previous year	0,6	6,4	7,6	2,3	1,5

MAT **(May)**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**
'moving annual total'	2.131,7	2.176,9	2.368,7	2.482,6	2.515,3	2.582,3
% increase versus the previous year	0,6	2,1	8,8	4,8	1,3	2,7

Figure 2: net expenditures NIHDI (public pharmacies) versus IMS turnover (2004 – 2010/2011)



[2] The term MAT 'Moving Annual Total' means: Total sum over one year: not the (usual) calendar year, but from month x (in this case may) of year y (for example 2010), up to and including month x-1 (in this case april) from year y+1 (for instance 2011).

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 2011) [3]

	2005	**2006**	**2007**	**2008**	**2009**	**2010**
Public pharmacies	2.205,5	2.155,1	2.288,8	2.568,9	2.670,1	2.714,3
Hospitals – ambulatory patients	451,3	477,7	570,0	671,8	736,3	814,1
Hospitals - hospitalised patients	513,5	503,0	502,3	510,2	497,4	484,4
Total	3.170,3	3.135,8	3.361,2	3.750,8	3.903,8	4.012,7
evolution in %						
Public pharmacies		-2,3	6,2	12,2	3,9	1,7
Hospitals – ambulatory patients		5,9	19,3	17,9	9,6	10,6
Hospitals - hospitalised patients		-2,1	-0,1	1,6	-2,5	-2,6
Total		**-1,1**	**7,2**	**11,6**	**4,1**	**2,8**

Similar recent NIHDI data for 2011, albeit it for the first three months only (*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 2011, 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 March), in 000 EURO (source note Insurance Committee, Evolution of the monthly expenditures) [4]

	2008	**2009**	**2010**	**2011**
Public pharmacies	621.218	671.844	672.025	690.802
Hospitals – ambulatory patients	158.318	178.737	188.438	219.042
Hospitals - hospitalised patients	133.614	132.853	122.692	123.510
Total	913.150	983.434	983.155	1.033.354
evolution in %	**2008/2007**	**2009/2008**	**2010/2009**	**2011/2010**
Public pharmacies	13,4	7,0	0,5	2,8
Hospitals – ambulatory patients	18,3	9,9	9,7	16.2
Hospitals - hospitalised patients	0,7	-1,4	-5,6	0,7
Total	12,1	6,3	1,4	5,1

[3] Standardized report in application of article 51, § 4 of the GVU Law (mandatory health insurance) - Sector 3: Pharmaceutical provisions – Posted expenditures 201012, 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 201012, 2011 May)

[4] (NIHDI, note CGU 2011/263 Evolution of the monthly expenditures on insurance for medical care. MARCH 2011, p.7, 2011 July)

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

New remuneration system for the pharmacists / changes to the wholesalers' mark-up

The new remuneration system for the pharmacists, which is applicable to drugs delivered in the public pharmacies (effective on 01.04.2010), ensures that properly conducted pharmaceutical practices be rewarded by a just and equitable compensation for the services provided.

The review aims at:

- abolishing the former distribution margin, this because of the economic evolution;
- re-assessing the pharmacist's role vis-à-vis the patient, coupled to greater recognition of a qualitative pharmaceutical follow-up on the part of the pharmacists (correct consumption of medicines, abiding by the therapy). The fact is that, effectively, the pharmacist is ever increasingly turning into the patient's guide in advising the latter about his or her optimal consumption of the medicines.

The pharmacist's remuneration is based on three pillars:

- First pillar: an economic margin coupled to the ex factory price covering the expenses incurred by the pharmacist's economic activities. The economic margin is included in the drug's selling price.
  ex factory price ≤ 60,00 euro: 6.04% of the ex factory price
  ex factory price ≤ 60,00 euro: 3.62 euro + 2% of the (ex factory price – 60.00 euro)
- Second pillar: a basic professional fee per delivery that constitutes the compensation for basic work performed, equal to 3.88 EUR (3.94 EUR as of 01.01.2011) per package. This basic professional fee is included in the drug's selling price.
- Third pillar: professional fees for specific pharmaceutical care (assistance with an initial delivery / making up a prescription for a non-brand specific drug / making the delivery of a drug registered in Chapter IV)

The specific professional fees are wholly assumed under the medical treatment insurance and are not a part of the selling price of the drug.
The selling price of a drug to the public consists of the ex factory price, the wholesaler's mark-up, the pharmacist's economic margin, the basic professional fee, and the VAT charge (6%).

Changing the wholesaler's mark-up:

The wholesaler's mark-up likewise changes in order to assure the budgetary neutrality of the review.
ex factory price ≤ 2.33 euro: wholesaler's mark-up = 0.35 euro
2.33 euro ≤ ex factory price ≤ 15.33 euro: wholesaler's mark-up 15% of ex factory price
15.33 < ex factory price: wholesaler's mark-up 2.3 euro + 0.9% of the (ex factory price – 15.33 euro)

This measure is budgetary neutral on the macro-economic plane, both for the pharmacists and for the medical treatment insurance.

Amendment to the Royal Decrees of 21.12.2001 in implementation of the Programme Law of 23.12.2009: cost saving measures (effective on 01.04.2010):

- Completion of definition of Class 3 drugs through addition of a number of references to national/European registration procedures, whereby 'hybrid' generics will also be counted amongst the Class 3 drugs.
- Extension of the reference price system: re-definition of the specialities involved, that is to say, with inclusion of salts, esters, ethers, isomers, mixtures, complexes,… + specific procedure for exemption claims for these specialities (55bis); adaptation of prices of original drugs in function of safety margin: limiting supplement at the expense of the patient up to 25% of the new reimbursement basis by a maximum of 10.80 euro.
- Price reductions for 'old drugs': price reduction after 12 years is to be 15% (instead of 14%), price reduction after 15 years is to be 17% (instead of 16%). Through the application of a new reimbursement basis within the context of the reference price system, a price reduction by 17% for 'old drugs' will be applied at the same time (translates into an accumulated price reduction by 41.9%).

EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES IN THE PUBLIC PHARMACIES

General

Table 6: net annual expenditures NIHDI for drugs 2003 – 2010

	2003	2004	2005	2006	2007	2008	2009	2010
Net expenditures NIHDI x 1,000,000 €	**2.063,3**	**2.213,0**	**2.203,6**	**2.161,1**	**2.297,9**	**2.611,1**	**2.680,8**	**2.711,4**

	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010
growth %	**7,4**	**7,3**	**min 0,4**	**min 1.9**	**6,3**	**13,6**	**2,6**	**1,1**

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

	Denomination	Growth 2008-2009	Growth 2009-2010	Net NIHDI 2010
	Total	2,61	1,14	2.711,4
C10A	LIPID MODIFYING AGENTS, PLAIN	10,6	5,8	249,0
L04A	IMMUNOSUPPRESSANTS	20,0	13,6	203,3
N06A	ANTIDEPRESSANTS	minus 7,5	minus 7,9	134,7
A02B	DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	minus 5,1	minus 13,3	116,7
N05A	ANTIPSYCHOTICS	9,7	9,3	113,2
R03A	ADRENERGICS, INHALANTS	3,7	3,7	111,1
B01A	ANTITHROMBOTIC AGENTS	9,9	minus 14,4	101,1
J05A	DIRECT ACTING ANTIVIRALS	13,1	13,2	79,1
A10A	INSULINS AND ANALOGUES	4,4	3,6	73,3
N03A	ANTIEPILEPTICS	12,9	11,6	69,4
C07A	BETA BLOCKING AGENTS	minus 0,4	2,7	64,4
L03A	IMMUNOSTIMULANTS	minus 0,7	minus 2,4	63,1
N02A	OPIOIDS	2,7	minus 1,6	60,4
A10B	BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	4,7	11,7	60,1
C09D	ANGIOTENSIN II ANTAGONISTS, COMBINATIONS	9,9	4,3	55,0
C09C	ANGIOTENSIN II ANTAGONISTS, PLAIN	minus 2,6	minus 8,5	54,0
M01A	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	minus 4,1	10,5	52,4
B02B	VITAMIN K AND OTHER HEMOSTATICS	4,2	7,1	51,0
J01C	BETA-LACTAM ANTIBACTERIALS, PENICILLINS	0,0	minus 2,0	50,5
R03B	OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS	4,0	minus 2,4	50,0
C09A	ACE INHIBITORS, PLAIN	minus 14,2	minus 11,3	47,7
J07B	VIRAL VACCINES	minus 24,0	minus 5,9	43,3
C08C	SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	1,2	minus 11,9	43,2
M05B	DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	minus 11,6	minus 8,1	41,4
L02B	HORMONE ANTAGONISTS AND RELATED AGENTS	minus 2,6	minus 3,3	39,4
N06D	ANTI-DEMENTIA DRUGS	8,3	5,6	35,7

C01D	VASODILATORS USED IN CARDIAC DISEASES	minus 5,3	minus 8,0	32,5
N04B	DOPAMINERGIC AGENTS	4,6	8,1	31,5
L01X	OTHER ANTINEOPLASTIC AGENTS	4,4	2,7	28,3
S01E	ANTIGLAUCOMA PREPARATIONS AND MIOTICS	6,0	8,3	27,0

The overview of the expenditures and the *established* growth per ATC3-class (*Table 7*) indicates that **30 of the 178 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: globally, the expenditures for the reimbursement of drugs in public pharmacies have become stabilized, underlying this (per class of drugs), we nonetheless note significant and very divergent evolutions.

A striking observation is the global, albeit small yet negative, increase in the number of patients treated (*Figure 3* and *Table 8*). Where relevant, the evolution per class will be discussed further in this report. In the evaluation of these data, one invariably has to take account of the 'accession' of the self-employed into the general system in 2008.

Figure 3: evolution of the net expenditures in public pharmacies versus the number of treated patients

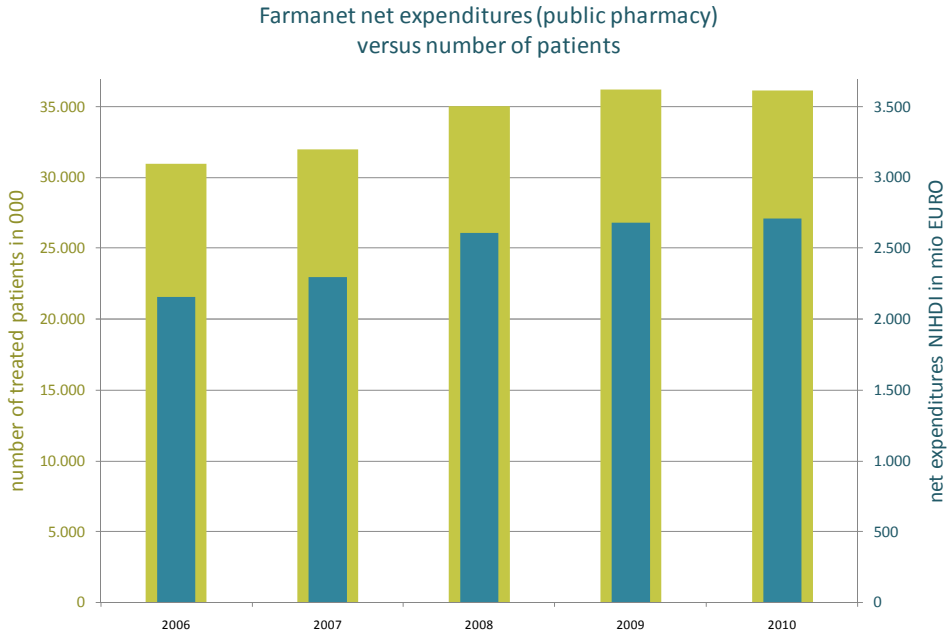


Table 8: evolution of the number of treated patients in public pharmacies (in 000)

	Denomination	Growth 2008-2009	Growth 2009-2010	Total 2010 (x 1.000)
	Total	3,3	minus 0,1	36.133,6
C10A	LIPID MODIFYING AGENTS, PLAIN	7,2	4,8	1.448,4
L04A	IMMUNOSUPPRESSANTS	7,5	6,6	74,7
N06A	ANTIDEPRESSANTS	0,8	1,4	1.151,8
A02B	DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	6,6	5,6	1.691,9
N05A	ANTIPSYCHOTICS	minus 0,3	0,4	369,9

R03A	ADRENERGICS, INHALANTS	7	3,2	984,6
B01A	ANTITHROMBOTIC AGENTS	32,9	7,7	1.231,0
J05A	DIRECT ACTING ANTIVIRALS	3,3	4,2	20,9
A10A	INSULINS AND ANALOGUES	2,6	2,9	136,7
N03A	ANTIEPILEPTICS	9,6	10,6	207,8
C07A	BETA BLOCKING AGENTS	1,8	1,6	1.249,5
L03A	IMMUNOSTIMULANTS	0,2	minus 0,6	8,1
N02A	OPIOIDS	5,4	7,8	838,4
A10B	BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	5,3	5,2	489,5
C09D	ANGIOTENSIN II ANTAGONISTS, COMBINATIONS	9,8	9,3	232,8
C09C	ANGIOTENSIN II ANTAGONISTS, PLAIN	minus 1,5	3,2	271,5
M01 A	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	1,9	0,3	3.101,3
B02B	VITAMIN K AND OTHER HEMOSTATICS	2,8	minus 1,8	0,3
J01C	BETA-LACTAM ANTIBACTERIALS, PENICILLINS	2,6	minus 1,8	2.942,7
R03B	OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS	1,4	minus 4,1	668,1
C09A	ACE INHIBITORS, PLAIN	2,6	minus 0,9	620,1
J07B	VIRAL VACCINES	4	minus 10,9	1.782,2
C08C	SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	1,9	minus 1,6	517,9
M05 B	DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	3,1	minus 0,9	195,9
L02B	HORMONE ANTAGONISTS AND RELATED AGENTS	1,6	0,7	55,4
N06D	ANTI-DEMENTIA DRUGS	9,2	7,1	46,8
C01D	VASODILATORS USED IN CARDIAC DISEASES	minus 3,8	minus 2,8	184,8
N04B	DOPAMINERGIC AGENTS	3,9	4,5	63,2
L01X	OTHER ANTINEOPLASTIC AGENTS	1,5	2,2	7,3
S01E	ANTIGLAUCOMA PREPARATIONS AND MIOTICS	2,2	2,2	196,9

Analysis

DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE

Figure 4: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class A02B Drugs for Peptic Ulcer and Gastro-Oesophageal Reflux disease

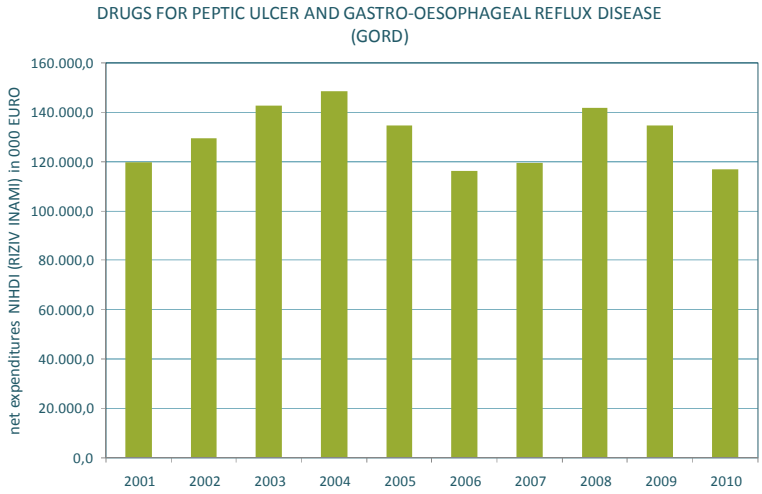
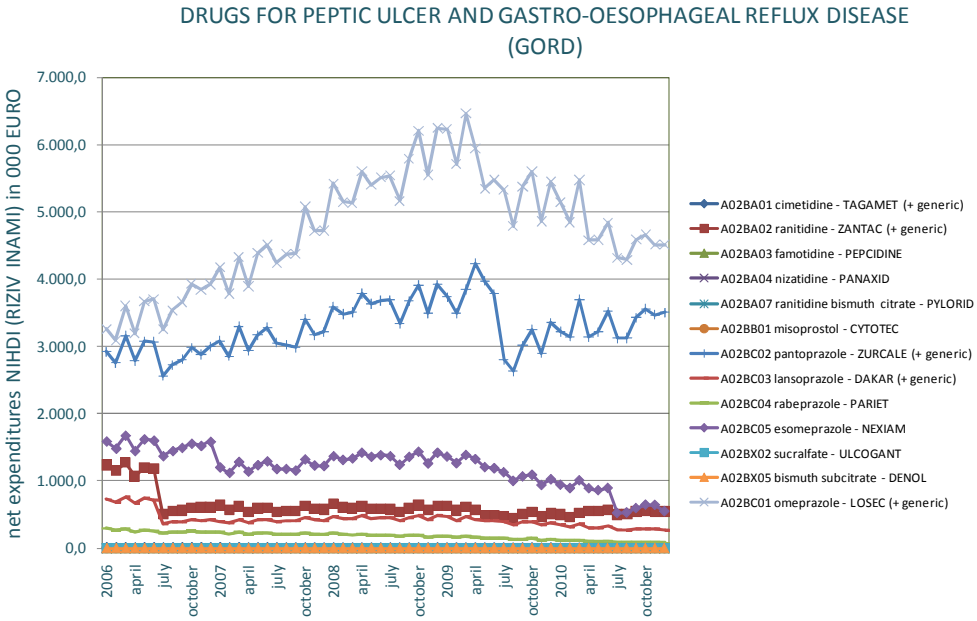


Figure 5: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class A02B Drugs Peptic Ulcer and Gastro-Oesophageal Reflux disease



The observed expenditures for the class A02B (Proton Pump Inhibitors - PPIs) continue the decline of 2009, thereby again reaching the lowest level of expenditures registered in 2006.

The strong drop in expenditures during 2010 (-13%) within this class is primarily caused by the drop in expenditures for omeprazole and esomeprazole (Nexiam®).
The decline in the number of patients treated with omeprazole in 2010 (-9.5%) largely explains the drop in expenditures for omeprazole.

In contrast, in the case of esomeprazole, the number of patients treated with the drug has strongly risen for 2010 (by 27%). In July 2010, Nexiam® was transferred from Chapter IV to Chapter II with an *a posteriori* control, coupled to a price decrease of circa -50% on all packages. This transfer accounts for the increase in the number of patients treated with Nexiam®, which remains without effect on the evolution of the expenditures caused by the major implemented price reduction.
On application of this transfer, the Drug Reimbursement Commission (CTG) estimated the expenditures for Nexiam® in 2010 to decline by circa 50%, down to 8.8 million euro. This estimation was confirmed by the Farmanet data, which show the expenditures for Nexiam® in 2010 to be 9.1 million euro.
Given that the number of reimbursable indications for NEXIAM via Chapter II is increasing significantly (fewer examinations, broader reflux treatment, treatment of NSAID-related ulcers and NSAID-co-prescription with risk), the CTG estimates that the expenditures in 2011 will reach the original level (17.5 million euro – status quo versus previous figure) and increase in 2012 by 1.4 million euro.

Table 9: Evolution of the number of patients with PPI treatment in 2006 – 2010

	Number of patients 2006	Number of patients 2007	Number of patients 2008	Number of patients 2009	Number of patients 2010
A02BC01 - OMEPRAZOL	500.148	612.449	786.918	788.154	713.060
A02BC02 - PANTOPRAZOL	176.992	177.759	195.280	428.755	616.663
A02BC03 - LANSOPRAZOL	45.862	54.477	59.606	49.773	39.175
A02BC04 - RABEPRAZOL	52.977	42.634	35.693	23.595	15.182
A02BC05 - ESOMEPRAZOL	90.605	94.949	102.993	87.157	110.400
TOTAL number of patients (*)	**781.539**	**893.462**	**1.079.033**	**1.220.188**	**1.355.041**

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

From 2006 until 2010, the number of patients treated with a PPI increased by 75% (from 2009 to 2010 by 11%), while the expenditures once again dropped down to the lowest level in 2010, as it had happened in 2006. From this it may be deduced that the measures undertaken did, indeed, have the desired effect. However, this effect of stabilized or declining expenditures will, unfortunately enough, be only temporary without the implementation of new measures for as long as the 'reservoir' of new patients for this group of proton pump-inhibitors is not exhausted.
It is notable that the number of patients treated with H2-antagonists remains on the decline.

The actual effect of the entry into force of the reference cluster for specialities based on pantoprazole in July 2009, with simultaneous application to this molecule of the price reduction measure for the drugs that have been reimbursable for over 12 years, is not reflected in a drop of expenditures for these specialities in 2010, seeing that these are stabilizing vis-à-vis 2009. This can be explained by the renewed significant rise in the number of patients treated with pantoprazole (+44% in 2010). Already in 2009, there happened a notable rise in start-up treatments with pantoprazole (mounting from 9% in January 2009 to 45% in December 2009). Pantoprazole has from January 2010 also been considered to be an inexpensive molecule within the PPIs, to be used in the start-up of new treatments, a measure that has been entered as one of the concrete prescription aims in the National Accord between Physicians and Health Insurance Funds 2009-2010.

In August 2010, the new guidelines for PPIs, as well as for statins, were adapted in order to promote correct prescriptions of these molecules within this class. In the process, the reimbursement Class C for these molecules was changed to Class B, and it was concluded that there are no therapeutic differences

between proton pump inhibitors amongst themselves. Moreover, a warning has been posted against the incorrect use of PPI (functional dyspepsia without typical reflux or without stomach ulcer-type pain and use amongst NSAID-treated patients without risk of ulceration). The effect of these changes on the expenditures for PPIs remains currently unclear.

Table 10 allows us to deduce from the volume in reality applied per patient that the omeprazoles are used in the largest volume per patient, namely 218 DDD per patient in 2010. Every patient treated with omeprazole receives this treatment on the average during 7 to 6 months, at a dosage of 1 DDD per diem. For esomeprazole (Nexiam®), the number of applied dosages per patient in 2010 has declined, this in spite of its eligibility for the more generous reimbursement criteria through transfer to Chapter II in July 2010.

Table 10: 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
2010	218,6	146,5	217,8	69,0	131,3

Figure 6: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class A10A Insulins and Analogues

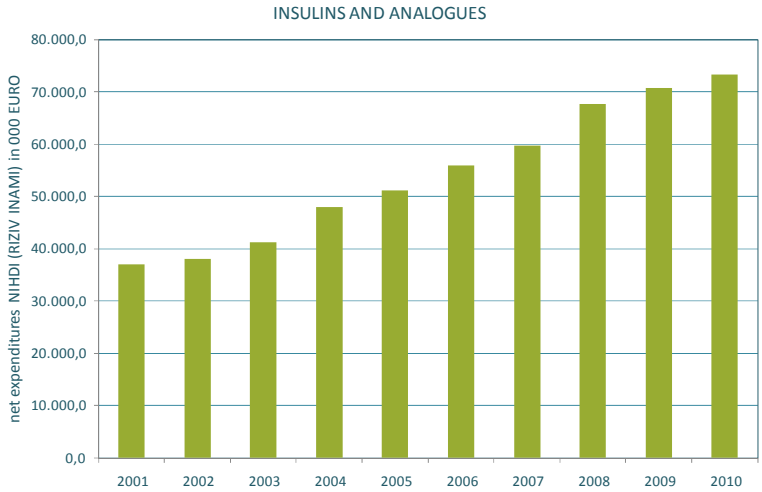
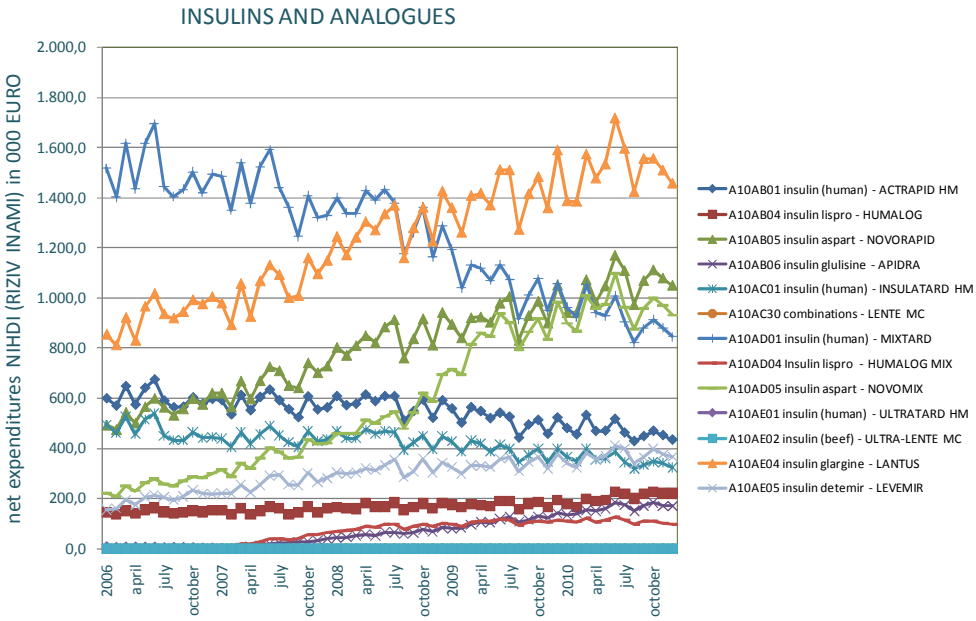


Figure 7: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class A10A Insulins and Analogues



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, although here also this increase appears to be stabilizing.

The same holds true for the evolution of the expenditures for Novomix®, registering a sharp rise in 2009, in consequence of the addition to the assortment of Novomix® 50 and Novomix® 70.

Figure 8 and *Figure 9* display a clear growth in expenditures for long-acting insulin-analogues (Lantus® and Levemir®). The increase in the expenditures for (oral) biguanides (*Figure 12*) may partially be explained by their use in combination with, for instance, Lantus ®[5].

Figure 8: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class A10AB fast-acting Insulins

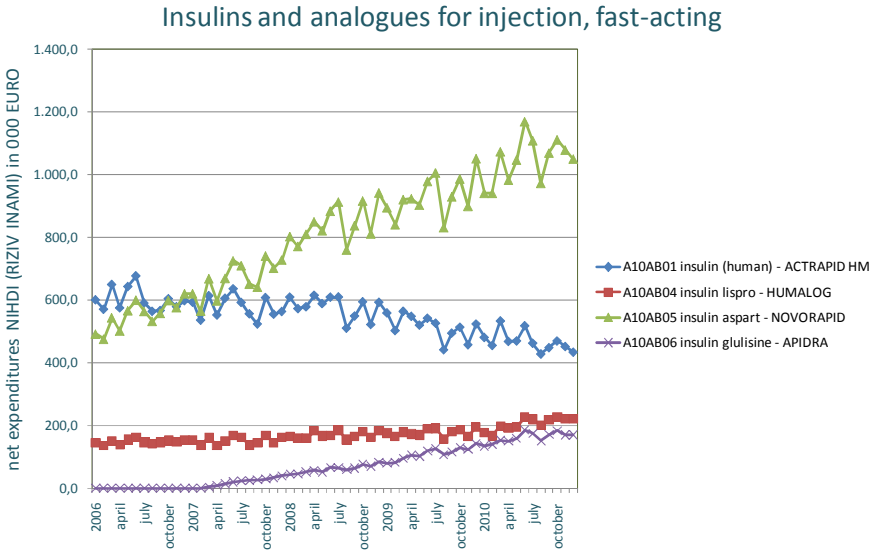
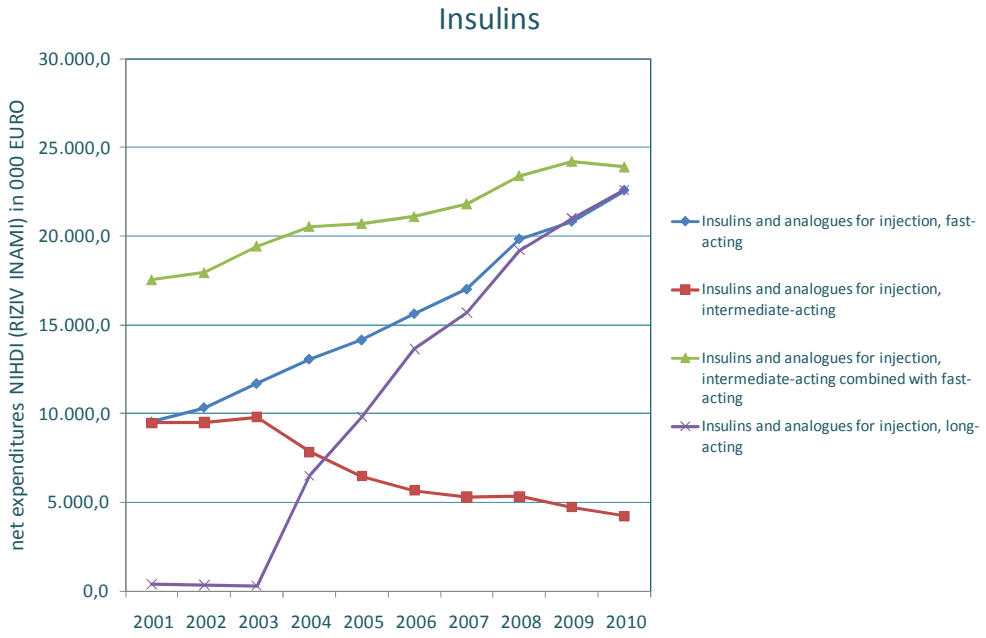


Figure 9: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class A10A Insulins and Analogues – per type



[5] The reimbursement conditions for, e.g., Lantus, provide for reimbursement as follows" … In the case of type 2 diabetes, the specialty may also be used in combination with oral antidiabetic agents in the following instances…"

BLOOD GLUCOSE LOWERING DRUGS, (excl. insulins)

Figure 10: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class A10B Blood Glucose Lowering drugs, with the exclusion of insulins

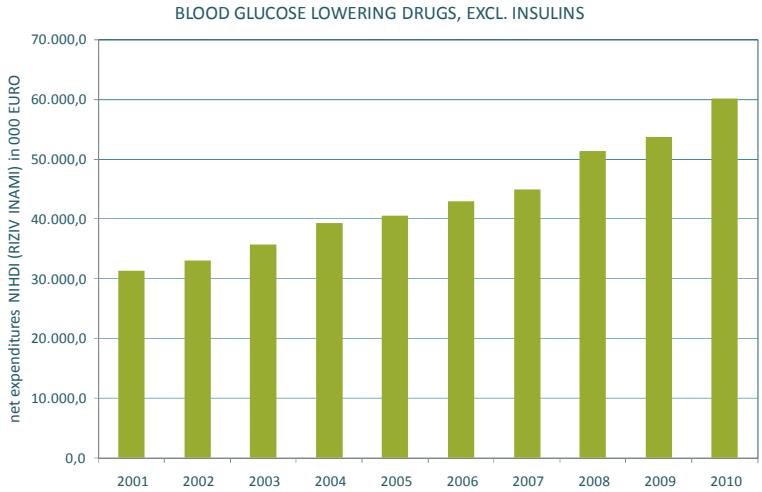
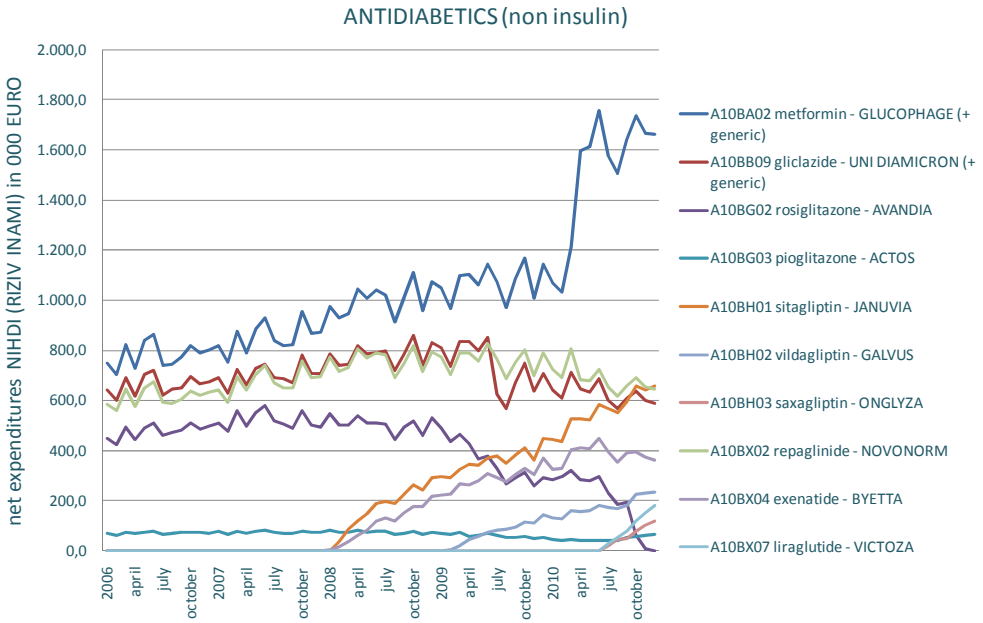


*Figure 11: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class A10B Blood Glucose Lowering drugs, with exclusion of Insulins (** restricted to the molecules in question)*

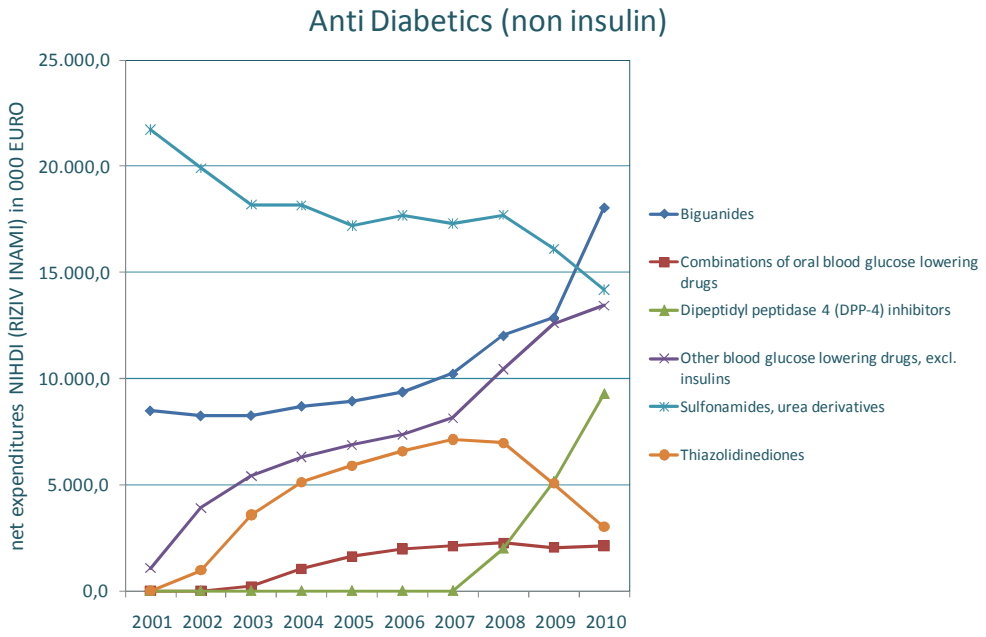


The expenditures for this class of oral antidiabetics keep growing steadily.
In contrast, the expenditures of metformin have, as it were, exploded as of March 2010 (+53% between the last quarter in 2009 and the last quarter in 2010).
Metformin is a first-choice preparation when drug treatment is necessary to deal with type 2-diabetes, certainly in the case of obese patients.

Both the price and the use of metformin are on the incline: the cost per DDD, which has been stable since 2006 at 0.17 €, has between 2009 and 2010 risen to 0.22 € (this price increase is caused by the new remuneration system for pharmacists); the number of DDD is steadily growing annually (9 % per annum in 2009 and 2010).

The increasing use of metformin during the last few years is, aside from the growing number of more and more diabetes type 2- patients, primarily due to the onset of new, more recent line treatments that are only reimbursable after inadequate treatment with metformin.

Figure 12: Evolution of the expenditures for oral antidiabetics in public pharmacies - per class



Aside from the remarkable rise in the use of metformin, both in mono- and in poly-therapy, for what concerns the mono-therapies it is the gliptins (DPP-4-inhibitors) (Januvia®, Galvus® and Onglyza®) that are causing the sharpest increase in expenditures (+ 80 % between 2009 and 2010), plus their combination use with metformin (Eucreas® and Janumet®), that register the strongest growth in the bi-therapies (+ 468% between 2009 and 2010). Furthermore, there is also a growing use of new antidiabetics (Byetta® and Victoza®).

Table 11: Price per DDD for oral antidiabetics

	Cost/DDD 2009	Cost/DDD 2010	DDD 2009	DDD 2010
A10BB09 Gliclazide (sulfamide)	0,33	0,25	26.773.342	30.384.802
A10BX02 Repaglinide (glinide)	0,69	0,64	13.231.388	12.784.667
A10BH01 Sitagliptine (glipitine)	1,51	1,51	2.860.581	4.503.079
A10BA02 Metformine	0,17	0,22	77.078.087	83.708.787
A10BX04 Exenatide (Byetta®)	3,01	2,98	1.143.937	1.547.962

When considered per individual speciality, it is noted that the expenditures for Januvia® (A10BH01 - sitagliptin) have currently reached the expenditure level of Novonorm® (A10BX02- repaglinide) and of Unidiamicron® (A10BB09 – Gliclazide); this together with a DDD-number that is considerably lower and a price per DDD of 1.51 euro.
These increasing expenditures for Januvia® may be partially explained by a switch that has occurred from rosiglitazone (Avandia® and Avandament®) to Januvia®.

The specialities based on rosiglitazone (Avandia®, in combination with metformin Avandamet®) have been taken off the market because of a negative benefit-to-risk ratio. On 24/09/10, the European Medicines Agency (EMA) ordered the suspension of the specialities based on rosiglitazone, an antidiabetic from the glitazone group. Following analysis of the data concerning the effectiveness and safety of rosliglitazone, with specific attention to cardiovascular risks, EMA has drawn the conclusion that the benefit-to-risk ratio was no longer positive. Hence, since recently, these products are no longer available in Europe.

Figure 13: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class B01A Antithrombotic agents

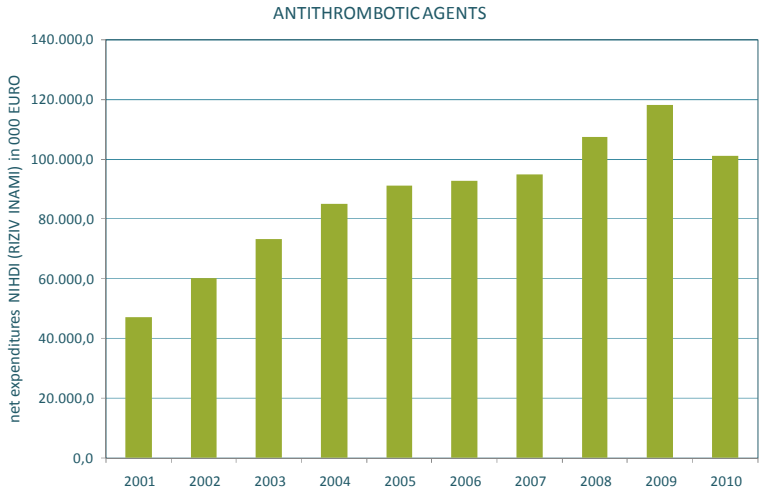
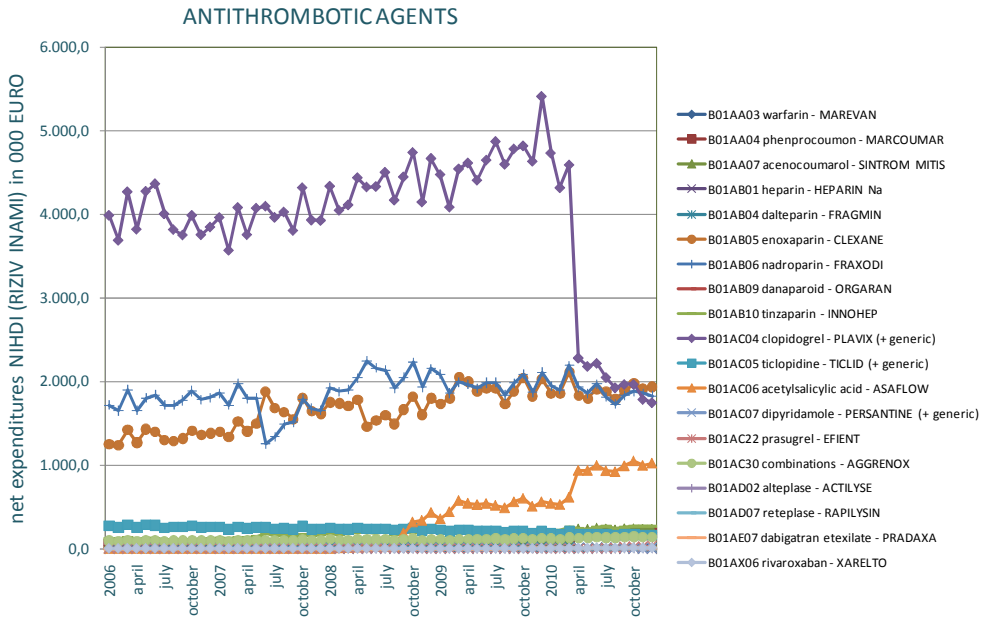


Figure 14: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class B01A Antithrombotic agents



The expenditures for Plavix® and the generics (B01AC04) have declined by half as of April 2010, the date of entry into force of the reference price system for this molecule. At the same time, the expenditures for acetylsalicylic acid (B01AC06) have risen by 50 %.

From the evolution of the number of patients treated with these molecules (*Table 12*), it may be deduced that these enormous changes in expenditures can only to a minor degree be explained by changes in the number of the patients treated; rather, they originate as a result of the entry into force of the reference price system and the change of the price per DDD.

Table 12: Evolution of the number of patients treated with clopidogrel and ASA from 2006 until 2010

	2006	2007	2008	2009	2010
CLOPIDOGREL – B01AC04	113.008	117.878	127.338	130.062 + 2%	123.203 - 5 %
ACETYLSALICYLZUUR – B01AC06	0	0	315.716	650.872 + 106 %	744.621 + 14 %

At the present time, the monthly expenditures for acetylsalicylic acid (B01AC06) amount to circa 40% of the monthly expenditures for clopidogrel, versus 10 % before the reference price system. With a DDD number that lies a lot lower, the price per DDD of specialities based on clopidogrel remains a lot higher than the price of specialities based on acetylsalicylic acid. The price increase per DDD for the drugs based on acetylsalicylic acid is wholly attributable to the changed system of pharmacists' remunerations (where the impact was most severely felt for very inexpensive drugs).

Table 13: Price per DDD for the antithrombotics

	DDD 2009	DDD 2010	Cost/DDD in 2009	Cost/DDD in 2010
B01AC04	36.944.320	36.379.831	1,51	0,88
B01AC06	223.049.368	257.600.386	0,03	0,04

In general, the expenditures for this class have dropped by 14% between 2009 and 2010. The price should drop even further in 2011, when the reference price system will have been in effect for the full year.

Figure 15: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class C09A ACE inhibitors

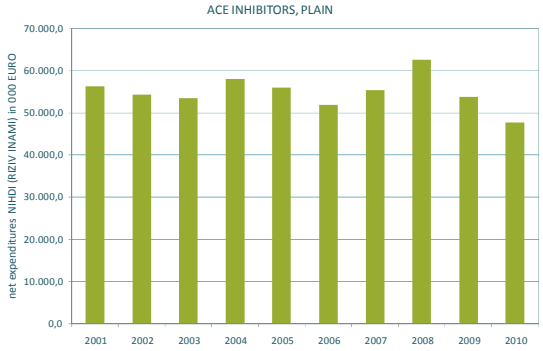


Figure 16: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class C09A ACE inhibitors and combination preparation

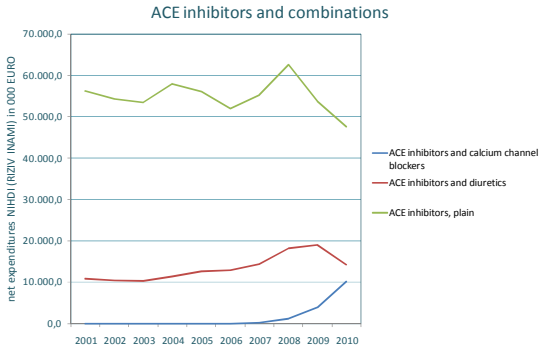
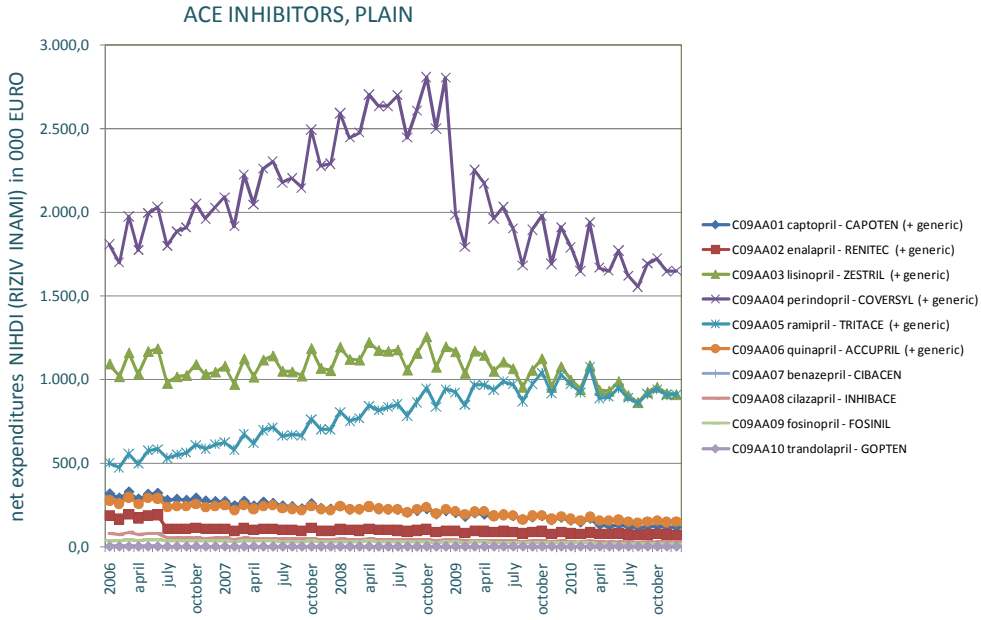


Figure 17: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class C09A ACE inhibitors



The drop of expenditures for ACE inhibitors continued into 2010. The expenditures for ramipril, which in 2009 had become the second most important molecule and which caused their upward evolution, have stabilized.

Notable, however, is the fast rise of expenditures for ACE inhibitors in combination preparations with calcium channel blockers (*Figure 16*). The evolution of these expenditures will be followed up further in a subsequent report.

Figure 18: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class C09C Antagonists, plain

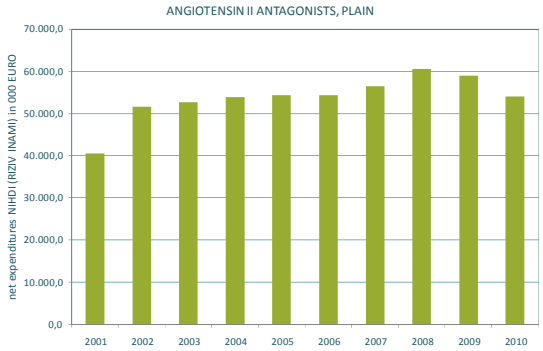


Figure 19: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class C09D Antagonists – combination preparations

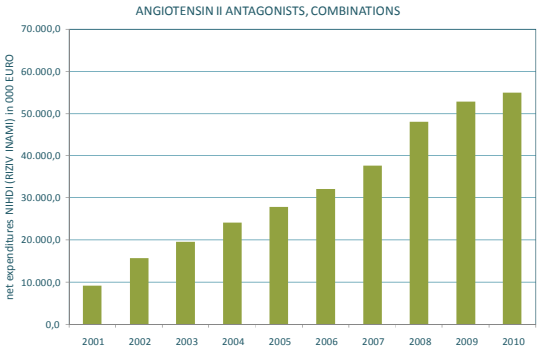
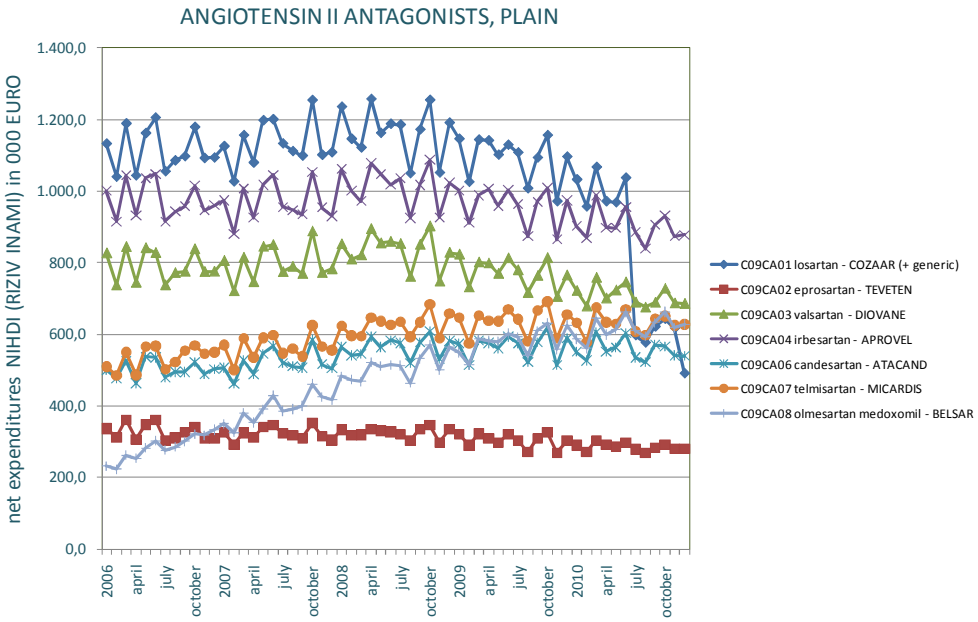


Figure 20: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class C09C Antagonists, plain



Within the Sartan class in monopreparations, the reference reimbursement for the molecule losartan entered into force in July 2010 (for the molecule valsartan, this will happen in the course of 2011). The realized savings for these reference clusters needs certainly to be monitored, seeing that they go hand in hand with the registration of the generics based on losartan and valsartan in Chapter I, in contrast to the reference specialities Loortan®, Cozaar® and Diovane®, which are being reimbursed in Chapter IV with an *a priori* control.

Figure 21: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC classes C09C and C09D Sartan combination preparations

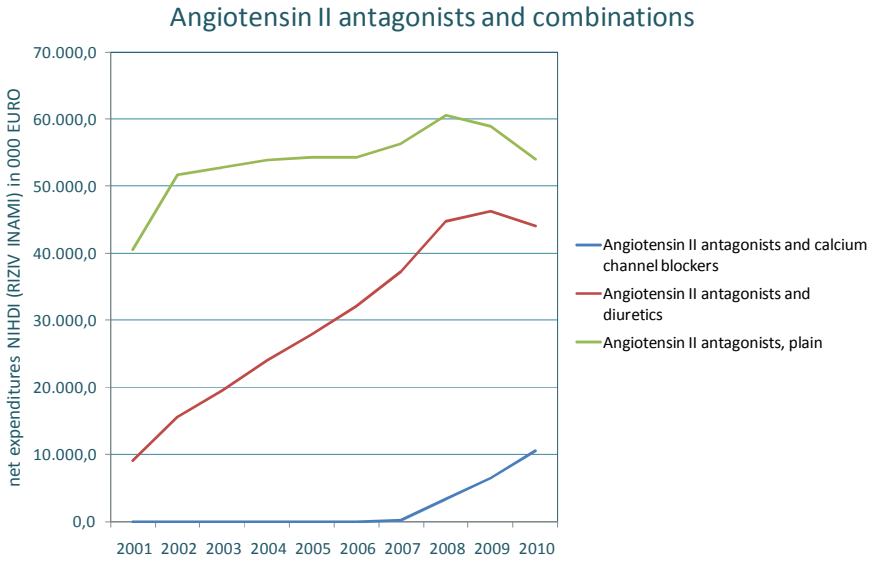
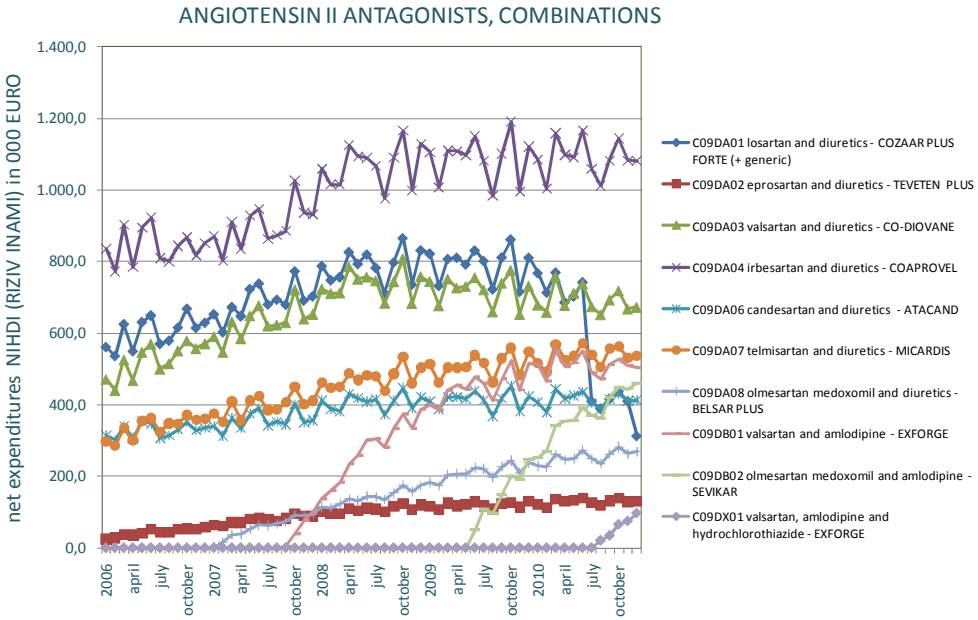


Figure 22: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC classes C09D Antagonists – combination preparations



Versus the decline in expenditures in 2009 for antagonists in monopreparations, we note a rise of 4.3% (10% in 2010) in the expenditures of the antagonists in combination preparations. The same 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 use of the combinations with a thiazide diuretic which seems to be stabilizing. It would be interesting to study in a subsequent report the concomitant usage of these fixed combinations with other antihypertension drugs.

EVOLUTION OF THE NUMBER OF PATIENTS TREATED WITH ACE INHIBITORS AND SARTANS

Although, for the time being, most patients are being treated with the monopreparations for ACE inhibitors and Angiotensin II antagonists (Sartans), it should be obvious that the use of combination preparations is gaining in importance (*Figure 23*).

Figure 23: evolution of the number of patients treated with ACE inhibitors and Sartans (and combination preparations)

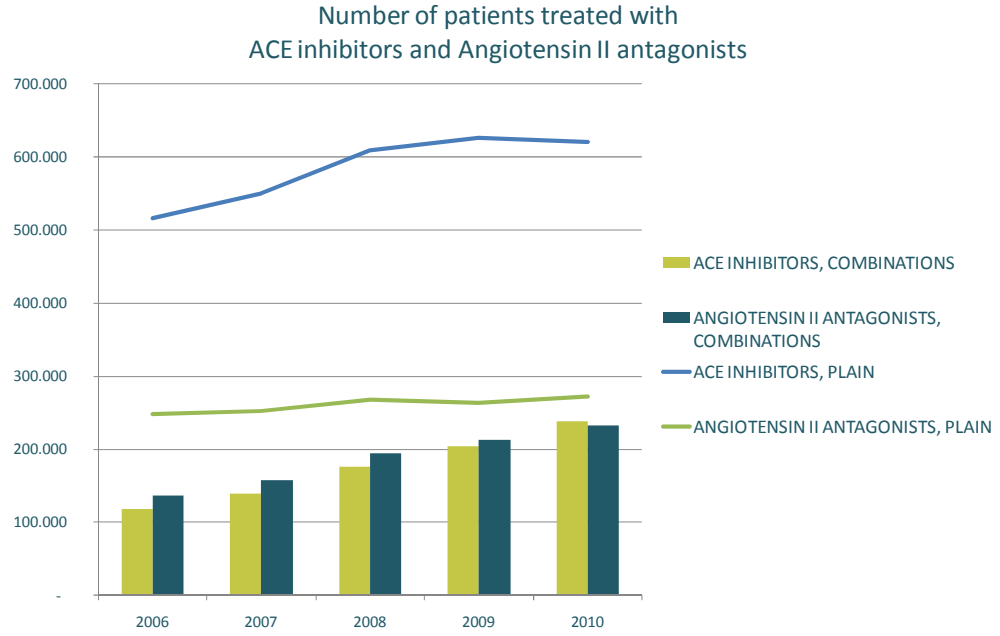


Figure 24: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class C10A Lipid modifying agents, plain

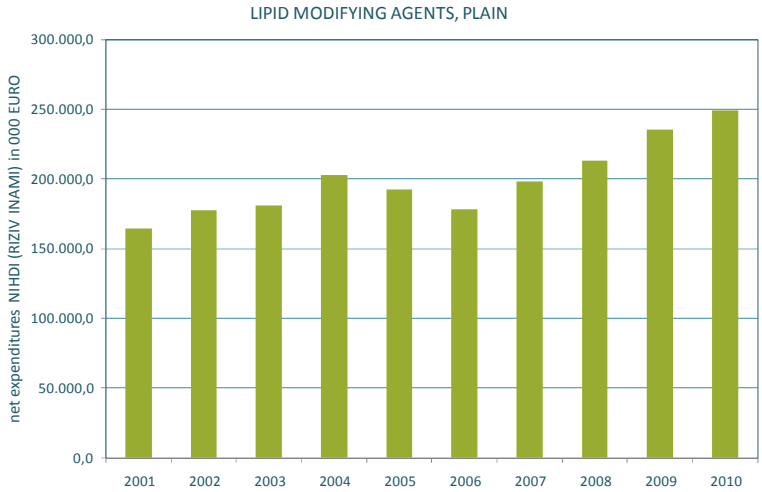
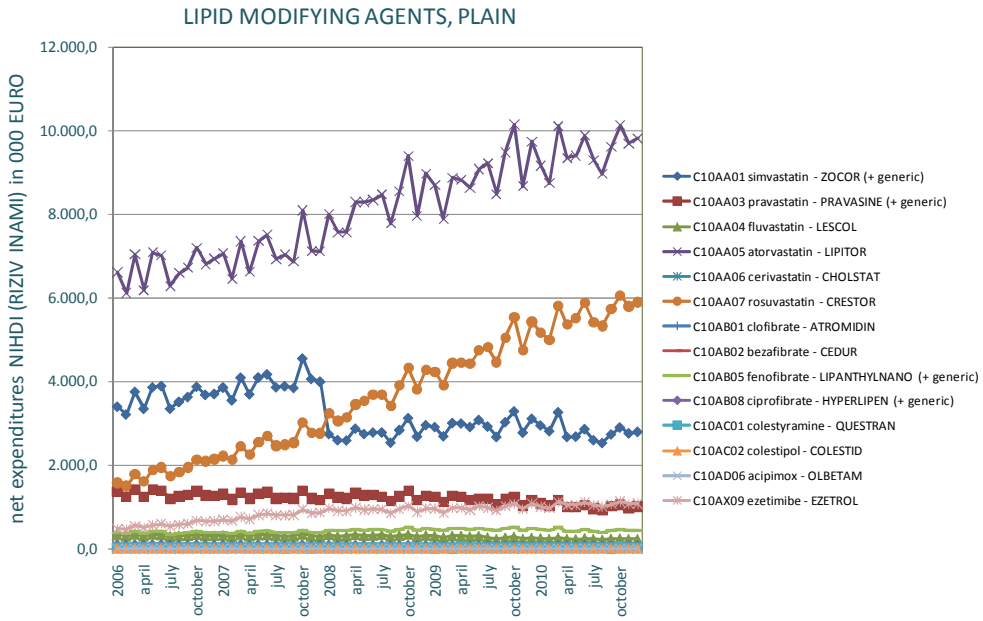


Figure 25: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class B01A Lipid modifying agents, plain



In 2010, the general expenditures for the lipid modifying agents continue to rise, displaying over a period of four years a steady increase from circa 180 million euro to 250 million euro. The trend in 2008 and 2009, when the expenditures for rosuvastatin (Crestor) and atorvastatin (Lipitor) show a further increase, continues.
The stagnation of the expenditures for the most inexpensive statin molecules (simvastatin and pravastatin) has been going on since 2008 and continues.

The measure entered into the National Accord between Physicians and Health Insurance Funds 2009-2010, taken within the context of a feasible savings of 42.5 million euro, appears, just like in 2009, to remain also in 2010 without effect on the prescription habits for statins.

In August 2010, the recommendations concerning the statins by the **Drug Reimbursement Commission** were changed in order to promote the prescription of the least expensive molecules within this class. It is still too early to be able to judge the effect of this measure. Furthermore, the observation that it pertains only to new patients amongst whom the treatment with a statin is started remains valid, which actually means that only a very small number of the total population is being treated with statins.

Table 14: Number of patients undergoing start-up treatment with statins in 2010 (C10AA)

	C10AA01		**C10AA03**		**C10AA04**		**C10AA05**		**C10AA07**		**TOTAL**
	simvastatin	**%**	**pravastatin**	**%**	**fluvastatin**	**%**	**atorvastatin**	**%**	**rosuvastatin**	**%**	
jan	11.835	58	1.466	7	99	0	3.083	15	3.882	19	20.365
feb	11.971	59	1.316	6	91	0	2.985	15	3.901	19	20.264
mar	13.599	59	1.483	6	91	0	3.485	15	4.499	19	23.157
apr	11.195	58	1.225	6	85	0	2.890	15	3.878	20	19.273
may	10.557	58	1.173	6	74	0	2.805	15	3.607	20	18.216
jun	11.134	59	1.271	7	73	0	2.886	15	3.598	19	18.962
jul	8.020	58	962	7	52	0	2.214	16	2.551	18	13.799
aug	8.314	59	921	7	53	0	2.094	15	2.618	19	14.000
sep	9.871	63	1.227	8	66	0	2.016	13	2.485	16	15.665
oct	11.513	67	1.371	8	52	0	1.985	11	2.365	14	17.286
nov	10.935	67	1.250	8	52	0	1.792	11	2.289	14	16.318
dec	10.529	66	1.177	7	53	0	1.911	12	2.348	15	16.018
	129.473	61	14.842	7	841	0	30.146	14	38.021	18	213.323

From the above Table it follows that, in the course of 2010, prescriptions by doctors for patients starting a treatment with statins have evolved towards a greater share for simvastatin, with a percentage for 2010 of 61%.
In comparison with 2009, we do not in 2010 notice changes in the percentages of the volume of new patients receiving treatment with the various statins.

For the total number of patients treated with a statin (n =1.337.316), the percentage of patients treated with a simvastatin has declined from 51% in 2009 to 49% in 2010.

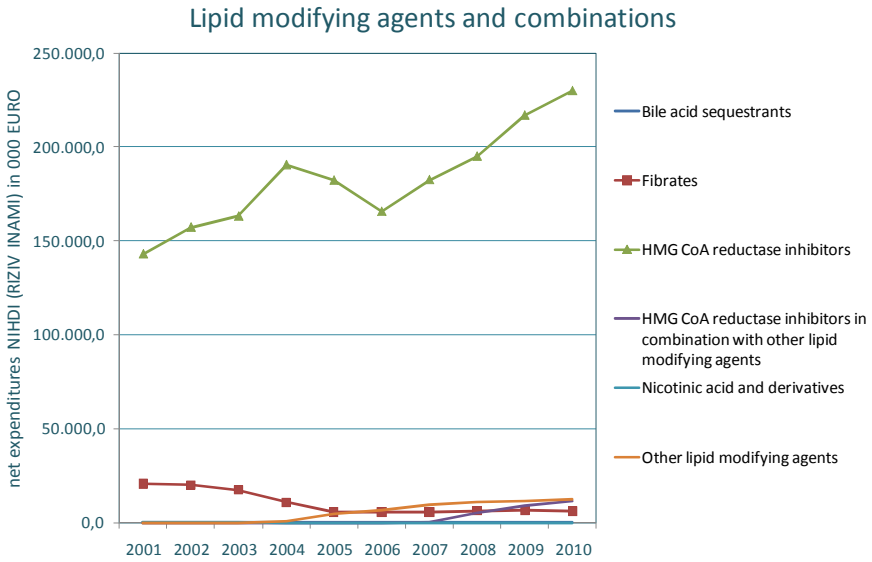
Table 15: Distribution of the treatments with a statin (C10AA - Inhibitors of the HMG-CoA reductase) with new patients and all treated patients in 2010.

		% volume new patients	% volume treated patients
C10AA01	SIMVASTATINE	**61%**	**49%**
C10AA03	PRAVASTATINE	7%	9%
C10AA04	FLUVASTATINE	0.4%	1%
C10AA05	ATORVASTATINE	**14%**	**22%**
C10AA07	ROSUVASTATINE	18%	20%

It further needs to be noted that lipid modifying agents can be combined in therapeutic use, namely by the addition of ezetimibe to a statin for patients with hypercholesterolemia, whereby a more pronounced

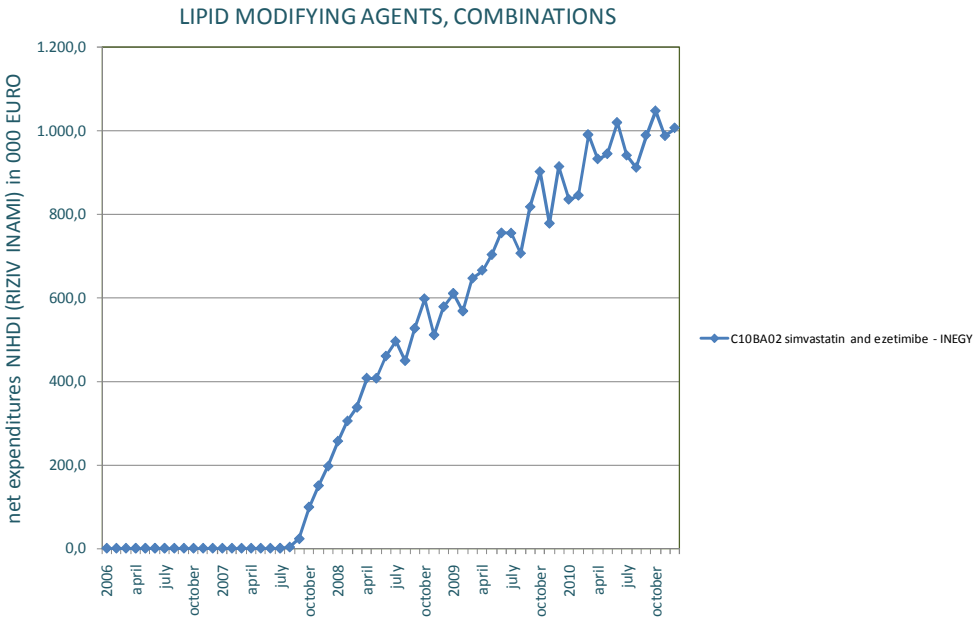
lowering of cholesterol or LDL-cholesterol is aimed at than what can be realized with a statin alone. It has not, however, been demonstrated that the addition of ezetimibe to a statin constitutes a better cardiovascular prevention in terms of morbidity and mortality.

Figure 26: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class C10A and C10B Lipid lowering agents and combination preparations



Since August 2007, the combination preparation Inegy® has been reimbursable (ezetimibe and simvastatin) with ATC C10B, the expenditures for which increased in 2010 to 11.5 million euro and ought to be added to the expenditures for the lipid modifying agents (C10A) in order to arrive at the actual total expense figure.

Figure 27: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class C01B Lipid modifying agents, combinations



In 2010, circa 1.47 million patients were treated with lipid modifying agents. Approximately 1.34 million of these patients were given a monopreparation statin.

Figure 28 illustrates the evolution of the number of patients treated (*cave* the different scales). Striking is the continuing, albeit declining, rise in the number of patients treated with monostatins (+ 10% in 2007, + 15% in 2008 (effect of the self-employed), + 7.6% in 2009 and + 5.1 % in 2010).
The new combination preparations at this time still account for only a small share, both in their usage and expense, but further follow-up of this future evolution is needed.

Figure 28: evolution of the number of patients (public pharmacies) treated with statins (and combination preparations)

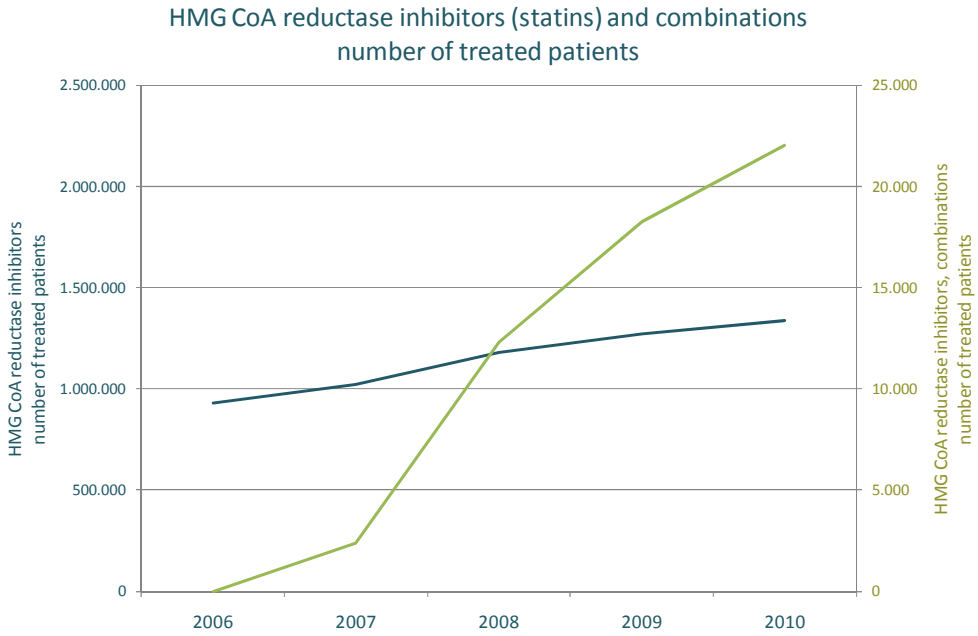


Figure 29: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class J05A Direct Acting Antiviral Agents

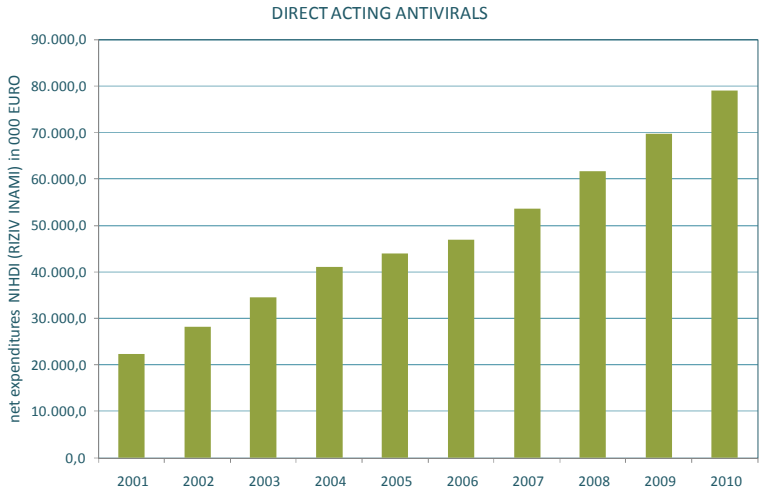
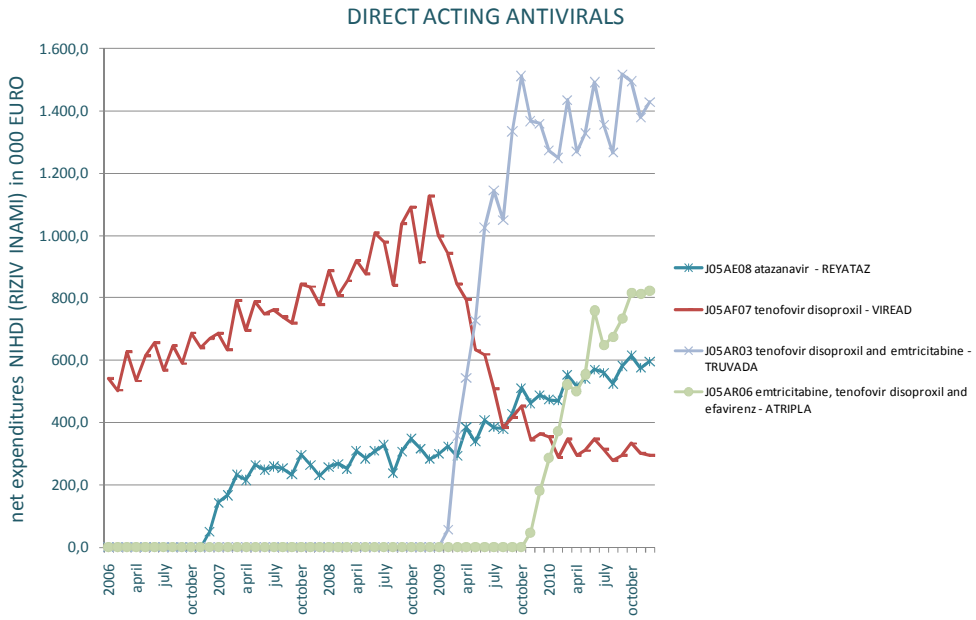


Figure 30: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class J05A Direct Acting Antiviral Agents



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.

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®. A sharp increase in expenditures for the fixed combinations is recorded.

Figure 31 clearly demonstrates that the constant and rapid rise in the (total) expenditures for this group of drugs is not, or is not only, to be explained by the growing (total) number of treated patients. Every year, the expenditures have been rising by more than 13% (2008 excluded), while the number of patients each year rose by less than 5%.

Figure 31: evolution of the expenditures versus the number of treated patients for direct-acting antiviral agents in public pharmacies

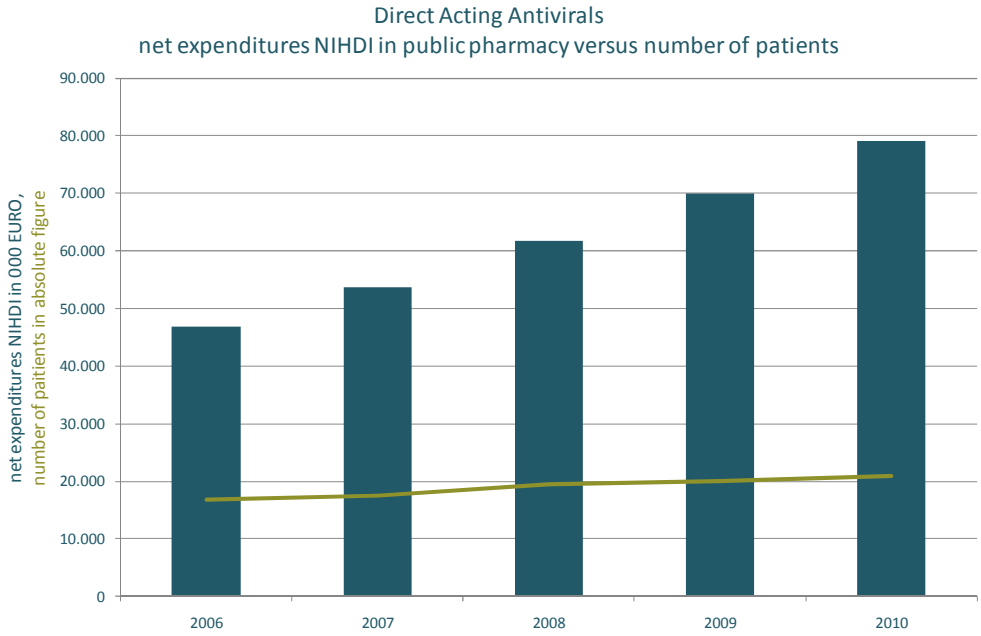


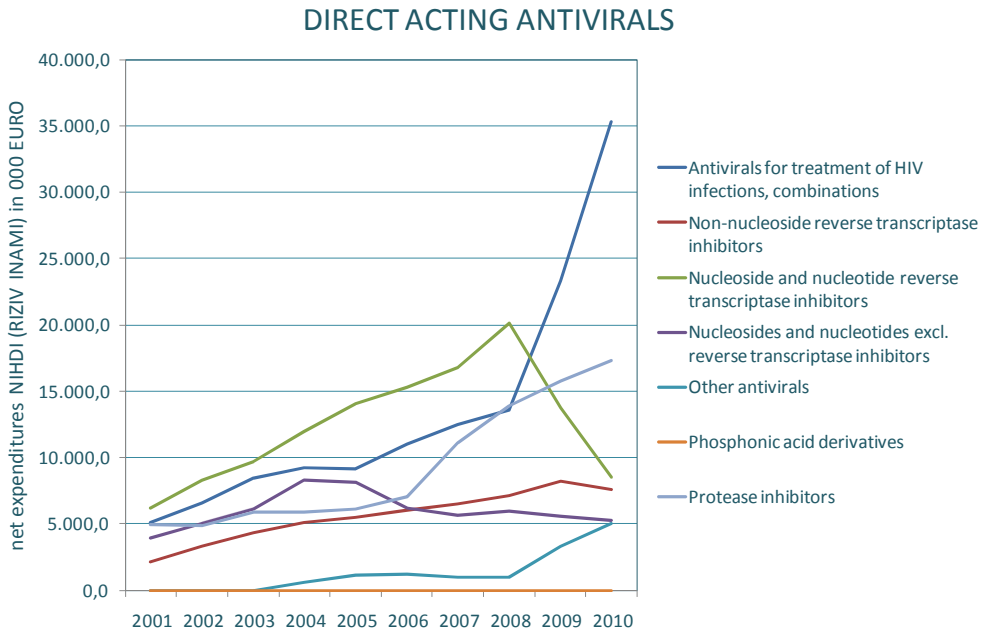
Figure 27 and *Figure 31*, however, do show that the evolution of the expenditures – in casu, their rapid increase – is primarily being determined by the evolution of the expenditures for protease inhibitors and, especially, antiviral combination preparations used in HIV treatments.

The evolution (increase) of the price per DDD, specifically for these two subclasses (J05AE and J05AR) of direct-acting antiviral agents (Table) can, however, partly explain the evolution of the expenditures.

Table 16: evolution of the average price per DDD for the direct-acting antiviral agents (2006-2009) in public pharmacies (in EURO)

		2006	2007	2008	2009	2010
J05AB	Nucleosides and nucleotides excl. reverse transcriptase inhibitors	17,1	16,4	16,5	15,4	14,1
J05AD	Phosphonic acid derivatives			50,9		
J05AE	Protease inhibitors	15,5	17,2	17,1	17,4	18,1
J05AF	Nucleoside and nucleotide reverse transcriptase inhibitors	9,0	8,9	9,0	8,8	8,4
J05AG	Non-nucleoside reverse transcriptase inhibitors	9,3	9,3	9,3	10,3	10,4
J05AR	Antivirals for treatment of HIV infections, combinations	16,7	16,7	16,7	19,6	19,6
J05AX	Other	31,8	31,7	37,3	37,3	37,2

Figure 32: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class J05A Direct Acting Antiviral Agents per class



IMMUNOSUPPRESSANTS

Figure 33: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class L04A Immunosuppressants

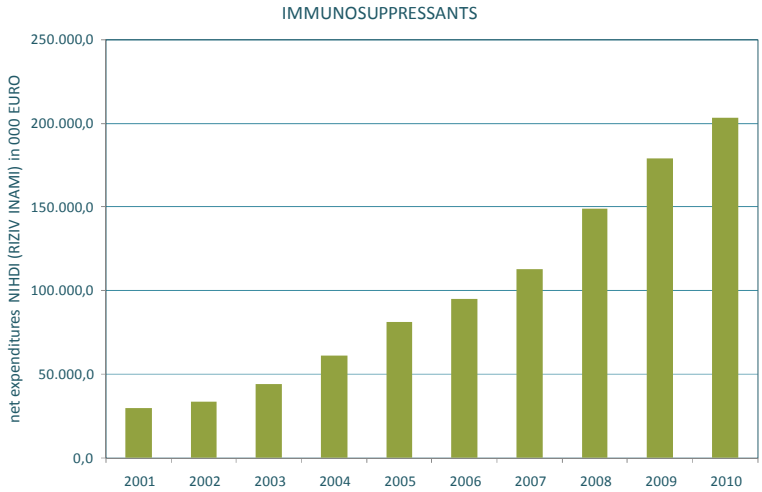
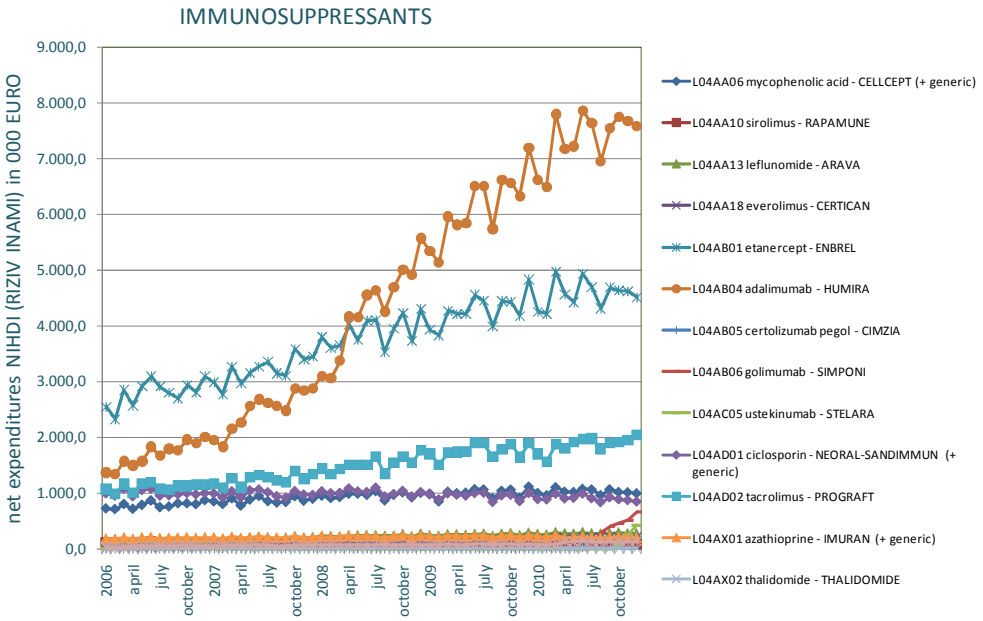


Figure 34: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class L04A Immunosuppressants



The ATC-3 class with the most notable rise in expenditures during last years in public pharmacies unquestionably remains for 2010 the class of the Immunosuppressants (L04A).
De expenditures in public pharmacies show an increase of 13.6% for 2010 and, as second class, thus reach in public pharmacies, beside the lipid modifying agents, an annual expenditure figure of more than 200 million euro.

The TNF-inhibitors Humira® and Enbrel® (L04AB) remain responsible for the most significant increases of the expenditures in public pharmacies. In 2010, we note the number of patients treated with these

molecules to be increasing further by, respectively, 18% and 10%. Between 2007 and 2010, the number of patients treated with these molecules (L04AB) has more than doubled (+ 116%).

Table 17: Evolution of the net expenditures for Humira and Enbrel in 2005-2010.

	2006	2007	2008	2009	2010
Enbrel L04AB01	33.538.207	38.442.386	46.743.844	51.313.037	55.163.644
Humira L04AB04	20.249.119	29.680.197	51.495.493	73.543.021	88.902.027
growth Enbrel	22,0%	14,6%	21,6%	9,8%	7,5%
growth Humira	42,8%	46,6%	73,5%	42,8%	20,9%

Table 18: Evolution of the number of treated patients per year with Humira and Enbrel

	2006	2007	2008	2009	2010
HUMIRA L04AB04	1.945	2.875	5.372	7.206	8.500
growth patients		47,8%	86,9%	34,1%	18,0%
ENBREL L04AB01	3.479	3.980	4.721	5.117	5.638
growth patients		14,4%	18,6%	8,4%	10,2%
Totaal L04AB	**5.424**	**6.855**	**10.093**	**12.323**	**14.138**[(1)]

[(1)]: In addition to this number, already 743 patients were in 2010 treated with the newly reimbursable specialities Cimzia® (174 patients) and Simponi® (569 patients).

Furthermore, within this class of immunosuppressants it is notable that, in the course of 2010, in the public pharmacies three new molecules became reimbursable, these being Cimzia® (certolizumab) in June 2010 and Simponi® (Golimumab) in July 2010 for the treatment of rheumatoid arthritis, and Stelara® (Ustekinumab) in October 2010 for the treatment of moderate to severe plaque psoriasis.

Within the class of the immunosuppressants (L04A), the TNF-inhibitors (L04AB), with expenditures in 2010 equal to 147 million euro, account for 73% of the total expenditures within this class.

Table 19: Reimbursable indications (and paragraph) and date of entry into force of the various TNF-inhibitors (L04AB) that are reimbursable in public pharmacies

	Rheumatoid arthritis	Polyarticular juvenile arthritis	Psoriatrica arthritis	Ankylosing spondylitis	Plaque psoriasis	Crohn Disease
Humira Adalimumab	§ 3070000 01/05/2004 (**)	-	§ 3620000 01/03/2006	§ 4070000 01/03/2007	§ 4870000 01/10/2008	§ 4550000 01/03/2008
Enbrel Etanercept	§ 2490000 01/02/2003 (**)	§ 2210000 01/07/2002	§ 2870000 01/02/2004	§ 3150000 01/09/2004	§ 3510000 01/02/2006	-
Simponi Golimumab	§ 5650100 01/07/2010	-	§ 5650200 01/07/2010	§ 5650300 01/07/2010	-	-
Cimzia Certolizumab	§ 5600000 01/06/2010	-	-	-	-	-
Stelara Ustekinumab	-	-	-	-	§ 5730000 01/10/2010	-

(**) On 1 May 2010: transfer from HAQ score to DAS 28 score as threshold or change of the DAS 28 score.

As appears from *Table 19*, not all anti-TNF drugs are reimbursable within the same indications and every molecule is in the course of the years given reimbursability for a variety of indications. The change of the reimbursement modalities for Humira and Enbrel in May 2010 (**), whereby the criteria for reimbursement were made more flexible, can partly explain the further rise in the number of patients and expenditures.

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 23.6%. In the second semester of 2009, two new molecules were made reimbursable within the hospital environment, namely Orencia® (Abatacept) in June 2009, and Roactemra® (Tocilizumab) in October 2009 for rheumatoid arthritis.

The available data and the most recent changes in the reimbursement modalities of the various anti-TNF drugs (amongst others for what concerns their reimbursable indications) do not at this time allow us to draw a relevant evaluation of the dissemination of their usage in the various indications over the different specialities (dermatology, rheumatology, gastroenterology,..). In a subsequent report, this issue will be discussed more thoroughly – where feasible, through a comparison of the available data with data taken from the registration system with rheumatologists (SAFE) and from epidemiological data.

ANTIEPILEPTICS

Figure 35: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class N03A Antiepileptics

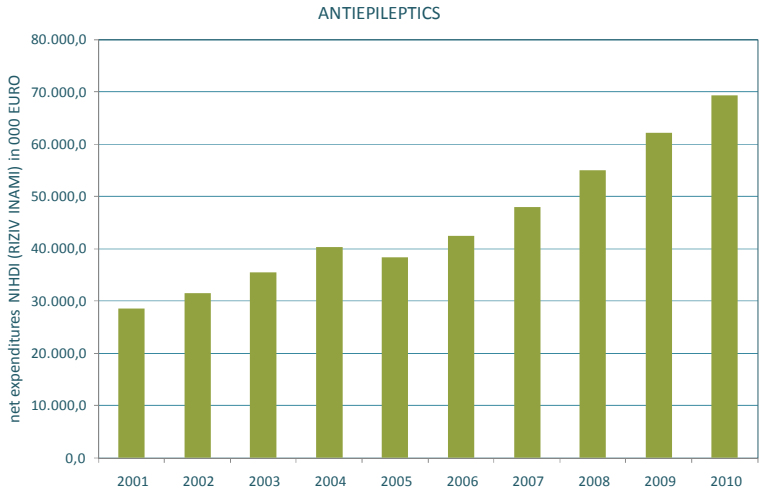
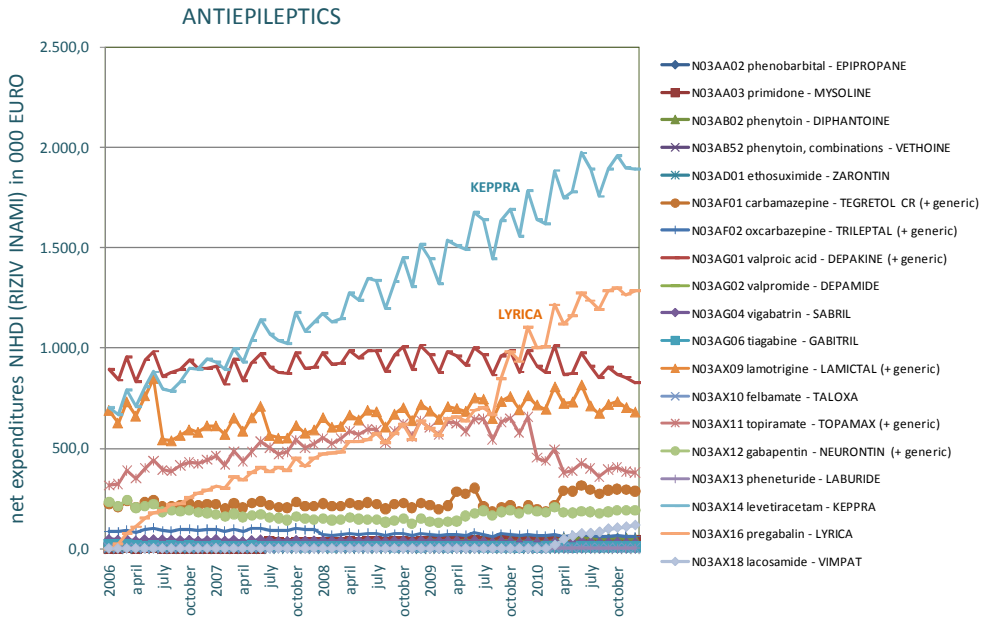


Figure 36: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class N03A Antiepileptics



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 presumably wholly due to the expansion of the reimbursement modalities with the indication 'neuropathic pains', and appears to be stabilizing in 2010.

The evolution of the number of treated patients confirms the need for continuing the follow-up of the evolution of some specific molecules within this class, where possible in function of the reimbursable indications.

Figure 37: evolution of the number of patients treated with anti-epileptics (2006 - 2009) in public pharmacies

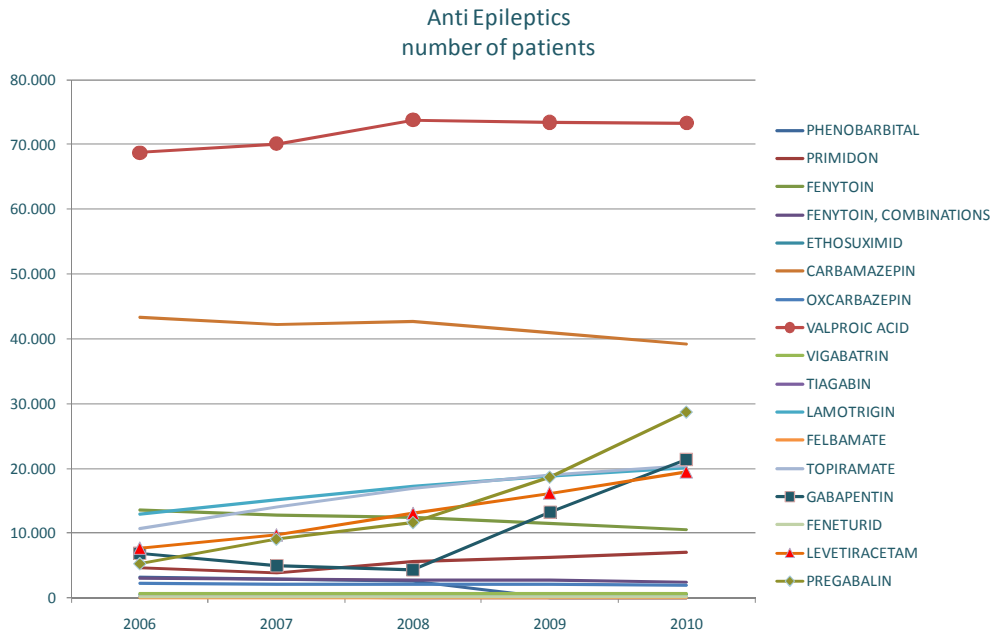


Figure 38: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class N05A Antipsychotics

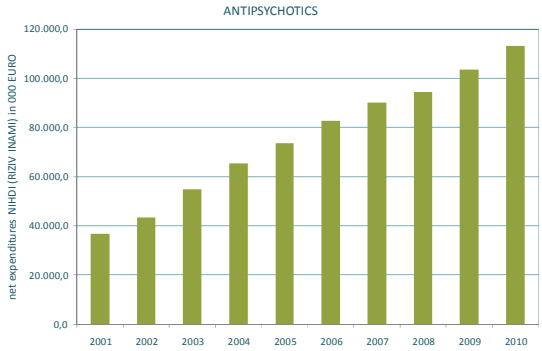


Figure 39: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class N06A Antidepressants

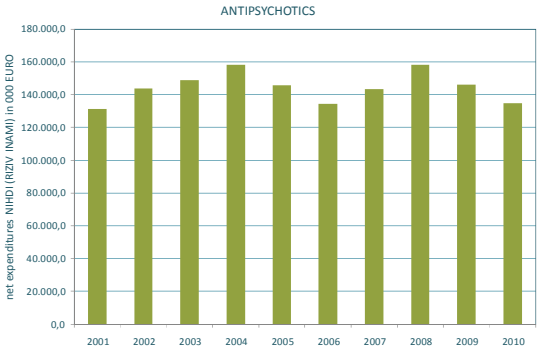
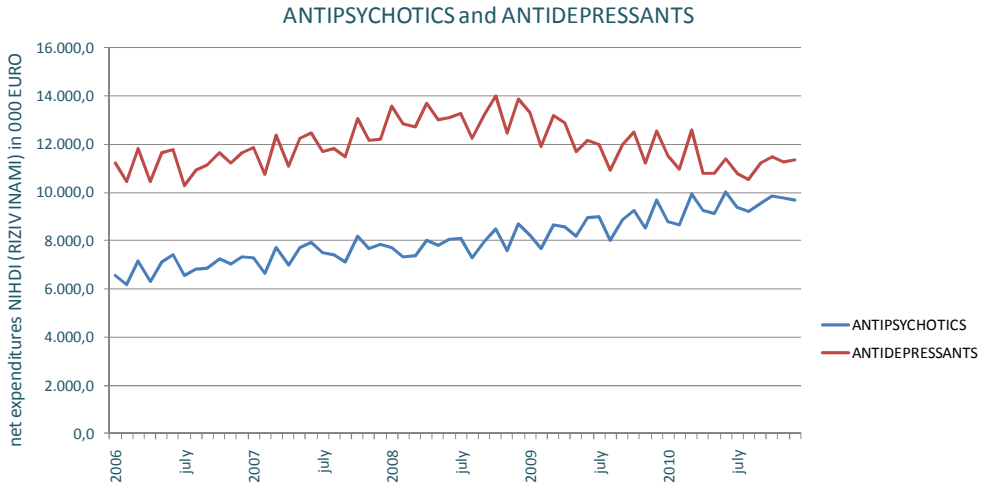
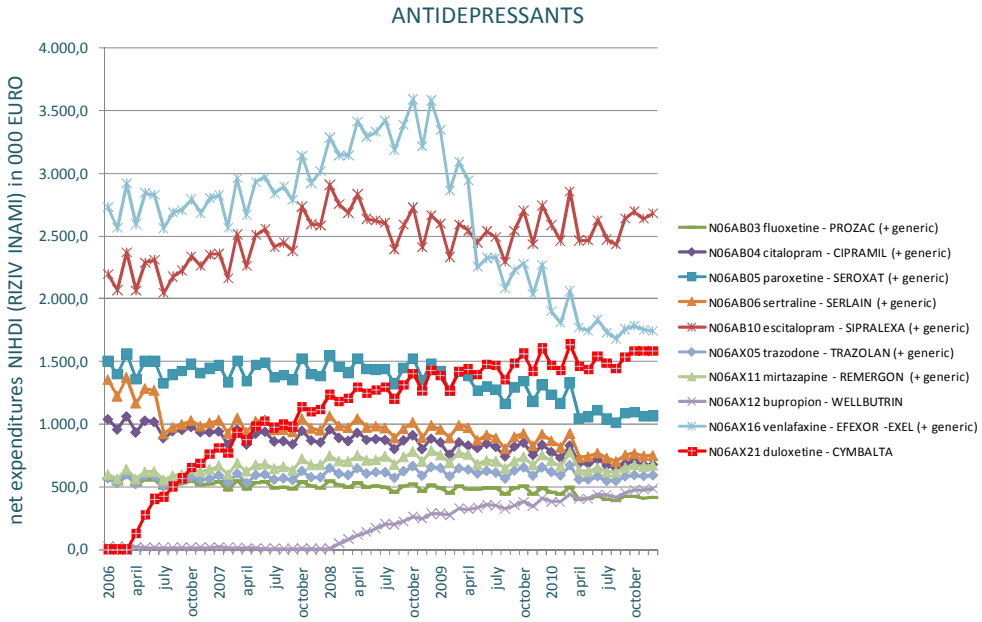


Figure 40: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class N06A Antidepressants and N05A Antipsychotics



ANTIDEPRESSANTS

Figure 41: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class N06A Antidepressants



In spite of the continued growth of the expenditures for Cymbalta® (reimbursable since April 2006), the expenditures for the entire group of antidepressants have been on the decline for the second consecutive year.
Wellbutrin® is the other molecule within this class for which expenditures are rising. The active component of Wellbutrin®, bupropion, is the same as for Zyban®, which has been registered as an aid to stop smoking. It is likely that Wellbutrin® is also being used within this indication: hence, off-label.
The expenditures for venlafaxine have been halved since its registration into the reference price system in 2009. These expenditures are largely exceeded by those of escitalopram (Sipralexa®), which has become the top anti-depressant in terms of expenditures, closely followed by duloxetine (Cymbalta®), which completes the picture for the top three places in expenditures.

Table 20: Price per DDD for antidepressants

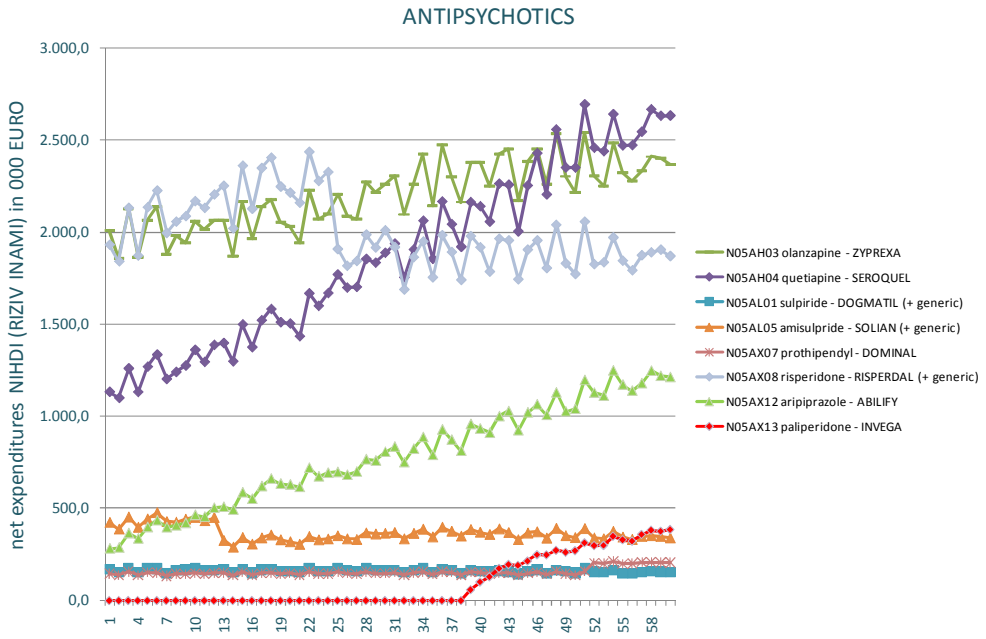
ATC-code		Price per DDD in 2009 (euro)	Price per DDD in 2010 (euro)
N06AB03	FLUOXETINE	0,42	0,37
N06AB04	CITALOPRAM	0,41	0,37
N06AB05	PAROXETINE	0,43	0,37
N06AB06	SERTRALINE	0,33	0,28
N06AB10	ESCITALOPRAM	0,62	0,57
N06AX12	BUPROPION (Wellbutrin®)	1,43	1,34
N06AX16	VENLAFAXINE	0,76	0,51
N06AX21	DULOXETINE	1,24	1,20

The price per DDD (in 2010) varies to a significant degree for this class of drugs. Amongst other reasons, this can be explained by the present availability of reimbursable large packaging and the registration of

the molecule into the reference prize system. Sipralexa® has been given an exemption from the application of the reference price system for citalopram..
The top 3 amongst the antidepressants registering the greatest expenditures in 2010 comprise the most recent and most costly molecules. Only the specialities based on bupropion (Wellbutrin®) represent a price per DDD that lies above the price for Cymbalta® (Duloxetine).

ANTIPSYCHOTICS

Figure 42: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class N05A Antipsychotics



The expenditures for the antipsychotics keep rising on a steady basis and are getting closer to the established expenditures for the antidepressants.
The expenditures for quetiapine (Seroquel®) account in 2010 for the largest figure within this class, followed by olanzapine (Zyprexa®). The expenditures for the molecule risperidone have, as of the entry into force of the reference cluster in January 2008, maintained the status quo. The molecules that, together with quetiapine, account for the strong rise in expenditures within this class are aripiprazole (Abilify®) and paliperidone (Invega®), all of which were formerly labelled “atypical antipsychotics”.

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

Name	2007	2008	2009	2010	% growth 2008-2009	% growth 2009-2010
Quetiapine (N05AH04) Seroquel®	31.630	38.744	46.865	54.764	**20,96** %	**16,85 %**
Olanzapine (N05AH03) Zyprexa®	42.588	43.972	44.000	44.294	0,06 %	0,67 %
Aripiprazol (N05AX12) Abilify®	11.379	14.276	17.240	20.453	**20,76** %	**18,64 %**
Risperidon (N05AX08) Risperdal® + generics	80.024	83.491	80.560	76.105	**- 3,51 %**	**- 5,53 %**
Paliperidone (N05AX13) Invega®	0	0	4.159	6.706	-	**61,24%**

Based on the evolution of the number of patients treated with various antipsychotics, it may be concluded that the number of patients treated with risperidone has been in decline for already two consecutive years, while we register a sharp rise in the number of patients treated with the new molecule paliperidone, which is the prime active metabolite of risperidone (with a largely comparable working mechanism). The benefit-to-risk ratio is likely comparable to that of risperidone.
Likewise for the atypical antipsychotics aripiprazole and quetiapine, the number of treated patients keeps on rising significantly for 2010, and this after an already notable increase in 2009.

The number of patients that in 2010 received a reimbursement for an antipsychotic drug exceeds herewith by far the epidemiological estimations for patients suffering from the most significant indications (schizophrenia and bipolar disorders).

These molecules are ever more frequently being used by seniors (> 65 years) resident in a nursing home and similar institutions.

Table 22: Distribution of the use of antipsychotics (N05A) amongst patients below and above 65 years of age

Age group	Number DDD	Number patients
≥ 65 years old	10.917.133	145.177
≥ 65 years old	30.871.017	224.478
Total	41.788.150	369.655

Thirty-nine percent of patients treated with an antipsychotic (N05A) are 65 years old or older, with this age group constituting 17% of the total population.
When the atypical antipsychotics of the classes N05AH (clozapine, olanzapine, quetiapine and clotiapine) and N05AX (prothipendyl, risperidone, aripripazole and paliperidone) are taken into consideration, we arrive at the same significant break-down of seniors above 65 years of age within the treated patient group: 33% for the N05AH and 40% for the class N05AX (and 26% in DDD).

Table 23: Distribution of the use of antipsychotics (N05A) amongst patients below and above 65 years of age (detail)

	Number patients (%)		Number DDD (%)	
ATC-code	< 65 years old	≥ 65 years old	< 65 years old	≥ 65 years old
N05AH	70.143 (66,6%)	35.120 (33,4%)	12.648.051 (74,2%)	4.391.415 (25,8%)
N05AX	82.311 (60,0%)	54.843 (40,0%)	9.929.975 (73,8%)	3.524.257 (26,2%)

Heightened mortality has been registered for all antipsychotics with chronic usage amongst seniors suffering from dementia, possibly as a result of the increased incidence of cerebral-vascular accidents [see Folia/Index June 2009]

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 24: 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 25*) 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 25: Division of the new treatments and all treatments with an SSRI in 2009

ATC-code	Name of the molecule	% of the volume of 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 43: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class R03A Adrenergics, Inhalants

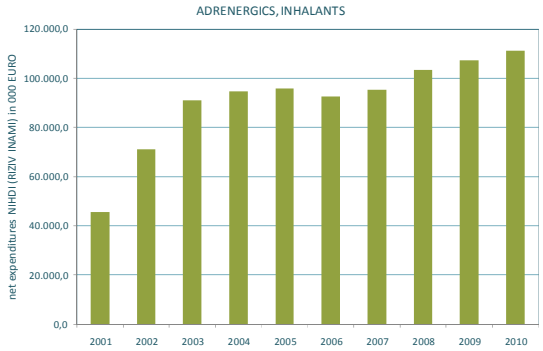


Figure 44: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class R03B Other Inhalants preparations

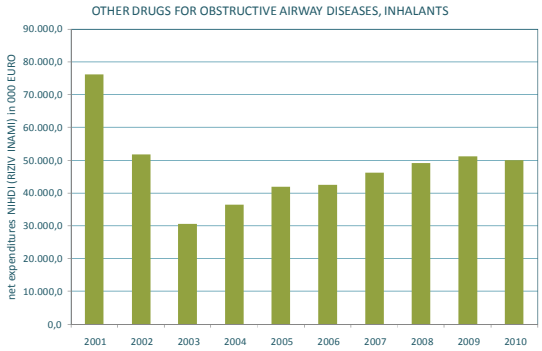


Figure 45: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class R03A Adrenergics, Inhalants

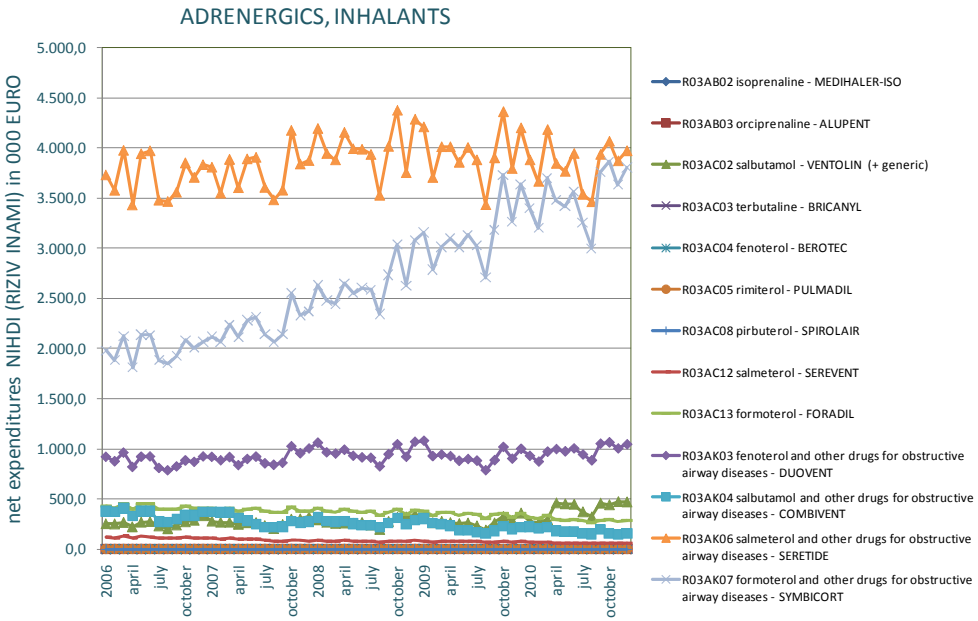
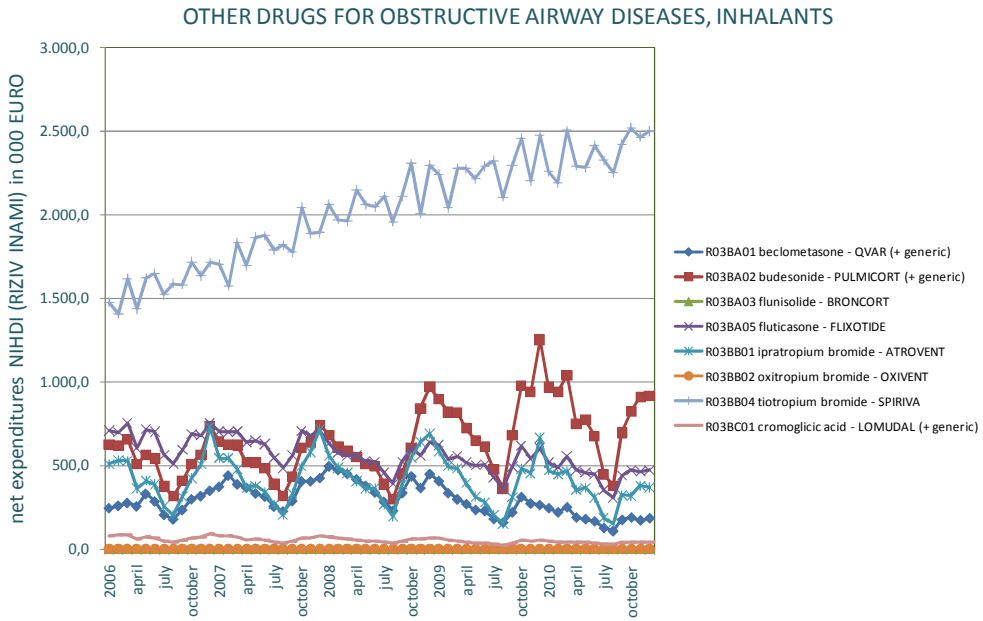


Figure 46: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class R03B other Inhalants Preparations



The observed rise in expenditures within the class R03A drugs (+ 3.7%), which in consequence reach an annual expenditure level exceeding 100 million euro in 2010, is due only to the increasing expenditures for the speciality Symbicort® (formoterol + corticoid), which hereby joins Seretide®(salmeterol + corticoid).

The fixed combination preparations LABA + corticosteroids have been approved for the treatment of asthma. For the treatment of COPD, first a bronchodilator is used and, only if the effect is insufficient, a corticosteroid will be added.
Symbicort® with a fast and long-acting Bèta-2-mimetic can, in contrast to salmeterol (Seretide®), also be used to treat attacks, aside from its use in maintenance treatment, which partially explains its success.

Table 26: number of patients treated with sympaticomimetics (R03A), anticholinergics and inhalation corticosteroids (R03B)

	2006	2007	2008	2009	2010
R03AC LABA	348.929	363.067	381.580	393.041	388.808
R03AK LABA + corticoïd	561.064	578.437	615.943	670.849	705.839
R03BA Glucocorticoïd	367.194	396.666	416.860	436.830	410.571
R03BB anticholinergicum	302.625	324.145	342.652	355.717	362.959

Figure 47: Evolution of the number of patients treated with LABA (R03AC), LABA + corticoids (R03AK), Glucocorticoids (R03BA) and Anticholinergics (R03BB)

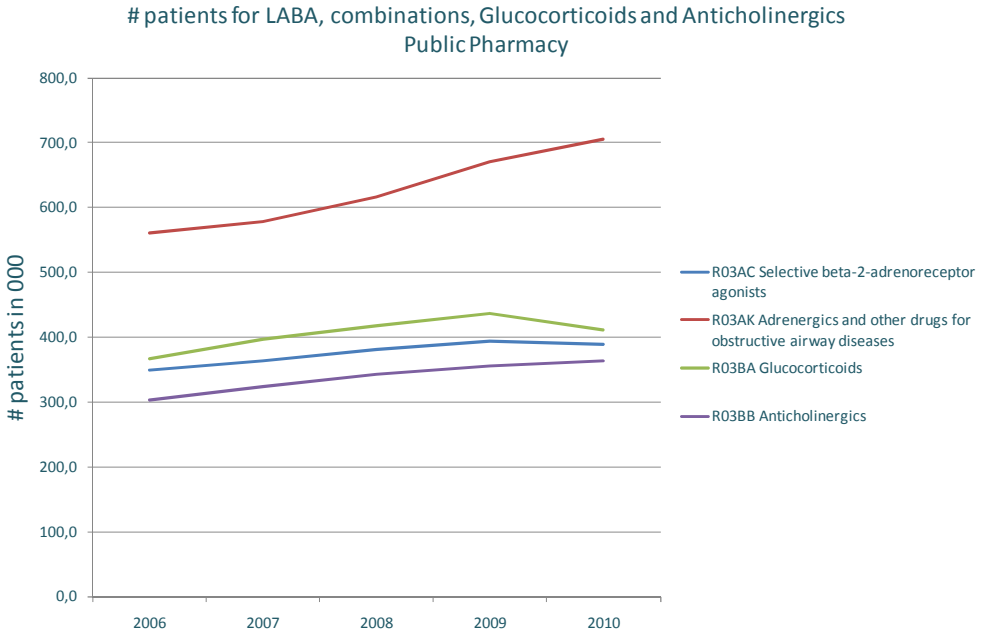


Figure 48: Evolution of the expenditures for LABA (R03AC), LABA + corticoids (R03AK), Glucocorticoids (R03BA) and Anticholinergics (R03BB)

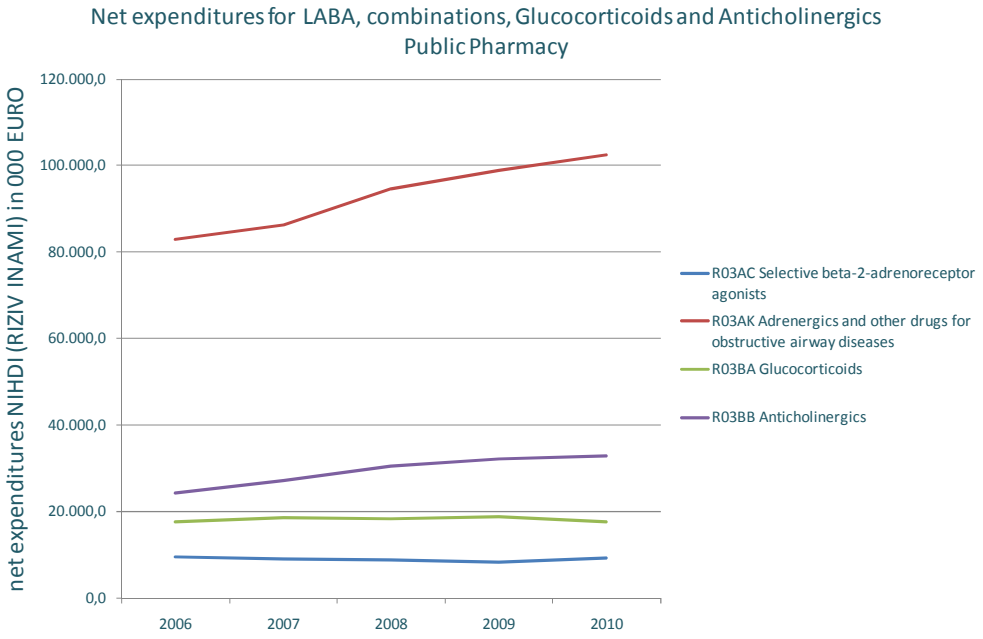


Table 27: Annual expenditures for sympaticomimetics (R03A), anticholinergics and inhalation corticosteroids (R03B)

	2006	2007	2008	2009	2010
R03AC	9.495.497	8.980.195	8.771.195	8.316.748	9.104.864
R03AK	83.021.061	86.241.875	94.556.600	98.825.604	102.459.603
R03BA	17.594.397	18.443.954	18.156.783	18.661.222	17.588.845
R03BB	24.111.337	26.987.909	30.399.565	32.016.903	32.833.278

The fixed combination preparations of LABA + corticosteroid (R03AK) dominate this class, both in terms of costs and in the number of patients and the number of prescribed DDD, in consequence of which they outpace the anticholinergics, glucocorticoids, and LABA monopreparations.
The expenditures of the class R03B (glucocorticoids and anticholinergics), primarily occasioned by Spiriva®, are stabilizing bit by bit. Nonetheless, it needs to be noted that the expenditures for the Pulmicort® spray suspension, which were stable until July 2008, have been on the rise following its transfer from Chapter IV to Chapter II. In 2010, these expenditures, amounting to 7.5 million euro for spray suspensions, are nearly double of what they were in 2008 (3.9 million euro).

Figure 49: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC H01C Hypothalamus hormones

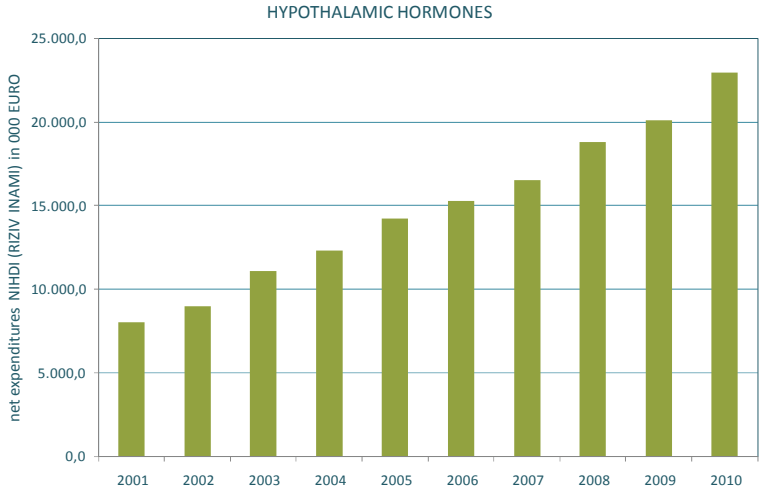
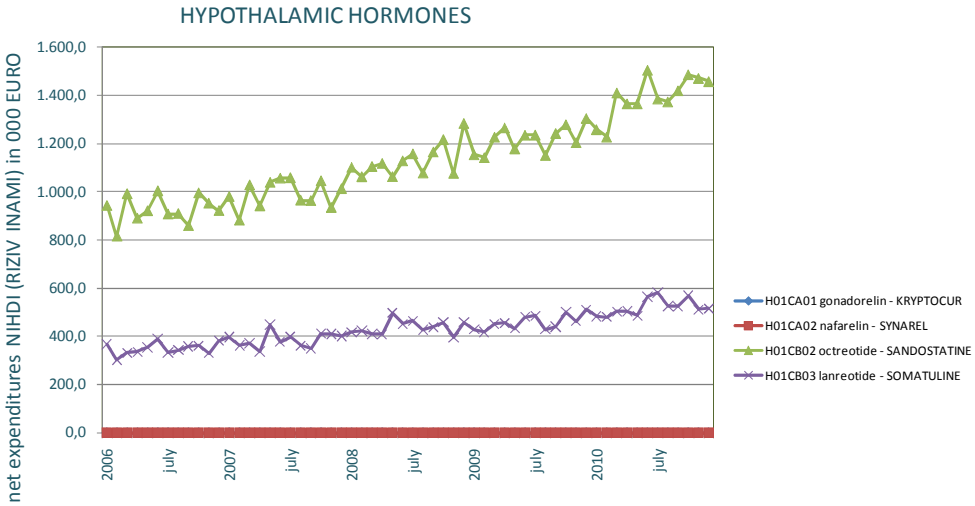


Figure 50: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class H01C Hypothalamic Hormones



There is no clear explanation for the continued rise of expenditures for octreotide in the public pharmacies (in reality to be attributed to the Long-Acting Repeatable packaging). The involved specialities are reimbursable under Class A (and Chapter IV) for the treatment of the acromegaly syndrome and of diarrhea that does not respond to a conventional treatment with antibiotics and antiperistaltics amongst patients with the "acquired immune-deficiency syndrome". This speciality is likewise reimbursable (Class B, Chapter I) for the treatment of patients displaying symptoms associated with functional gastroenteropancreatic endocrine tumours. The expenditures are for 83% (and rising) reimbursable in Class B.

A possible explanation for the acceleration in the rise of the expenditures as of begin 2010 is the reimbursement (since February 2010) of the pharmaceutical speciality Octreoscan® when the latter is used for the visual localisation by means of emission computed tomography (SPECT) of gastroentero-pancreatic neuroendocrine tumours and carcinoid tumours, and in consequence, the enhanced detection of these kinds of tumours.

Figure 51: evolution of the net expenditures NIHDI (public pharmacies 2001 - 2010) for ATC class H03A Thiroid preparations

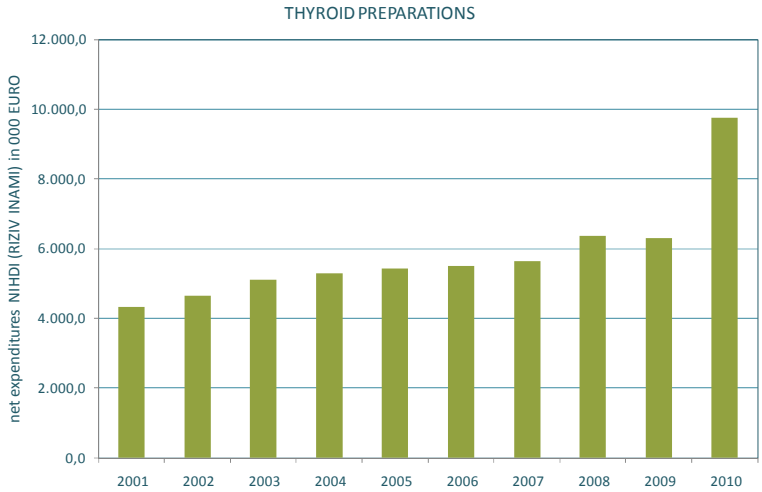
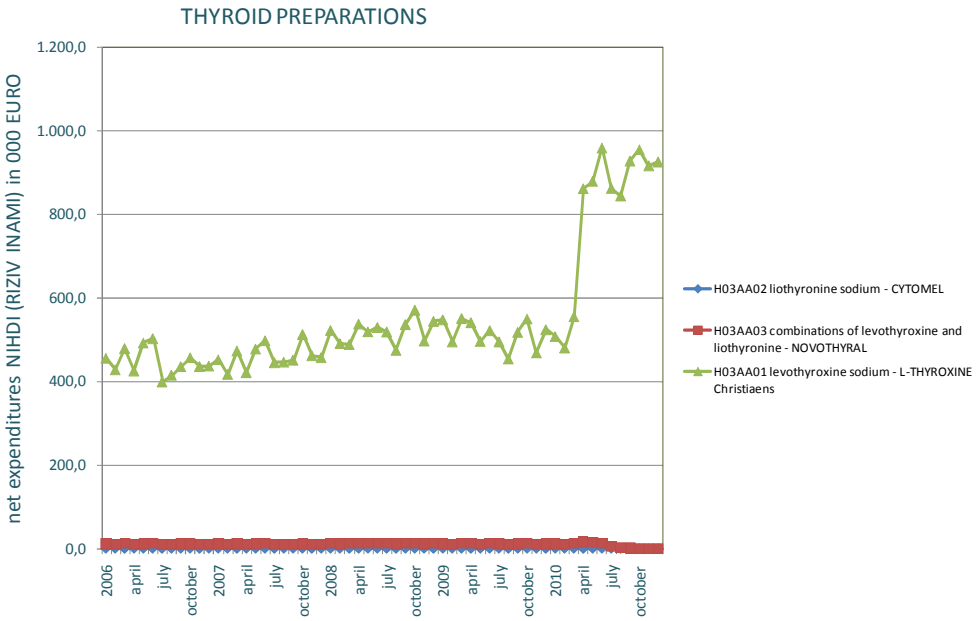


Figure 52: evolution of the net expenditures NIHDI per month (public pharmacies 2006 - 2010) for ATC class H03A Thyroid preparations



The sudden sharp rise in the expenditures for levothyroxine is to be explained by the introduction of the new remuneration system for pharmacists. It pertains here to a drug that is priced at an exceptionally low ex factory cost, whereby, through the introduction of the renewed margin system, the public retail price has been substantially increased (in some instances doubled). In the practice, there appears no notable change in the evolution of the use (*Figure 33*) or in the number of treated patients (*Table 28*).

Figure 53: evolution of the use of L-Thyroxine (ATC Class H03A Thyroid hormones – H03AA01) per month (public pharmacies 2006 - 2010)

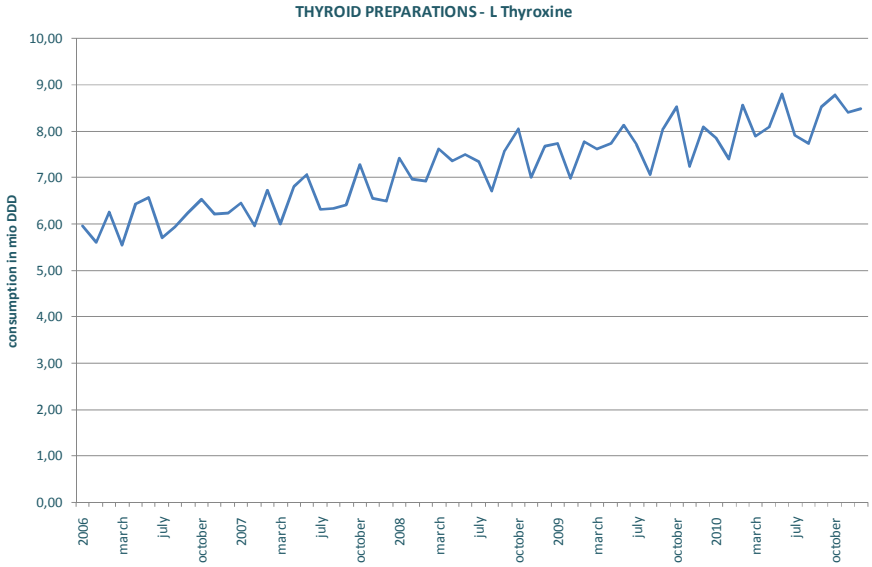


Table 28: Evolution of the number of patients treated with thyroid hormones (ATC H03)

	2006	2007	2008	2009	2010
H03A	360.851	384.545	428.623	450.660	474.766

EXPENDITURES FOR PHARMACEUTICAL SPECIALITIES IN HOSPITALS

General

Table 29: net annual expenditures NIHDI for drugs 2006 - 2009 (doc PH)

Net expenditures NIHDI x 1,000,000 EUR

	2006	2007	2008	2009
Hospitals	**975,5**	**1.057,8**	**1.171,4**	**1.205,9**

Growth %

		2006-2007	2007-2008	2008-2009
Hospitals		8,4	10,7	2,9

Table 30: 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	OVERIGE CYTOSTATICA	41,9	21,7	13,9	195,1
2	3	No	L04A	IMMUNOSUPPRESSIVA	21,7	37,3	23,6	102,5
3	2	No	B03X	OVERIGE MIDDELEN BIJ ANEMIE	-3,7	-2,4	-1,6	90,8
4	4	Yes	B05B	INTRAVENEUZE OPLOSSINGEN	-3,1	3,7	-1,7	61,5
5	5	No	J06B	IMMUNOGLOBULINEN	6,8	7,1	10,3	45,5
6	6	Yes	V08A	RONTGENCONTRASTMIDELEN, GEJODEERD	-1,2	1,0	-2,3	40,3
7	8	No	L01C	ALKALOIDEN EN OVERIGE NATUURLIJKE PRODUCTEN	-1,9	4,8	4,5	39,6
8	7	Mix	B01A	ANTITHROMBOTICA	-2,2	-0,4	-4,2	36,5
9	9	Yes	N01A	ALGEMENE ANESTHETICA	-1,5	5,6	-2,2	35,4
10	10	No	B02B	VITAMINE K EN OVERIGE HAEMOSTATICA	15,7	7,9	-5,1	34,0
11	11	Yes	J01C	BETALACTAM-ANTIBIOTICA, PENICILLINES	0,6	5,9	-4,2	33,0
12	13	No	L03A	CYTOKINES EN IMMUNOMODULERENDE MIDDELEN	8,8	10,0	10,3	32,3
13	12	Mix	J01D	OVERIGE BETALACTAM-ANTIBIOTICA	-0,8	4,2	-5,5	30,4
14	14	No	L01B	ANTIMETABOLIETEN	31,5	25,9	6,1	29,9
15	16	Mix	A16A	OVERIGE PREPARATEN I.V.M. MAAGDARMKANAAL EN STOFWISSELING	43,3	30,8	12,0	27,8
16	15	Yes	N05A	ANTIPSYCHOTICA (NEUROLEPTICA)	0,2	5,5	5,5	27,6
17	18	Yes	M05B	MIDDELEN MET INVLOED OP DE BOTSTRUCTUUR EN -MINERALISATIE	-14,2	3,2	10,1	21,8
18	22	No	S01L	MIDDELEN BIJ VASCULAIRE AANDOENINGEN VAN HET OOG	17,6	228,0	33,4	20,2
19	17	Mix	V03A	ALLE OVERIGE THERAPEUTISCHE MIDDELEN	0,1	22,6	-7,1	19,8
20	19	Mix	J02A	ANTIMYCOTICA VOOR SYSTEMISCH GEBRUIK	-1,1	11,8	8,0	19,5
21	20	No	B05A	BLOEDPRODUCTEN EN VERWANTE MIDDELEN	-6,9	1,2	1,7	16,2
(25)	21	No	L01D	CYTOTOXISCHE ANTIBIOTICA EN AANVERWANTEN	6,6	-1,6	-15,2	13,4

(*) expenditures calculated on the basis of:

- the available doc PH data: 1st semester 2006 to and including the 2nd semester 2009 (NIHDI data), whereby total expenditures= expenditures ambulant + expenditures outside of the forfait + 4 x expenditures within the forfait

The overview of the (virtual) expenditures and the *noted growth* per ATC3-class shows that **21 of the 171 classes** are responsible for **80% of the expenditures in hospitals.**

The 3 ATC-3 Classes that occupy the highest ranking in this overview, e.g., the Classes L01X, L04A, and B03X, represent one-third of the expenditures in hospitals. It pertains here to classes that are excluded from the 'drug forfait' regime.

In a following report, it will be possible to present an analysis of the evolution of the expenditures for iodinated X-ray contrast agents. For this class of drugs, an important impact is expected on the expenditures because of a number of measures centred on medical imaging[6]
and an NIHDI information campaign around the subject of the rational prescription of medical imaging (NIHDI, 2011)[7].

[6] National accord between Physicians–Health Insurance Funds 2011 of 13 December 2010: the structural measures 11/09 and 11/10 mentioned in point 4.4.1 and the structural measure 11/17 mentioned in point 4.4.2.

[7] Medical imagery
Rational prescription
Awareness campaign on the exposure risks to ionizing radiation
http://www.riziv.be/care/nl/doctors/promotion-quality/medical_imagery/pdf/medical_imagery.pdf

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.

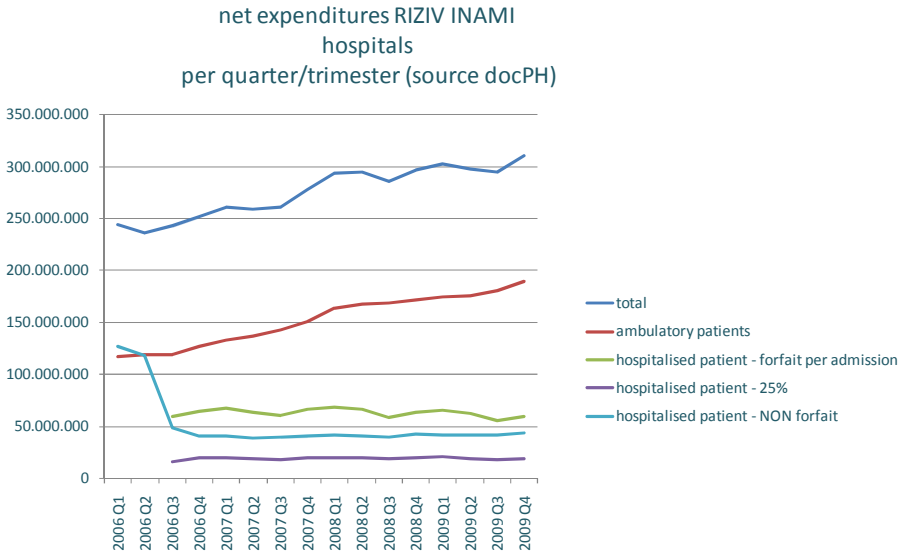
Because of the partial reimbursement (25% of the reimbursement base is still being billed according to the conventional method, namely billing by unit used), it is possible to monitor the real drug use without its being absorbed by a drug reimbursement total based on APRDRG (All Patients Refined Diagnosis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

We note in the process that with the doc N data, the invoicing data for a given period make reference to the period during which the payment of the drugs was **posted**. With doc PH data, the invoicing data for a given period refer to the period during which the drugs were **delivered**. Doc PH data are invariably made available at a later time given that the date for a delivery year are selected out of the posted data from a period of eighteen months (the defined year and the semester that follows that particular year in question).

Figure 54: 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 mounting increase in the expenditures for ambulatory patients that occurred as of the 4th quarter in 2006 and persisted until the 1st quarter in 2008 has slowed as of the 2nd quarter in 2008. This slowing of the growth figures persisted into the 3rd quarter of 2009, from which moment onwards we once again recorded a notable, stronger increase.

The total expenditures in hospitals keep rising, although the strong growth in 2007 and 2008 has, in fact, declined once again in 2009. 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 31: fixed amounts national budget for forfait per admission for the period July 2006 to July 2011 (source, Permanent Audit, May 2011)

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
1/7/2009- 30/6/2010	228,393
1/7/2010 - 30/6/2011	219,026

On an **annual basis,** we arrive at the following amounts (*Table 32*) for the various types of expenditures.

Table 32: net expenditures NIHDI period 2006-2009 (source doc PH – in Mil EURO) – break-down expenditures hospitals

	2006	**2007**	**2008**	**2009**
Ambulatory patients [1]	481,4	562,1	671,7	718,9
Hospitalized patients total	494,1	495,6	499,7	487,0
- hospitalized patients – NON forfait [2]	333,7	159,5	165,0	169,2
- hospitalized patients – forfait [3]	35,6	77,2	78,2	75,5
- forfait per admission [4]	124,8	258,9	256,5	242,3
Total hospital	**975,5**	**1.057,8**	**1.171,4**	**1.205,9**

[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).

Because of problems with the transfer of doc PH data from the insurance companies to the NIHDI (at present, data from 3 insurance companies are still missing), validated doc PH data are currently only available up to the end of 2009.

In order to get an idea of the evolution of the expenditures as of 2010, recourse is taken to more recent doc N data (*Table 33*).

Table 33: net expenditures NIHDI period 2006-2009 (source doc N – in million EURO) – break-down of expenditures for hospitals (source, permanent audit, May 2011, key Table 3.1.1. and Table 3.1.5.2.)

	2006	2007	2008	2009	2010
Hospitals – ambulatory patients	477,7	570,0	671,8	736,3	814,1
Hospitals – hospitalized out of forfait (100%)	399,6	166,5	167,8	174,0	181,4
Hospitals – hospitalized in forfait (25%)	21,4	77,3	79,1	77,1	72,1
hospitals - forfait per admission	82,0	258,5	263,2	246,3	230,9
hospitals – hospitalized patients (total)	503,0	502,3	510,2	497,4	484,4
total hospitals	**980,7**	**1.072,3**	**1.181,9**	**1.233,8**	**1.298,4**
evolution in %					
Hospitals – ambulatory patients		19,3	17,9	9,6	10,6
Hospitals – hospitalized out of forfait (100%)			0,8	3,7	4,2
Hospitals – hospitalized in forfait (25%)			2,3	-2,5	-6,6
hospitals - forfait per admission			1,8	-6,4	-6,2
hospitals – hospitalized patients (total)		-0,1	1,6	-2,5	-2,6
total hospitals		**9,3**	**10,2**	**4,4**	**5,2**

It appears from these figures that the observed stronger growth of the expenditures for ambulatory patients in hospitals as noted in graphic (doc PH) (*Figure 54*) as of the 3rd quarter in 2009 is continuing into 2010.
The total expenditures in the hospitals continue to rise, albeit at a slower pace than during the strong increase experienced in 2007 and 2008.

Evaluation of the consumption of medicines (either in forfait or out forfait) in hospitals

Source: Evaluation of the forfaitarisation of the medicines in hospitals' – Work group of the Multipartite Consultation structure [8]

This analysis is based on doc PH data from acute general hospitals (hence only those hospitals where the drug forfait regime is of application) over a period of 4 years
Data pertain to 4 semesters prior to the entry into force of the hospital forfait on 1/7/2006 and to 4 semesters following it.

Table 34: evolution of the consumption of medicines (expressed in DDD) in acute hospitals over a 4-year 2 years prior to the entry into force of the hospital forfait, 2 years after it (source note CGV 2011/182 (Work group of the Multipartite Consultation structure , 2011 May)

	1/7/04 through 30/6/05	**01/07/05 through 30/06/06**	**1/7/06 through 30/6/07**	**01/07/07 through 30/6/08**
	Year-2	**Year-1**	**Year1**	**Year2**
Out of forfait	16.888.560 (13%)	18.427.804 (14%)	17.636.552 (14%)	18.548.319 (14%)
In forfait	113.744.90 (87%)	110.551.581 (86%)	107.039.773 (86%)	110.627.083 (86%)
Total	**130.633.463**	**128.979.385**	**124.676.325**	**129.175.402**

Growth%	vs jaar -2
Out of forfait	9,8
In forfait	-2,7
Total	**-1,1**

Table 34 shows that the consumption of the drugs falling under the forfait regime declined in the course of 3 years (respectively minus 2.8% in year - 2 versus year -1, and minus 3.2% in year 1 versus year -1), and, subsequently, in the second year of the forfaitarisation rose slightly (increase of 3.4% in year 2 versus year 1).

During the studied period, the total drug consumption (expressed in DDD) dropped slightly (minus 1.1%). This drop is completely attributable to a decrease in the consumption of forfait drugs (minus 2.7%). For the drugs excluded from the forfait, we do notice a rise in their consumption (9.8%). However, when we consider the period 1 year prior to the entry into force of the forfait up to 2 years after it, we note that the consumption of medicines excluded from the forfait regime has remained fairly stable.

Notable is the fact that the consumption ratio for 'in forfait medicines'/'out forfait medicines' has neither risen nor changed since the introduction of this forfait.

[8] Note CGV 2011/182 (Work group of the Multipartite Consultation structure, 2011 May 2011).

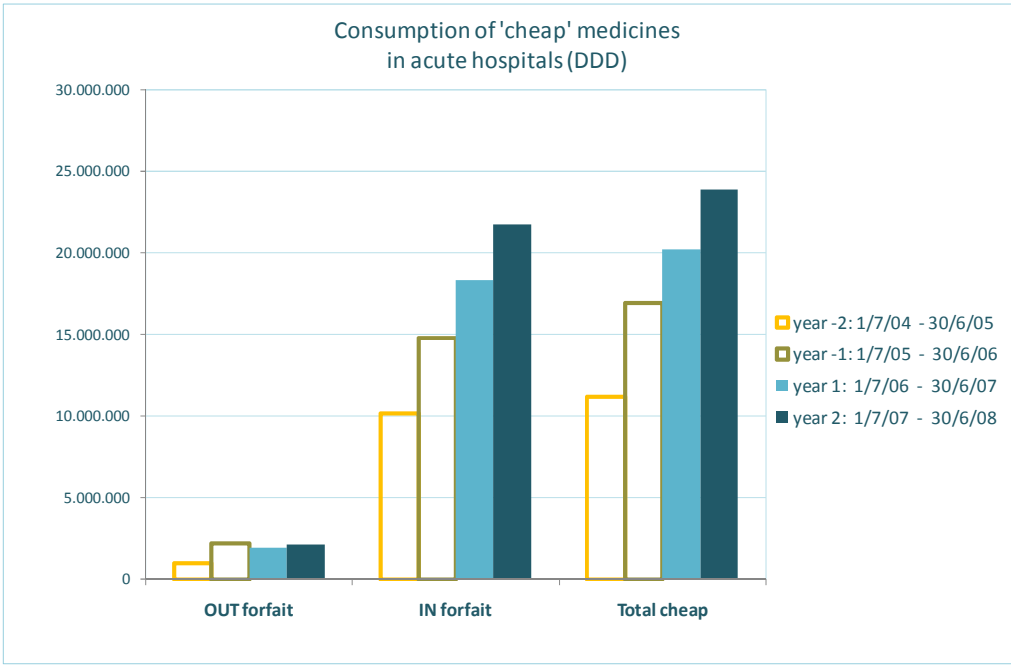
Evaluation of the consumption of "cheap" medicines (either in forfait or out forfait) in hospitals

Source: Evaluation of the forfaitarisation of the medicines in hospitals' – Work group of the Multipartite Consultation structure [9]

This analysis is based on doc PH data of acute general hospitals (hence only those hospitals where the drug forfait regime is of application) over a period of 4 years
Data pertain to 4 semesters prior to the entry into force of the hospital forfait on 1/7/2006 and 4 semesters following it.

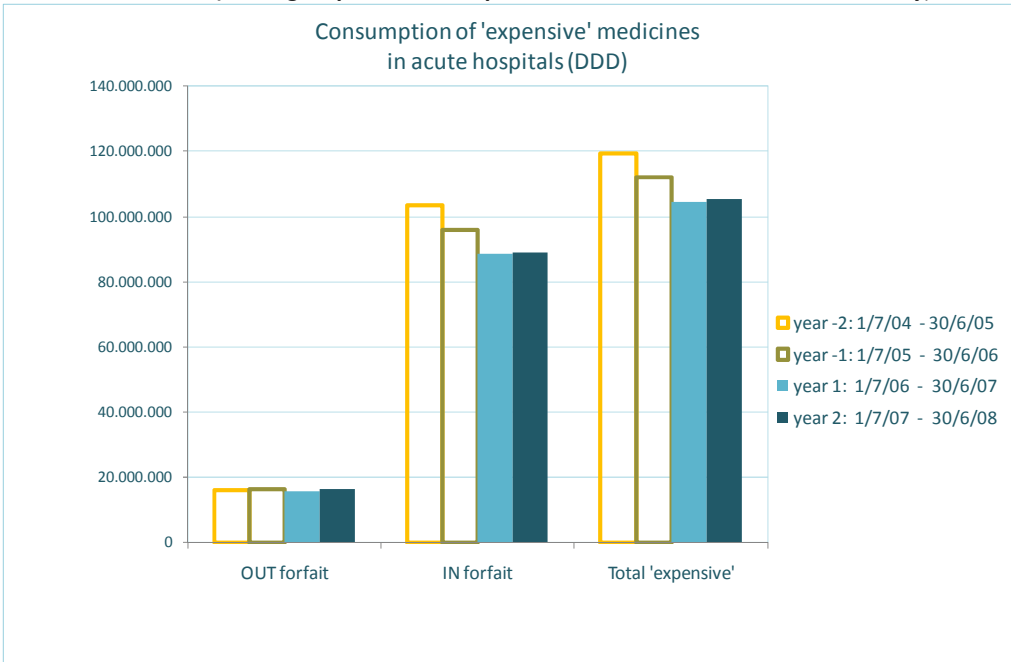
As 'cheap' medicines are considered: reproduced and generic drugs and the original reference specialities whose retail price is equal to the reimbursement basis
As 'expensive' medicines are considered: the original specialities under patent and the original reference specialities whose retail price differs from the reimbursement basis.

*Figure 55: evolution in the consumption of 'cheap' medicines (expressed in DDD) in acute hospitals over a 4-year period 2 years prior to the entry into force of the hospital forfait, and 2 years after it (**source: note CGV 2011/182** (Work group of the Multipartite Consultation structure, 2011 May)*



[9] Note CGV 2011/182 (Work group of the Multipartite Consultation structure , 2011 May)

*Figure 56: evolution in the consumption of 'expensive' medicines (expressed in DDD) in acute hospitals over a 4-year period: 2 years prior to the entry into force of the hospital forfait, and 2 years after it (**source: note CGV 2011/182** (**Work group of the Multipartite Consultation structure, 2011 May**)*



It appears from this analysis that in the course of the studied period, the consumption of 'cheap' medicines more than doubled: a rise from 11.2 million DDD to 23.9 million DDD (increase of 114%), whereas the consumption of 'expensive' medicines dropped from 119.5 million DDD to 105.3 million DDD (drop of 12%).

For medicines that fall under the forfait (IN forfait) we note that, following the entry into force of the forfait, the consumption of 'cheap' medicines keeps rising (increases versus the previous year of 24% in year 1 and 19% in year 2).
During the year prior to the entry into force of the forfait, we already recorded a significant increase of 45 % (year -1). A possible explanation for this may be that the hospitals anticipated on the introduction of the hospital forfait.

For what concerns the 'expensive' medicines, we note that their consumption following the introduction of the forfait declines during the first year (minus 7.4%) and then remains well nigh stable (0.2%). Here too we note that the decline of 7.4% in year 1 was already preceded by a drop of 7.5% in year -1, which again may point to the hospitals' anticipation on the forfaitarisation.

For drugs excluded from the forfait (OUT forfait), the consumption rate following the entry into force of the forfait remains reasonably stable (both for 'cheap' and for 'expensive' medicines).

In *Table 35*, for the 20 most important ATC Classes (level 2) the percentage 'cheap' medicine in total consumption (DDD) in the 2nd year following the forfaitarisation is compared with the consumption 2 years prior to it. These 20 ATC-2 Classes represent 90% of the consumption (in DDD).

*Table 35: evolution of the consumption of medicines (expressed in DDD) in acute hospitals over a 4-year period: 2 years prior to the entry into force of the hospital forfait and 2 years after it: consumption broken down per ATC2 Class, evolution of the 'cheap' medicine percentage of (**source: note CGV 2011/182** **(Work group of the Multipartite Consultation structure, 2011 May**))*

		1/7/04 through 30/6/05 Year-2		01/07/07 through 30/06/08 Year2	
ATC	Description	Total (DDD) (cheap + expensive)	Proportion cheap/total (%)	Total (DDD) (cheap + expensive)	Proportion cheap/total (%)
J01	ANTIBACTERIELE MIDDELEN VOOR SYSTEMISCH GEBRUIK	7.224.998	18 %	6.898.838	50 %
C09	MIDDELEN AANGRIJPEND OP HET RENINE-ANGIOTENSINESYSTEEM	3.584.237	5 %	4.054.303	49 %
C08	CALCIUMANTAGONISTEN	2.116.544	7 %	2.476.664	**70 %**
L01	CYTOSTATICA	3.737.236	**23 %**	3.833.327	**51 %**
A02	MIDDELEN BIJ AANDOENINGEN DIE VERBAND HOUDEN MET MAAGZUUR	5.244.170	55 %	5.800.699	**68 %**
C07	BETA-BLOKKERS	2.082.712	3 %	2.190.503	48 %
N02	ANALGETICA	2.999.072	33 %	3.099.643	56 %
C10	HYPOLIPEMIERENDE MIDDELEN	1.398.736	43 %	2.234.105	54 %
N06	PSYCHOANALEPTICA	2.403.890	13 %	2.184.575	40 %
N01	ANESTHETICA	14.051.963	15 %	13.679.440	18 %
B05	BLOEDVERVANGINGSMIDDELEN EN PERFUSIEVLOEISTOFFEN	21.285.103	1 %	20.599.591	2 %
M01	ANTI_INFLAMMATOIRE EN ANTIREUMATISCHE MIDDELEN	2.142.791	8 %	1.883.050	23 %
A10	ANTIDIABETISCHE MIDDELEN	3.499.969	8 %	3.749.026	13 %
N05	PSYCHOLEPTICA	2.409.762	0 %	2.338.915	9 %
C03	DIURETICA	5.530.458	4 %	5.243.885	6 %
B02	ANTIHEMORRAGICA	9.410.720	0 %	11.243.751	0 %
H02	CORTICOSTEROIDEN VOOR SYSTEMISCH GEBRUIK	7.937.551	0 %	7.724.302	0 %
D03	WOND- EN ULCUSMIDDELEN	10.570.997	0 %	40.567	0 %
B01	ANTITHROMBOTICA	14.171.024	0 %	14.848.999	0 %
C01	CARDIACA	6.895.133	2 %	4.997.434	2 %
		128.697.067	**8 %**	**118.757.618**	**19 %**

In contrast to 'year -2', where only for 1 ATC Class the ratio cheap/total consumption is more than 50%, we note that in 'year 2' for some 8 ATC Classes at least half of the consumption concerns 'cheap' medicines.
For the Calcium Antagonists and agents related to stomach acid (ATC Classes C08 and A02), this ratio is even as high as 70%.
It is notable that also for the L01 Class (out forfait, consumption primarily for non-hospitalized patients), the percentage of the 'cheap' medicines has sharply increased.

DOSSIER – ORPHAN DRUGS

These drugs are assuming an ever more significant share in the drug budget. The number of orphan drugs, as well as the affected population, keeps on growing.

At the end of 2010, of the 59 orphan drugs that were licensed by the EMA in Belgium, 47 are reimbursable. In addition, there are still 2 other reimbursable orphan drugs that at the national level have been licensed under the orphan drug statute, which makes for a total of 49 reimbursable orphan drugs. Amongst the non-reimbursable orphan drugs we find 6 for which the application procedure towards their eventual reimbursability is in progress, 6 were turned down for reimbursability status (for most of them there are alternatives) and 1 drug was made reimbursable in 2011.

The reimbursability procedure provides for the support of a College of Orphan Drugs for 28 of the 49 reimbursable orphan drugs. At the end of 2010, the Colleges had processed the dossiers of 2.237 patients, being 700 new patients in 2010 (versus the 389 in 2009). By the end of July 2011, the dossiers of 413 new patients were added to that number. In 2010, 6 new Colleges of Orphan Drugs were formed, amongst which 5 for new drugs and 1 for a new indication of a medicine that was already reimbursable in a different indication (Tracleer for the prevention of digital ulcers amongst patients with systemic sclerosis vs Tracleer for the treatment of pulmonary arterial hypertension). In 2010, 5 other orphan drugs were made reimbursable (without College).

When we follow the evolution of the expenditures for orphan drugs in the hospital environment, we not only notice rapid growth from one year to the next, but we also observe that the share of the expenditures for orphan drugs within the hospital expenditures for drugs keeps rising, going from 1.45% in 2004 to 6.66% in 2009, and to almost 7.5% in 2010. During that same period, (from 2004 to end 2009), the number of reimbursable orphan drugs has risen from 5 to 37.

Table 36: Evolution of the expenditures NIHDI for orphan drugs (in 000 EURO)

	2004	2005	2006	2007	2008	2009	2010 (6 months)
Total orphan drugs	14.390	25.255	29.235	45.326	77.125	89.236	51.815
Total hospital	995.531	1.050.675	1.098.441	1.182.940	1.296.936	1.340.561	694.001
%	1,45	2,44	2,66	3,83	5,95	6,66	

Figure 57: Evolution of the number and the expenditures NIHDI in Belgium for orphan drugs

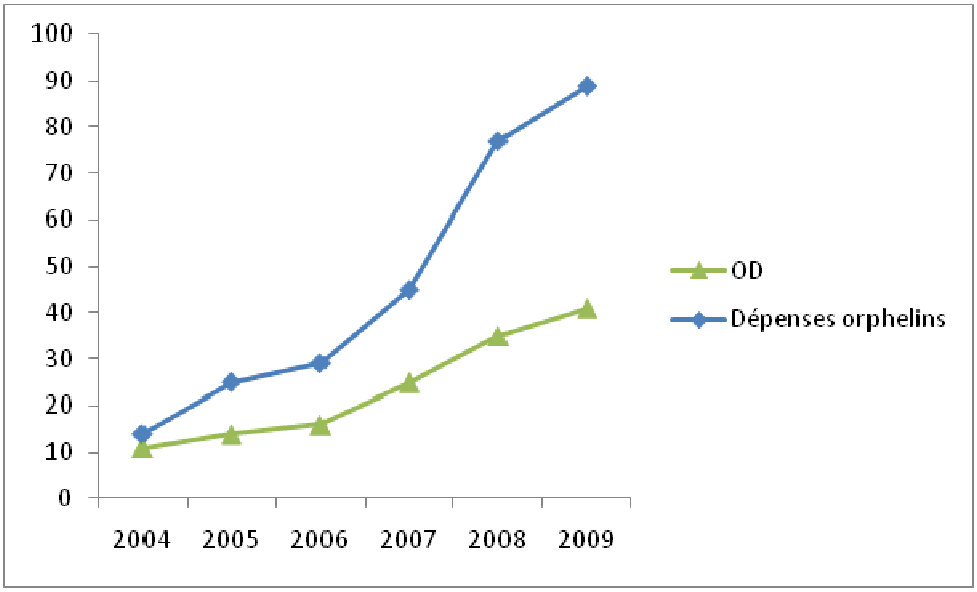
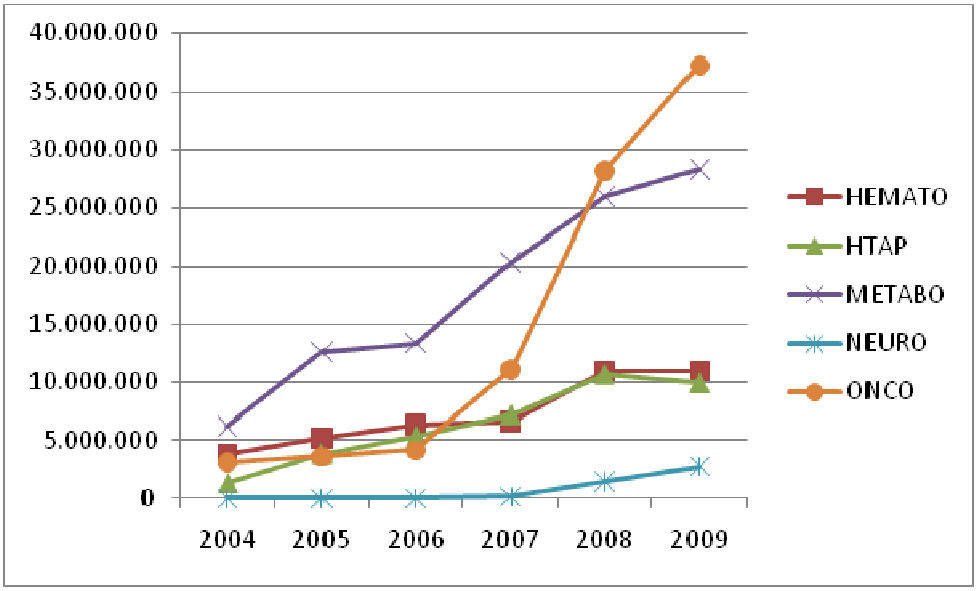


Figure 57 illustrates the evolution of the expenditures for orphan drugs in function of the number of reimbursable orphan drugs between 2004 and the end of 2009.

When we consider the evolution of the expenditures more closely with reference to the type of orphan drug, we note that 2 categories display a remarkable growth qua cost, as appears from *Figure 58*.

Figure 58: Evolution of the expenditures NIHDI in Belgium for orphan drugs per type of pathology



It pertains here, on the one hand, to the use of drugs in the oncology, for which the rise of the expenditures is especially significant as of 2006. The reimbursement of a significant portion of new drugs essentially explains this increase. For, in effect, where in 2006 the number of reimbursable drugs was 2, this number had increased to 15 between 2006 and the end of 2009. The expenditures rose from 4 million to more than 37 million €.

The other domain showing a significant and steady rise of the expenditures is the one related to the treatment of metabolic diseases. The expenditures in this area increase from 6.2 million € in 2004 to 28.3 million euro in 2009 for, respectively, 6 and 13 reimbursable drugs. When we calculate the average annual cost per patient (all metabolic diseases together), we note a rising trend, going from 172.000 €/annum/patient in 2005 to 215.000 €/annum/patient in 2009. The explanation for this increase is the growth in the number of paediatric patients, as most drugs are being administered according to a posology proportional to the patient's weight or his or her body surface area. The expenditures rose to 23 million € for 107 patients treated in 2009.

The expenditures for pulmonary arterial hypertension likewise experience a steady growth, albeit clearly less significant than the expenditures for metabolic disorders.
Nonetheless, we note that in these expenditures, the ones for Flolan (reimbursable as of 2010) and Remodulin have not been included; the cost for these 2 products was partially assumed by the Special Solidarity Fund.

In 2010, a contribution of the Special Solidarity Fund for a treatment with Remodulin was approved for 41 patients. For 29-39% of these patients, the contribution was approved for a treatment within the indication area that may be eligible for 'traditional' reimbursement.

Flolan has since May 2010 been 'temporarily' registered into the list of reimbursable specialities – this by agreement between the NIHDI and the claimant – conform to the provisions in article 81 of the RD of 21 December 2001. This temporary registration is coupled to the completion of an observational study to be conducted by the claimant organisation for the purpose of obtaining confirmation of hypotheses pertaining to the effectiveness of this medicine in the practice, and coupled to budget-control techniques. At the time of the editing of this report, the decision about the registration of Remodulin into the list of reimbursable specialities is still pending.
It should be evident that acceptance or rejection of reimbursement for both these specialities – and the modalities in this regard – will have a significant impact not only on the consumption of, and the expenditures for, these specialities themselves, but just as much on those of the alternatives.
In a subsequent report – when more extensive data have become available – this issue will be discussed further in greater depth.

A clear trend for what concerns taking charge of patients with pulmonary arterial hypertension is the ever more popular recourse to polytherapy. Currently, out of a total of 675 patients for whom a dossier was submitted to the College for Orphan drugs, 2/3 of these are on monotherapy and 1/3 on bi- or even tri-therapy, which results in a significant increase in the average cost per annum per patient.

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).
This avenue has thus so far been explored only sparingly

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 01.01.11 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**. 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)

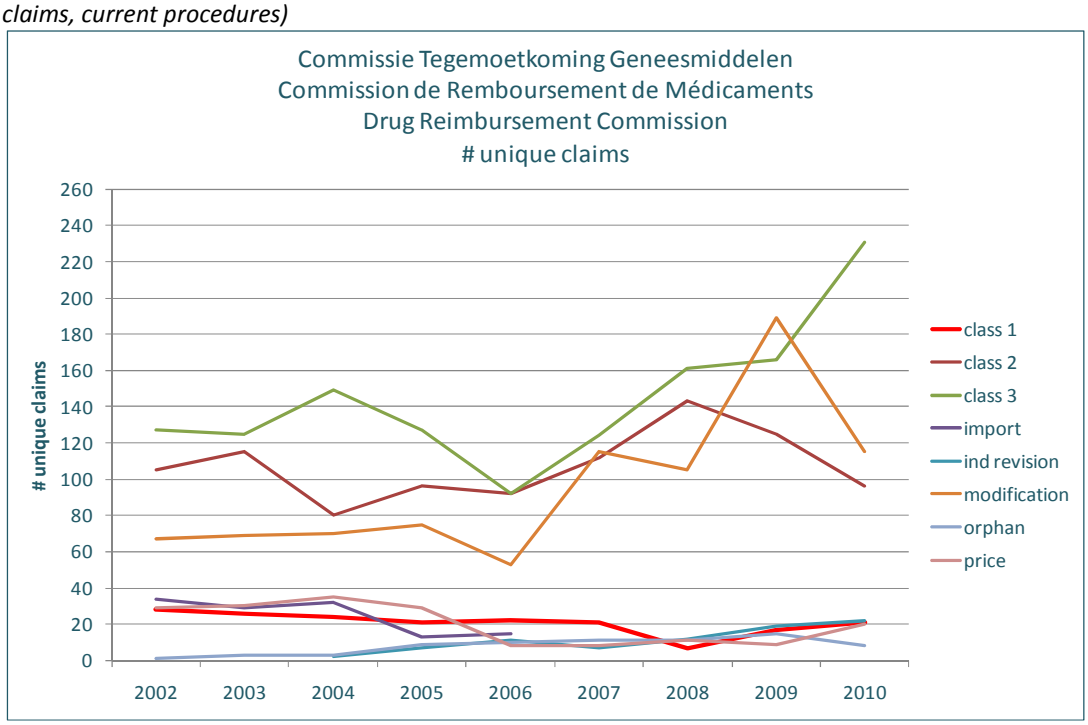
The number of dossiers (claims) submitted in 2010 via the CTG-procedure (RD 21.12.2001) lies considerably higher that the fairly steady number of the previous years, showing once again significant differences depending on the type of application (see *Figure* 59: number of claims *per year (unique dossiers – including* ***completed procedures, withdrawn claims, current procedures)***

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) – 17 (seventeen)/21 (twenty-one).
- The number of applications for orphan drugs in 2010 was 8 (eight).
- 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 3 drugs).
- The large number of 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).

NOT added to these data: for 2010, 227 (two hundred and twenty-seven) processed claims Class 3 – administrative procedure (average processing time to notification of the decision: 45 calendar days), nor are 898 (eight hundred and ninety-eight) 'procedures article 97 – administrative proposals for change/corrections to the list'.

Figure 59: 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 37 shows for the period 2006-2010 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 (24% and 22 % no proposal), and that for these same drugs it is more common to propose that they not be reimbursed (21% and 13%).

Table 37: number of unique claims for registration in the list of reimbursable specialities versus proposal of the Drug Reimbursement Commission (2006-2010)

2006 - 2010							
	positive		negative		no proposition		total
	number	%	number	%	number	%	number
class 1	36	55	14	21	16	24	66
class 2	362	79	42	9	56	12	460
class 3	659	96	17	2	7	1	683
modification	436	85	51	10	26	5	513
orphan	29	64	6	13	10	22	45
total	1522	86	130	7	115	7	1767

Table 38 shows for the period 2006-2010 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 38: decisions by the Minister in function of the proposal by the CRM (unique dossiers 2006 - 2010)

2006 - 2010											
	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	48	65,8	14	19,2	2	2,7	2	2,7	7	9,6	73
positive prop	36	100									36
negative prop	2	10,5	9	47,4	2	10,5	1	5,3	5	26,3	19
no prop	10	55,6	5	27,8			1	5,6	2	11,1	18
class 2	390	81,9	62	13,0	4	0,8	4	0,8	16	3,4	476
positive prop	349	94,8	9	2,4	2	0,5	2	0,5	6	1,6	368
negative prop	6	12,0	35	70,0			1	2,0	8	16,0	50
no prop	35	60,3	18	31,0	2	3,4	1	1,7	2	3,4	58
class 3	663	96,2	18	2,6	1	0,1	1	0,1	6	0,9	689
positive prop	655	98,5	3	0,5			1	0,2	6	0,9	665
negative prop	4	23,5	13	76,5							17
no prop	4	57,1	2	28,6	1	14,3					7
modification	449	86,7	46	8,9	2	0,4	16	3,1	5	1,0	518
positive prop	420	95,7	2	0,5	2	0,5	12	2,7	3	0,7	439
negative prop	7	13,2	41	77,4			3	5,7	2	3,8	53
no prop	22	84,6	3	11,5			1	3,8			26
orphan	39	81,3	6	12,5					3	6,3	48
positive prop	28	96,6	1	3,4							29
negative prop	3	37,5	3	37,5					2	25,0	8
no prop	8	72,7	2	18,2					1	9,1	11
total	1589	88,1	146	8,1	9	0,5	23	1,3	37	2,1	1804

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 (85 %)

The Drug Reimbursement Commission 2002 – 2011

On 1 January 2012, the Drug Reimbursement Commission (CTG) will have been active for ten years. The Commission is responsible for the formulation of proposals towards amendments to the list of reimbursable specialities, and this on the basis of the procedures as described in the Royal Decree of 21 December 2001 concerning the establishment of the procedures, terms, and conditions pertaining to the reimbursement of the costs of the mandatory insurance for medical treatment and reimbursements of costs of pharmaceutical specialities.
The Commission's mission combines the mission of the Technical Council for the Pharmaceutical Specialities (TRSF - of which it is the successor) and that of the Transparency Commission.

An evaluation was drawn up of the impact of 'decisions' (in this instance 'proposals') of the Technical Council for the Pharmaceutical Specialities and those of the Drug Reimbursement Commission. 'Decisions' were deemed to have been made by the CTG in cases where the registration of the speciality in casu on the list of reimbursable specialities became effective after 30 June 2002. All packaging was charged.

Figure 63 illustrates that more than half (55%) of the expenditures for the reimbursement of pharmaceutical specialities in the public pharmacies are expenditures for those specialities for which the 'decision' had been taken by the CTG. At the same time, it demonstrates the fairly rapid rate at which 'new' pharmaceutical specialities are being 'accepted' into the Belgian therapeutic arsenal – and, hence, the fairly high access to new drugs for patients.

Figure 60 compares the number of individual 'decisions' taken by the CTG with the number of (still reimbursable) packages for which the 'decision' was taken by the TRFS. The larger number of reimbursable packages for the account of the CTG can nearly fully be explained by the great number of 'decisions' for generic pharmaceutical specialities (see *Figure 62*). Only for oncolytic medicines are the new 'original' specialities the determining factor.

Figure 60: number of reimbursable pharmaceutical specialities in Belgium on 01.01.2011 (all packages) - claims Drug Reimbursement Commission versus claims Technical Council for Pharmaceutical specialities.

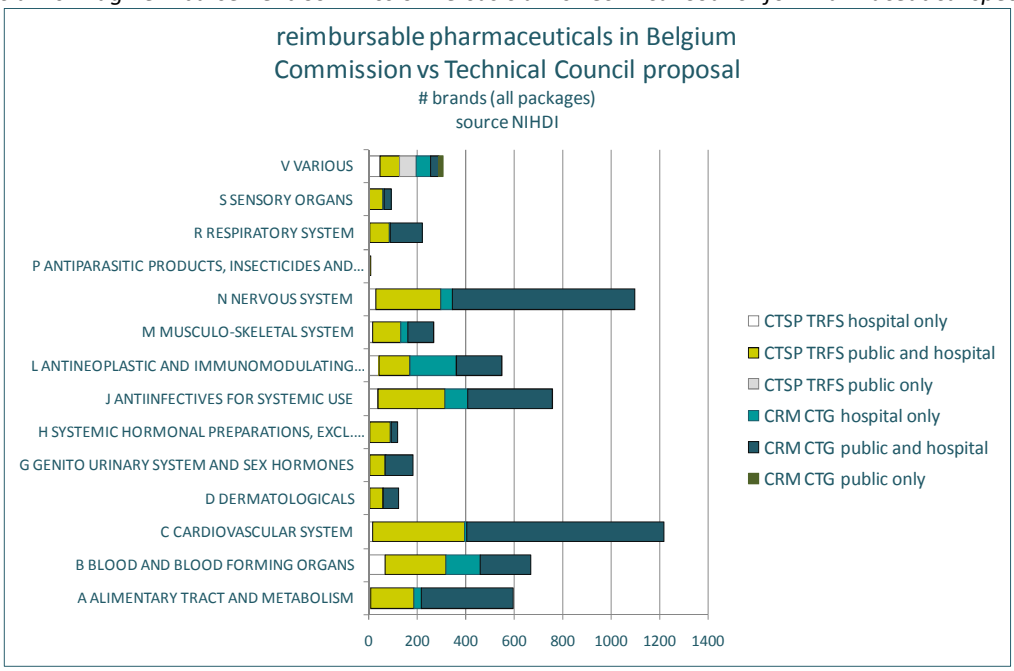


Figure 61: number of reimbursable pharmaceutical specialities in Belgium (original specialities) on 01.01.2011 (all packages) - claims Drug Reimbursement Commission versus claims Technical Council for Pharmaceutical Specialities.

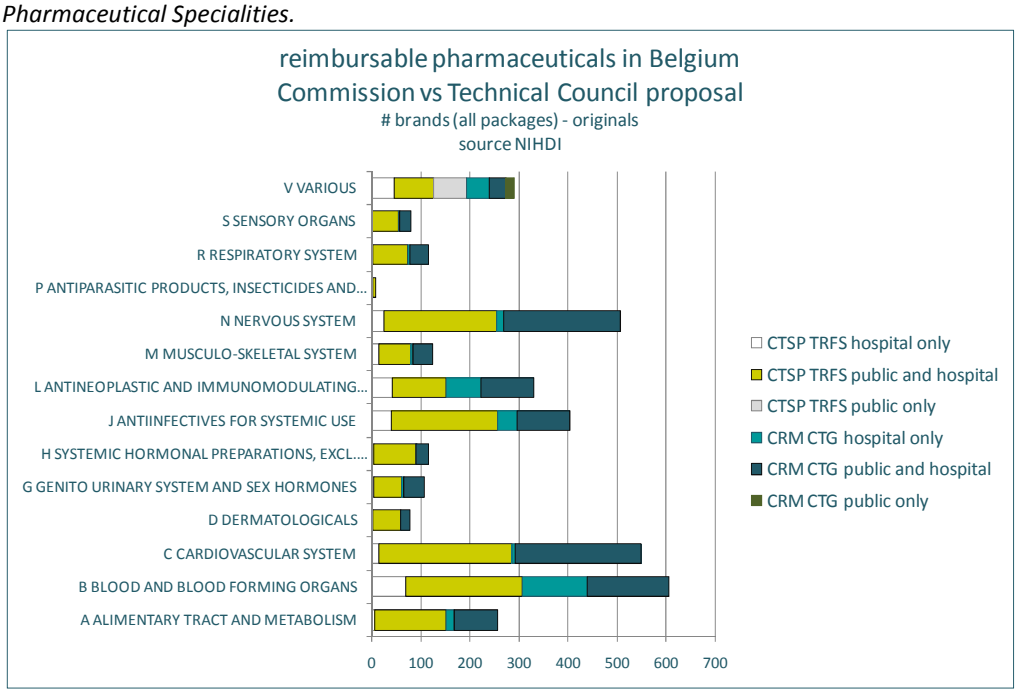


Figure 62: number of reimbursable pharmaceutical specialities (generics) in Belgium on 01.01.2011 (all packages) - claims Drug Reimbursement Commission versus claims Technical Council for Pharmaceutical Specialities.

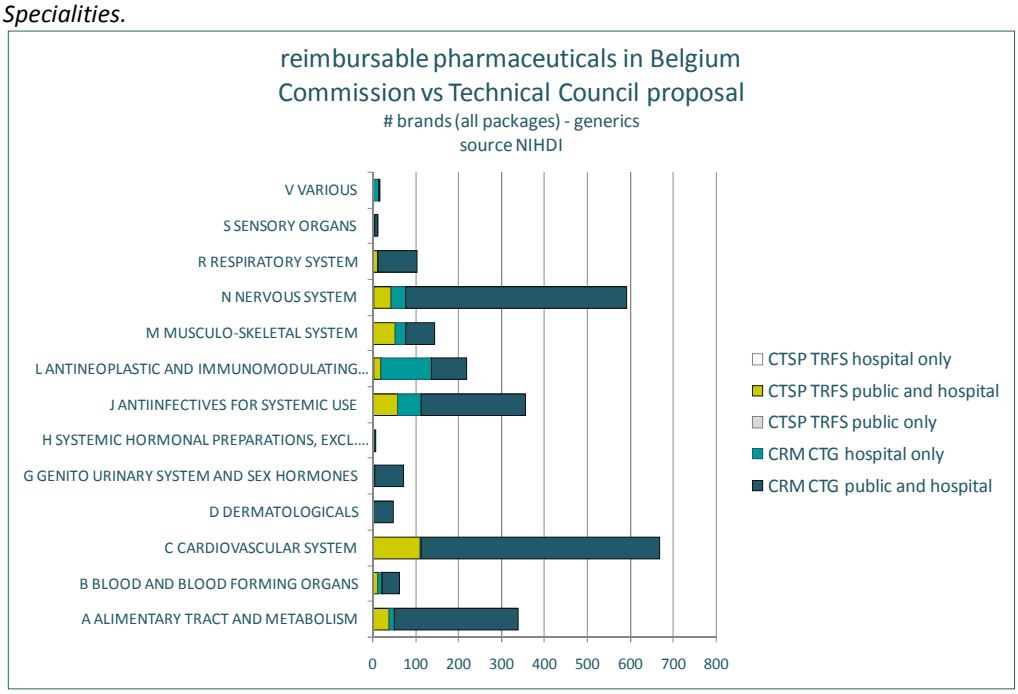
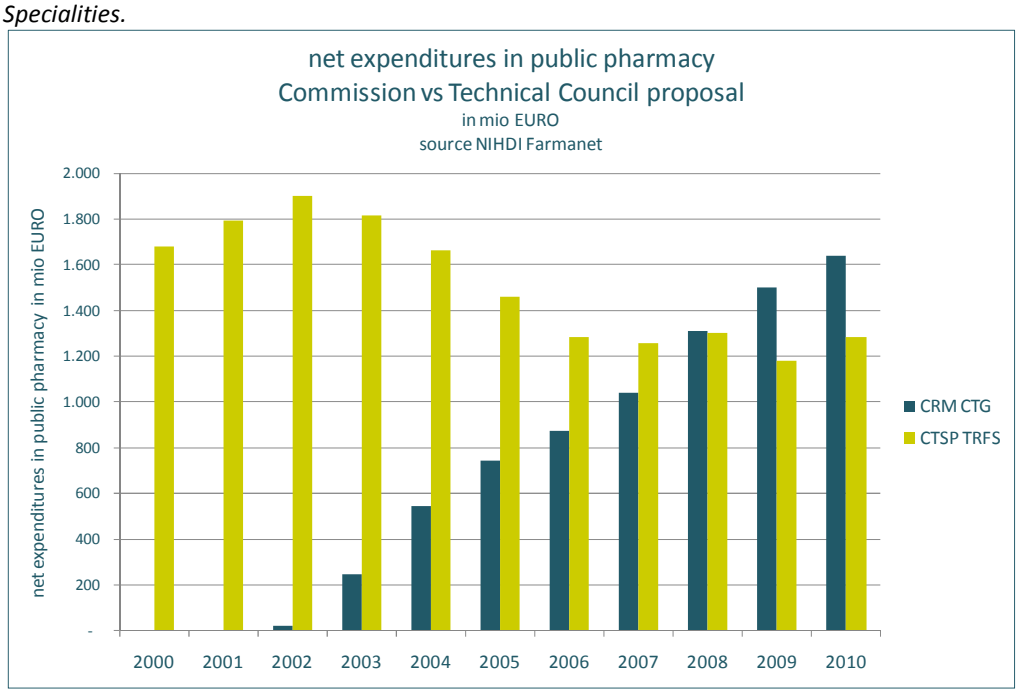


Figure 63: net expenditures NIHDI in public pharmacies for reimbursable pharmaceutical specialities (all packages) - claims Drug Reimbursement Commission versus claims Technical Council for Pharmaceutical Specialities.



DOSSIER - THERAPEUTIC ADDED VALUE

The procedure for amendments to the list of reimbursable specialities (RD 21 December 2001) provides that the Minister competent for Social Affairs take a decision concerning the acceptance or rejection, the modifying, or the scrapping of pharmaceutical specialities on this list. This entails a decision about the reimbursement base, the reimbursement conditions, the reimbursement category, and the reimbursement group (and, case pertaining, the term and the elements to be evaluated for the individual review) (article 4), such decision to be taken after an evaluation of one or more of the following criteria.

1° The therapeutic value
2° The price of the speciality and the reimbursement basis proposed by the claimant
3° the importance of the speciality in the medical practice in function of the therapeutic and social needs
4° The budgetary impact on the insurance factor, taking into account the budgetary objectives
5° The ratio between the insurance costs and the therapeutic value

Article 5, § 1 of this RD determines that the therapeutic value of a speciality be expressed by the Commission (or by the Secretariat in case of an administrative processing of the claim) in one of the three 'added value' classes:
Class 1 is defined as specialities with a demonstrated therapeutic added value versus existing therapeutic alternatives …

Article 6 holds that the definitive determination of the added value class be made by the Minister, on the proposal of the Commission, except in instances where the Commission is late in formulating a proposal, in which case the Minister shall make the decision, and in instances where the Minister is late in taking a decision, in which case the most recent proposal by the claimant organisation will be adopted.

With the RD of 11 February 2010, implementation was given in the RD of 21 December 2001 (article 81) to the possibility for concluding agreements between the NIHDI and the claimants for temporary registration of pharmaceutical specialities in the list of reimbursable pharmaceutical specialities.
".. ".. in case the Drug Reimbursement Commission does not deem the claimant's proposed basis for reimbursement to be in proportion with the evaluation of the criteria stated in § 2, or should the Commission be of the opinion that the registration in the list of reimbursable specialities contains points of uncertainty with respect to budgetary issues… " (art 35bis, § 7 of the Law of 14 July 1994). That possibility was created for (and, hence, limited to), amongst others, drugs for which added value Class 1 was claimed, and for orphan drugs.

The introduction of this new procedure could, however, have the unintended effect that businesses – in order to be able to make full use of this new possibility – might well submit more frequent 'claims' for added value Class 1 for drugs (without any demonstrable added value), or in the traditional reimbursement procedure give preference to a 'no proposal' or to a negative proposal.

At the same time, this procedure heightens the risk that the Commission would formulate no proposal, or formulate a negative one, with a view to satisfying the basic conditions for starting the procedure for such agreements wherein – to the Commission inaccessible - flexible solutions for financial /budget control can be applied.

An initial evaluation of the application of these new procedures for concluding agreements allows a (temporary) insight into such workings and, at the same time, also provides a picture of the evaluation and recognition of the therapeutic added value as conducted by the Commission and the Minister (and the granting of added value Class 1).

For the analysis, all claims for registration into the list of reimbursable specialities were taken into account for which the added value Class 1 or 'orphan drug' was requested (unique claims: with simultaneous claims for varying dosages /packages for specialities, the claims are being 'pooled' in case the contract partner, the type of claim, day 0, active component, proposal by the Commission, and the Minister's decision prove identical).

For the purpose of this analysis, it was checked if applications pertained to an initial or a repeat claim (second or third claim following a previous rejection or a halt to the procedure). In the event of a stopped procedure (at the organisation's request or in case the maximum term of the suspension (90 days) had been exceeded), the Commission's proposal and/or the Minister's decision was considered to be negative. No decision by the Minister was considered as a positive decision.
Seeing that not in all cases the procedure was halted by the organisation because a negative decision was anticipated (but likewise for administrative reasons), the data no doubt show an all too negative picture. The results for 2010 need to be looked at with some reservations: at the time of the analysis there were still 7 Class 1 drugs and 1 orphan drug in procedure.

Figure 64: Claims for registration in the list for reimbursable specialities – Class 1 – therapeutic added value (2002 - 2010).

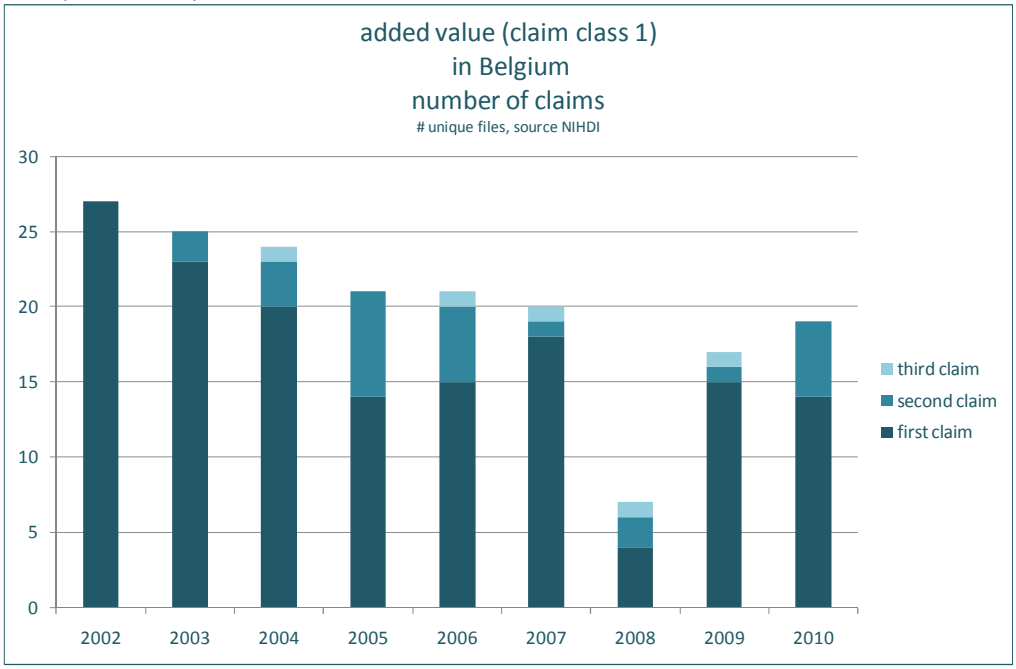


Figure 65: Claims for registration in the list for reimbursable specialities - Orphan drugs (2002 - 2010).

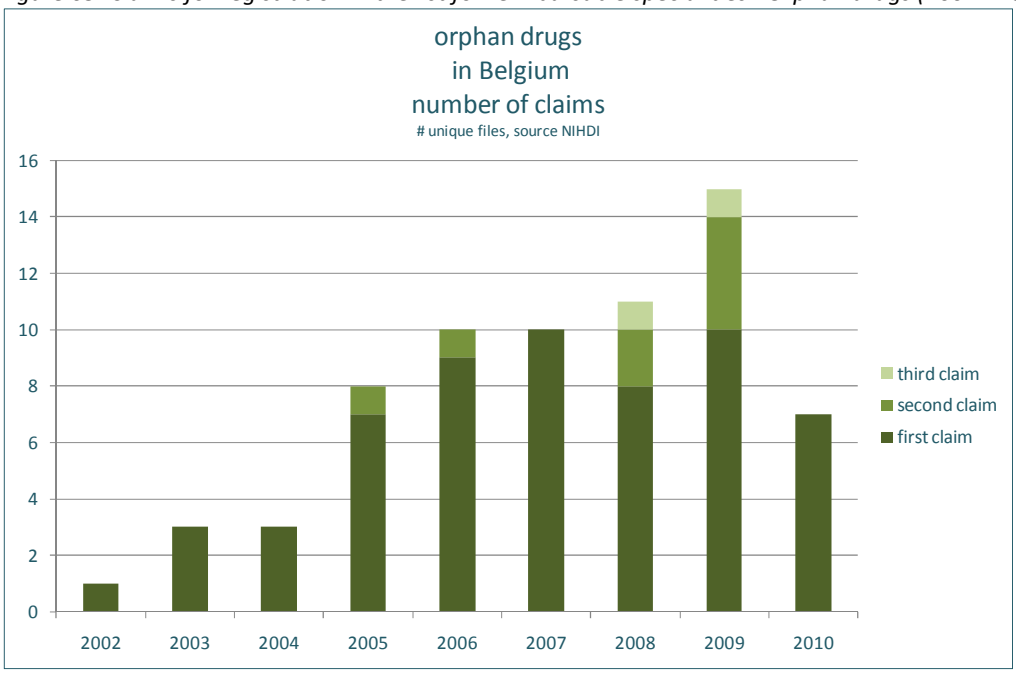


Table 39: Claims (and repeats) for registration in the list of reimbursable specialities – Class 1 and Orphan drugs (2002 - 2010): decision by the Minister

	decision	claim	2002	2003	2004	2005	2006	2007	2008	2009	2010
class 1	positive	first	20	15	7	4	11	9	4	7	4
		second		2	1	5	4	1	1	1	2
		third					1	1	1	1	
			74%	**68%**	**33%**	**43%**	**76%**	**55%**	**86%**	**53%**	**50%**
class 1	negative	first	7	8	13	10	4	9		8	4
		second			2	2	1		1		2
		third			1						
			26%	**32%**	**67%**	**57%**	**24%**	**45%**	**14%**	**47%**	**50%**
	decision	**claim**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
orphan	positive	first	1	3	1	5	7	9	4	8	4
		second					1		2	2	
		third							1	1	
			100%	**100%**	**33%**	**63%**	**80%**	**90%**	**64%**	**73%**	**67%**
orphan	negative	first			2	2	2	1	4	2	2
		second				1				2	
		third									
			0%	**0%**	**67%**	**38%**	**20%**	**10%**	**36%**	**27%**	**33%**

Table 40: Claims (and repeats) for registration in the list of reimbursable specialities – Class 1 and Orphan drugs (2002 - 2010): proposal by the Drug Reimbursement Commission

	motion	claim	2002	2003	2004	2005	2006	2007	2008	2009	2010
class 1	positive	first	17	11	9	1	6	7	4	6	3
		second		2		4	3	1			2
		third					1	1		1	
			63%	**52%**	**38%**	**24%**	**48%**	**45%**	**57%**	**41%**	**42%**
class 1	negative	first	4	7	8	8	6	6		5	4
		second				1	1		1		2
		third			1						
			15%	**28%**	**38%**	**43%**	**33%**	**30%**	**14%**	**29%**	**50%**
class 1	no proposition	first	6	5	3	5	3	5		4	1
		second			3	2	1		1	1	
		third							1		
			22%	**20%**	**25%**	**33%**	**19%**	**25%**	**29%**	**29%**	**8%**

	motion	claim	2002	2003	2004	2005	2006	2007	2008	2009	2010
orphan	positive	first		3	1	5	4	6	3	6	4
		second							2	2	
		third							1	1	
			0%	**100%**	**33%**	**63%**	**40%**	**60%**	**55%**	**60%**	**67%**
orphan	negative	first			1	2	2	2	4	2	1
		second				1				1	
		third									
			0%	**0%**	**33%**	**38%**	**20%**	**20%**	**36%**	**20%**	**17%**
orphan	no proposition	first	1		1		3	2	1	2	1
		second					1			1	
		third									
			100%	**0%**	**33%**	**0%**	**40%**	**20%**	**9%**	**20%**	**17%**

From *Table 39* and *Table 40* it appears that for more than 50 % of the claims for specialities with claimed added value (Class 1), the decision for registration in the list is positive.
The Drug Reimbursement Commission, however, formulates in somewhat less than 50% of the cases a positive proposal and for some one-quarter of the claims no proposal at all.
For Orphan drugs, these results lie 50% higher. More than 75% of the claims result in a positive decision, based on over 60% positive proposals by the Commission.

In reality, the end results – if account is taken only of the last decision (for instance, in case of a repeat submission) – lie considerably (*Table 41* infra). Seventy percent of the claims for Class 1 drugs are registered in the list, and 83% of the claims for Orphan drugs.

Table 41: Claims for registration in the list of reimbursable specialities – Class 1 and Orphan drugs (2002 - 2010): decision by the Minister

	decision	2002	2003	2004	2005	2006	2007	2008	2009	2010	total
class 1	positive	20	17	8	9	16	11	6	9	6	102
		80%	**77%**	**50%**	**60%**	**80%**	**65%**	**100%**	**75%**	**46%**	**70%**
	negative	5	5	8	6	4	6		3	7	44
		20%	**23%**	**50%**	**40%**	**20%**	**35%**	**0%**	**25%**	**54%**	**30%**

		2002	2003	2004	2005	2006	2007	2008	2009	2010	total
orphan	positive	1	3	1	5	8	9	7	11	4	49
		100%	**100%**	**50%**	**71%**	**89%**	**100%**	**78%**	**85%**	**67%**	**83%**
	negative			1	2	1		2	2	2	10
		0%	**0%**	**50%**	**29%**	**11%**	**0%**	**22%**	**15%**	**33%**	**17%**

For what concerns the evaluation of the unintended effects of the creation of the procedure for concluding agreements, the available data (for about a one-year span) do not permit us to draw conclusions: There are – in the figures – no indications of 'more' (possibly unjustified) claims for Class 1. And there are no indications that the Commission is apt to more frequently formulate either no proposals or negative proposals (*Figure 66*, *Figure 67* and *Figure 68*).

Figure 66: Class 1 and orphan drugs: decisions concerning the registration in the list of reimbursable specialities (claims 2002 – 2010)

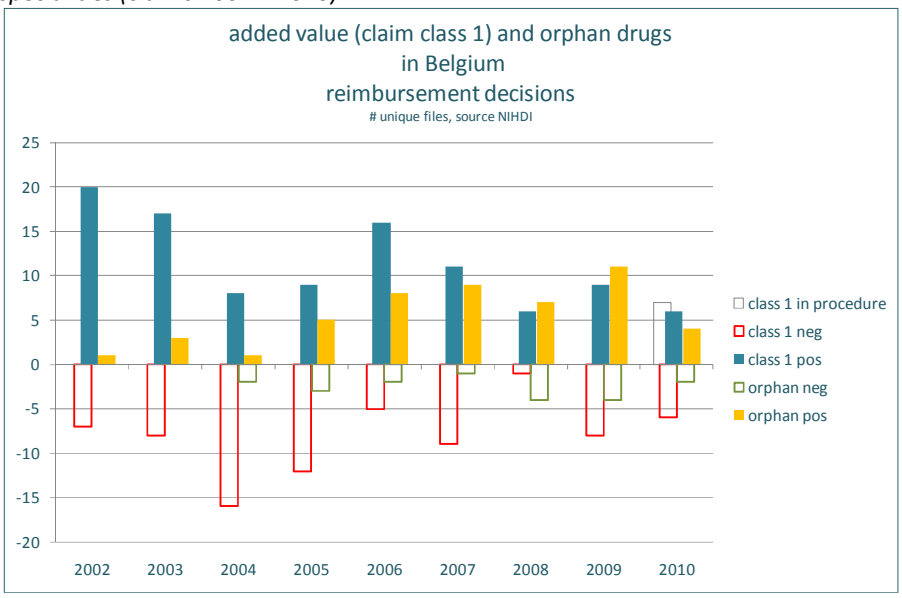


Figure 67: Class 1: decisions concerning the registration in the list of reimbursable specialities (detail) (claims 2002 – 2010)

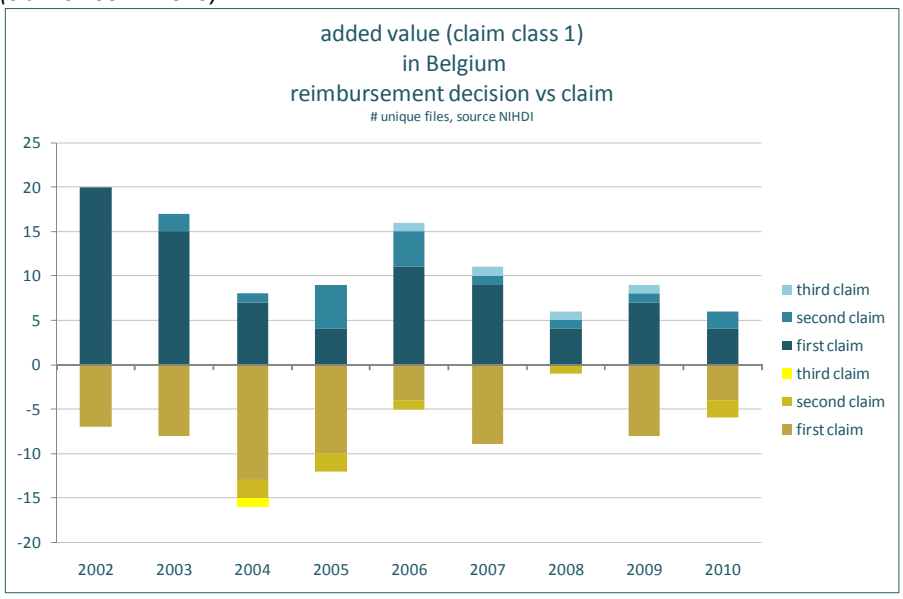
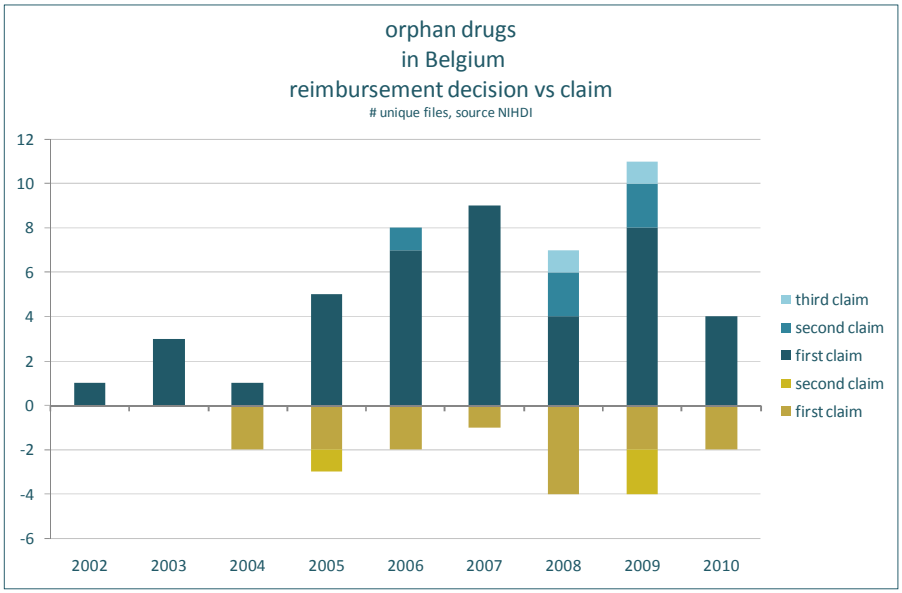


Figure 68: orphan drugs Class 1: decisions concerning the registration in the list of reimbursable specialities (detail) (claims 2002 – 2010)



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.
BCFI. (2010). *Gecommentarieerd Geneesmiddelenrepertorium.*
RIZIV. (2011 mei). *Gestandaardiseerd verslag in toepassing van artikel 51, § 4 van de GVU Wet - Sector 3: Farmaceutische Verstrekkingen - Geboekte Uitgaven 201012.*
RIZIV. (2011). *Medische Beeldvorming - Rationeel Voorschrijven - Sensibilisering voor het blootstellingsrisico aan ioniserende straling.* Brussels.
RIZIV. (2011 juli). *nota CGV 2011/263 Evolutie van de maandelijkse uitgaven van de verzekering voor geneeskundige verzorging. MAART 2011, p 7.*
Werkgroep van de Multipartiete Overlegstructuur . (2011 mei). *Nota CGV 2011/182 Evaluatie van de forfaitarisering van de geneesmiddelen in ziekenhuizen.*

ATTACHMENT 1:

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

SPECIALITY		
TAXOTERE (docetaxel)	*20 mg injection vial concentrate for solution for infusion 10 mg/ml* *80 mg injection vial concentrate for solution for infusion 10 mg/ml*	*Modification*
effective as of : 01-01-2010 *hospital: * and ***	- treatment of **local advanced or metastasized breast cancer** - treatment of **local advanced or metastasized non-small cell lung cancer** - treatment in combination with doxorubicin of patients with **local advanced or metastasized breast cancer** - treatment of **metastatic hormone-resistant prostate cancer** **- adjuvant treatment of operable breast cancer** - treatment of **local advanced or metastasized non-small cell lung cancer in combination with cisplatin** - treatment with **cisplatin and 5-fluorouracil of patients with metastasized adenocarcinoma of the stomach** - **induction treatment in combination with cisplatin and 5-fluorouracil of patients with local advanced non-metastasized squamous cell carcinoma of the hypopharynx, larynx, oral cavity, or oropharynx**	BI : 1.870.000 €
SPRYCEL (dasatinib)	*30 film-coated tablets 100 mg*	*orphan drug*
effective as of : 01-01-2010 *hospital: * and ***	- treatment of chronic myeloid leukemia with an entitled patient 18 years of age or older and in whom the **chronic myeloid leukemia is found in the chronic phase** - treatment of **chronic myeloid leukemia** with an entitled patient 18 years of age or older and in whom the chronic myeloid leukemia **is found in an accelerated phase or blast crisis phase**	BI : -

	- treatment of **acute lymphoblast leukemia**	

CAELYX (doxorubicine)	*2 mg/ml 1 injection vial concentrate for solution for infusion 1 x 25 ml ; 1 x 10 ml*	*Modification*
*effective as of : 01-01-2010 hospital: * and ***	treatment, in combination with VELCADE, for patients with **multiple myeloma** who display a progression of the disease and that have undergone at least one previous treatment schedule that contained at least one stem cell transplant	BI : 220.000 € - 370.000 €.

AVASTIN (bevacizumab)	*Injection vial concentrate for solution for infusion 400 mg/16 ml; injection vial concentrate for solution for infusion 100 mg/4 ml*	*Modification*
*effective as of : 01-02-2010 hospital: * and ***	First-line treatment of patients **with metastasized triple negative breast cancer** in combination with paclitaxel.	BI : 500.000 € year 1, 900.000 € year 2 and 1.300.000 € year 3

ERBITUX (cetuximab)	*5 mg/ml solution for infusion, Injection vial 1 x 100 ml Injection vial 1 x 20 ml*	*Claim Class 2*
*effective as of : 01-02-2010 hospital: * and ***	- treatment of a **metastasized colorectal carcinoma of which the K-RAS gene has not mutated** - treatment of a stage III or IV **local advanced non-metastasized squamous cell carcinoma of the oropharynx, hypopharynx, or larynx**	BI : -

OXALIPLATIN SANDOZ (oxaliplatin) **OXALIPLATIN HOSPIRA (oxaliplatine)**	*5 mg/ml solution for infusion: 1 vial 50 mg; 1 vial 100 mg* *5 mg/ml solution for infusion 1 vial 40 ml*	*Modification*

effective as of : 01-02-2010 *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 : -

IRINOTECAN MYLAN (irinotecan)	*500 mg/25 ml concentrate for solution for infusion, 1 injection vial 1 x 25 ml*	*Claim Class 3*
effective as of : 01-02-2010 *hospital: * and ***	- treatment of **metastasized colorectal cancer** - **second-line treatment of metastasized colorectal cancer**	BI : -

CARBOPLATIN SANDOZ (carboplatin)	*Concentrate for solution for infusion* *5 injection vials 50 mg* *1 injection vial 1 x 150 mg* *1 injection vial 1 x 450 mg*	*Claim Class 3*
effective as of : 01-02-2010 *hospital: * and ***	-Treatment of a**dvanced ovarian carcinoma**	BI : -

SUTENT (sunitinib)	*12.5 mg 30 hard capsules* *25 mg 30 hard capsules* *50 mg 30 hard capsules*	*Individual review*
effective as of : 01-02-2010 *hospital: * and ***	- Treatment of an unresectable and/or metastasized malignant gastro-instantinal stroma tumor (DIST) - Treatment of an **advanced and/or metastasized renal cell carcinoma** (stage IV)	BI: -

ATRIANCE (nelarabine)	*5 mg/ml solution for intravenous infusion 6 vials*	*Individual review*
effective as of : 01-02-2010 *hospital: * and ***	Treatment of a patient with **acute T-cel lymphoblastic leukemia or a T-cel lymphoblastic lymphoma**	BI : -

YONDELIS (trabectedine)	*Powder for concentrate for solution for intravenous infusion 0,05 mg/ml* *0,25 mg 1 vial 0,05 mg/ml* *1 mg 1 vial 0,05 mg/ml*	*Modification*

effective as of : 01-02-2010 *hospital: * and ***	Treatment, in combination with pegylated liposome doxorubicin, of patients with **platinum sensitive recurrent epithelial ovarian cancer**	BI : €981.290,49

AFINITOR (everolimus)	*5 mg 30 tablets* *10 mg 30 tablets*	*orphan drug*
effective as of : 01-03-2010 *hospital: * and ***	Treatment of clearcell **advanced renal carcinoma** with patients whose illness has become progressive conform to the RECIST criteria during or following a VEGF or VEGF-R-directed therapy.	BI : 2.132.000€ per year

GEMCITABINE MYLAN (gemcitabine)	*38 mg/ml, injection vial powder for solution for infusion* *1 vial 200 mg* *1 vial 1000 mg*	*Claim Class 3*
effective as of : 01-03-2010 *hospital: * and ***	-Treatment of **non-small cell lung cancer** -Treatment of a **local advanced or metastasized adenocarcinoma of the pancreas** -Treatment of **local advanced or metastasized bladder cancer** -Treatment, in combination with carboplatin, of **advanced recurrence of an ovarian epithelial carcinoma** -Treatment of an **advanced recurrence of an ovarian epithelial carcinoma**, -Treatment, in combination with paclitaxel, of **local advanced metastasized or local recurrent breast cancer**	BI : -

FLUDARA (fludarabine)	*50 mg injection vial powder for solution for infusion and injection; 5 vials*	*Modification*
effective as of : 01-03-2010 *hospital: * and ***	Treatment of a patient with **B-cell chronic lymphatic leukemia**	BI : -

GEMZAR (gemcitabine)	*Powder for solution for infusion* *1 x 200 mg; 1 x 1000 mg* *Powder for solution for infusion*	*Modification*

GEMCITABINE SANDOZ (gemcitabine)	*1 x 200 mg; 1 x 1000 mg*	
VINORELBINE ACTAVIS (vinorelbine)	*Powder for solution for infusion 10 vials 1 ml; 10 vials 5 ml*	
VINORELBINE "Ebewe Pharma" (vinorelbine)	*Powder for solution for infusion 5 vials 1 ml/10 mg; 5 vials 5 ml/50mg*	
MYOCET (doxorubicine)	*Liposome colloid for infusion 2 vials 50 mg*	
CAELYX (doxorubicine)	*2 mg/ml concentrate for solution for infusion 1 vial 10 ml; 1 vial 25 ml*	
IRINOTECAN ACTAVIS GROUP (irinotecan)	*20mg/ml concentrate for solution for infusion: 1 vial 5 ml; 1 vial 2 ml; 1 vial 25 ml*	
IRINOTECAN MYLAN (irinotecan)	*20 mg/ml concentrate for solution for infusion: 1 vial 5 ml; 1 vial 2 ml*	
IRINOTECAN EBEWE (irinotecan)	*40 mg/2 ml concentrate for solution for infusion: 1 vial 5 ml; 1 vial 2 ml*	
CAMPTO (irinotecan)	*20mg/ml solution for infusion: 1 vial 15 ml; 1 vial 5 ml; 1 vial 2 ml*	
IRINOSIN (irinotecan)	*20 mg/ml concentrate for solution for infusion: 1 vial 25 ml; 1 vial 2 ml; 1 vial 5 ml*	
IRINOTECAN HOSPIRA (irinotecan)	*40 mg/2 ml concentrate for solution for infusion, 1 vial 2 ml; 100 mg/5 ml concentrate for solution for infusion, 1 vial 5 ml; 500 mg/25 ml concentrate for solution for infusion, 1 vial 25 ml*	
*effective as of : 01-03-2010 hospital: * and **	Deletion in the various regulatory texts of the notices concerning the issuance of an authorization to the patient by the consulting doctor prior to third-party payer invoicing.	BI : -

TAXOTERE (docetaxel)	*160 mg/8 ml concentrate for solution for infusion, 1 vial 8 ml*	*Claim Class 2*
*effective as of : 01-03-2010 hospital: * and **	- Treatment of **local advanced or metastasized breast cancer** - Treatment of **local advanced or metastasized non-small cell lung carcinoma** - treatment , **in combination with**	BI : -

	doxorubicin, of metastasized or local advanced breast cancer - treatment of **metastatic hormone-resistant prostate cancer** - adjuvant treatment of operable **breast cancer** - treatment of **local advanced or metastasized non-small cell lung cancer in combination with cisplatin** - treatment with cisplatin and 5-fluorouracil of patients with **metastasized adenocarcinoma of the stomach** - induction treatment, in combination with cisplatin and 5-fluorouracil, of **local advanced non metastasized squamous cell carcinoma of the hypopharynx, larynx, oral cavity, or oropharynx**	
VOTRIENT **(pazopanib)**	*200 mg 90 coated tablets* *400 mg 60 coated tablets*	*Claim Class 2*
effective as of : 01-03-2010 *hospital: * and ***	First-line treatment of an **advanced and/or metastasized renal cell carcinoma** (stage IV)	BI : -
HYCAMTIN **(topotecan)**	*0.25 mg 10 hard capsules* *1 mg 10 hard capsules*	*Individual review*
effective as of : 01-03-2010 *hospital: * and ***	Second-line treatment of a **recurrent small-cell lung cancer**	BI : -
GEMCITABINE HOSPIRA **(gemcitabin)** **GEMCITABINE EG** **(gemcitabin)**	*1 vial 200 mg; 1 g; 2 g concentrate for solution for infusion* *38 mg/ml concentrate for solution for infusion* *1 vial 5.26 ml* *1 vial 39.5 ml* *1 vial 26.3 ml* *1 vial 52.6 ml*	*Claim Class 2*
effective as of : 01-04-2010 *hospital: * and ***	-treatment of **non-small cell lung cancer** -treatment of **local advanced or metastasized adenocarcinoma of the pancreas**	BI : -

	-treatment of **local advanced or metastasized bladder cancer** -treatment of **advanced recurrence of an ovarian epithelial carcinoma** , - treatment, in combination with paclitaxel, of **local advanced metastasized or local recurrent breast cancer**	
BLEOMYCINE TEVA (bleomycine)	*15 U, powder for solution for injection 1 vial 10 ml*	*Claim Class 3*
effective as of : 01-04-2010 *hospital: * and ***	treatment of: **- Squamous cell carcinomas of head and neck, external genitalia or cervix** **- Hodgkins lymphoma** - Moderate and severe malignant **non-Hodgkins lymphoma** with adults **- Testicular carcinomas** - Intrapleural therapy of **malignant pleural effusion**	BI : -
AVASTIN (bevacizumab)	*25 mg/ml concentrate for solution for infusion, 100 mg/4 ml; 400 mg/16 ml*	*Modification*
effective as of : 01-05-2010 *hospital: * and ***	First-line treatment, in combination with interferon alpha -2a , of patients with **advanced and/or metastasized renal cell cancer**	BI : 1.483.000 €.
MABTHERA (rituximab)	*500 mg/50 ml concentrate for solution for infusion, 1 vial 50 ml* *100 mg/10 ml concentrate for solution for infusion, 2 vials 10 ml*	*Modification*
effective as of : 01-05-2010 *hospital: * and ***	treatment of a **non-Hodgkins lymphoma**	BI : -
VELCADE (bortezomib)	*1 mg powder for solution for injection 1 vial 1 ml*	*Claim Class 2*
effective as of : 01-06-2010 *hospital: * and ***	treatment of a **multiple myeloma**	BI : 1.160.627 € - 2.321.254 € saving
MABTHERA (rituximab)	*500 mg/50 ml concentrate for solution for infusion, 1 vial 50 ml* *100 mg/10 ml concentrate for solution for infusion, 2 vials 10 ml*	*Modification*

effective as of : 01-06-2010 *hospital: * and ***	Treatment, **in combination with chemotherapy** containing fludarabin, of a **recurring or refractory B-cell chronic lymphocytic leukemia**	BI : 612.536 €

IRESSA **(gefitinib)**	*30 tablets 250 mg*	*Claim Class 2*
effective as of : 01-07-2010 *hospital: * and ***	treatment **in monotherapy** of a **local advanced or metastasized non-small cell lung carcinoma with an activating EGFR-TK mutation**	BI : 6.288.406 €

LEDERTREXATE **(methotrexaat)**	*5 mg/2 ml solution for injection vial 12 x 2 ml*	*Claim Class 2*
effective as of : 01-08-2010 *hospital: * and ***	treatment of choriocarcinoma and other trofoblastic tumours; psoriasis and rheumatoid arthritis	BI : -

CISPLATINE TEVA **(cisplatine)**	*1 mg/ml concentrate for solution for infusion* *1 vial 10 ml* *1 vial 50 ml* *1 vial 100 ml*	*Claim Class 3*
effective as of : 01-08-2010 *hospital: * and ***	Treatment of advanced or metastasized testicular carcinoma; advanced or metastasized ovarian carcinoma; advanced or metastasized bladder carcinoma; advanced or metastasized squamous cell carcinoma of head and neck; advanced or metastasized non-small cell lung carcinoma; advanced or metastasized small cell lung carcinoma; treatment of cervical carcinoma	BI : -

TAXOTERE **(docetaxel)**	*20 mg/1 ml concentrate for solution for infusion:* *80 mg/4 ml concentrate for solution for infusion:*	*Claim Class 2*
effective as of : 01-09-2010 *hospital: * and ***	- treatment of **local advanced or metastasized breast cancer** - treatment of **local advanced or metastasized non-small cell lung cancer** - treatment in combination with doxorubicin of patients with **metastasized or local advanced breast cancer**	BI : -

	- treatment of **metastatic hormone-resistant prostate cancer** **- adjuvant treatment of operable breast cancer** - treatment of **local advanced or metastasized non-small cell lung cancer in combination with cisplatin** - treatment with **cisplatin and 5-fluorouracil of patients with metastasized adenocarcinoma of the stomach** - **induction treatment in combination with cisplatin and 5-fluorouracil of patients with local advanced non metastasized squamous cell carcinoma of the hypopharynx, larynx, oral cavity or oropharynx**	
HERCEPTIN (trastuzumab)	*powder for solution for infusion 1 vial 150 mg*	*Modification*
effective as of : 01-10-2010 *hospital: * and ***	Treatment , in combination with capecitabin or 5-fluorouracil and cisplatin, of **metastasized adenocarcinoma of the stomach or the gastro-oesophageal transition with an amplification of the gene of the Human Epidermal growth factor Receptor-2**	BI : 16 724 € per patient
IRINOTECAN MYLAN (irinotecan)	*40 mg/2 ml concentrate for solution for infusion, 1 vial 2 ml* *100 mg/5 ml concentrate for solution for infusion, 1 vial 5 ml*	*Claim Class 3*
effective as of : 01-11-2010 *hospital: * and ***	- treatment of **metastasized colorectal cancer** - **second-line treatment of metastasized colorectal cancer**	BI : -
GEMCITABINE MYLAN (gemcitabine) **GEMCITABIN EBEWE (gemcitabine)**	*200 mg concentrate for solution for infusion, 1 vial 10 ml* *1 g powder for solution for infusion 1 vial 50 ml* *10 mg/ml concentrate for solution for infusion, 1 vial 200 mg* *1 vial 500 mg* *1 vial 1000 mg*	*Claim Class 3*

GEMCITABINE FRESENIUS KABI (gemcitabine)	*38 mg/ml powder for solution* *1 vial 10 ml* *1 vial 50 ml* *1 vial 100 ml*	
effective as of : 01-11-2010 *hospital: * and ***	- treatment of **non-small cell lung cancer** - treatment of **local advanced or metastasized adenocarcinoma of the pancreas** - Treatment of **local advanced or metastasized bladder cancer** - treatment, **in combination with carboplatin,** of entitled patients with **advanced recurrence of ovarian epithelial carcinoma** - treatment, **in combination with paclitaxel,** of **local advanced metastasized or local recurrent breast cancer**	BI : -
TEMOMEDAC (temozolomide)	*5 hard capsules 140 mg* *5 hard capsules 180 mg*	*Claim Class 3*
effective as of : 01-11-2010 *hospital: * and ***	- **First-line treatment of malignant glioma** (WHO grade IV) - **second-line treatment** of malignant glioma (WHO grade IV)	BI : -
ERBITUX (cetuximab)	*5 mg/ml solution for intravenous infusion* *1 vial 20 ml; 1 vial 100 ml*	*Modification*
effective as of : 01-11-2010 *hospital: * and ***	F**irst-line treatment in combination with cisplatin** of **recurrent and/or metastasized squamous cell ccarcinoma of the head and neck area**	BI : -
NEXAVAR (sorafenib)	*200 mg 112 coated tablets*	*Individual review*
effective as of : 01-12-2010 *hospital: * and ***	treatment of **advanced renal carcinoma**	BI : - (cost of 21.468 € per patient not exceeded)
IRINOTECAN MYLAN (irinotecan)	*20 mg/ml concentrate for solution for infusion, 1 vial 25 ml*	*Claim Class 3*
effective as of : 01-12-2010 *hospital: * and ***	- treatment of **metastasized colorectal cancer** - second-line treatment of **metastasized colorectal cancer**	BI : -

ATTACHMENT 2

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
2008 – 2010

PROPOSALS OF THE CRM in function of the TYPE OF CLAIM

Table 42: number of unique claims for registration in the list of reimbursable specialities versus proposal of the Commission for the Reimbursement of Medicines (2010)

2010							
	positive		negative		no proposition		total
	number	%	number	%	number	%	number
class 1	5	45 %	4	36 %	2	18 %	11
class 2	65	90 %	6	8 %	1	1 %	72
class 3	198	95 %	7	3 %	3	1 %	208
modification	72	78 %	18	20 %	2	2 %	92
orphan	4	80 %	1	20 %			5
total	344	89 %	36	9 %	8	2 %	388

Table 43: 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 proposition		total
	number	%	number	%	number	%	number
class 1	7	58 %	1	8 %	4	33 %	12
class 2	90	85 %	5	5 %	11	10 %	106
class 3	149	99 %	1	1 %	1	1 %	151
modification	163	91 %	11	6 %	6	3 %	180
orphan	9	60 %	3	20 %	3	20 %	15
total	418	90 %	21	5 %	25	5 %	464

Table 44: 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 proposition		total
	number	%	number	%	number	%	number
class 1	4	67 %			2	33 %	6
class 2	95	83 %	9	8 %	11	10 %	115
class 3	141	96 %	6	4 %			147
modification	81	83 %	12	12 %	5	5 %	98
orphan	6	75 %	1	13 %	1	13 %	8
total	327	87 %	28	7 %	19	5 %	374

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

Table 45: decisions of the Minister in function of the proposal of the CRM (unique dossiers 2010)

2010											
	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**	**58,3%**	**2**	**16,7%**			**2**	**16,7%**	**1**	**8,3%**	**12**
positive prop	5	100 %									**5**
negative prop	1	20,0%	2	40,0%			1	20,0%	1	20,0%	**5**
no prop	1	50,0%					1	50,0%			**2**
class 2	**61**	**81,3%**	**7**	**9,3%**	**1**	**1,3%**	**3**	**4,0%**	**3**	**4,0%**	**75**
positive prop	60	89,6%	2	3,0%	1	1,5%	2	3,0%	2	3,0%	**67**
negative prop	1	14,3%	4	57,1%			1	14,3%	1	14,3%	**7**
no prop			1	100%							**1**
class 3	**199**	**95,2%**	**7**	**3,3%**	**1**	**0,5%**	**1**	**0,5%**	**1**	**0,5%**	**209**
positive prop	197	99,0%					1	0,5%	1	0,5%	**199**
negative prop			7	100%							**7**
no prop	2	66,7%			1	33,3%					**3**
modification	**62**	**66,0%**	**14**	**14,9%**			**16**	**17,0%**	**2**	**2,1%**	**94**
positive prop	59	81,9%	1	1,4%			12	16,7%			**72**
negative prop	2	10,0%	13	65,0%			3	15,0%	2	10,0%	**20**
no prop	1	50,0%					1	50,0%			**2**
orphan	**4**	**66,7%**	**1**	**16,7%**					**1**	**16,7%**	**6**
positive prop	4	100%									**4**
negative prop			1	100%							**1**
no prop									1	100%	**1**
total	**333**	**84,1%**	**31**	**7,8%**	**2**	**0,5%**	**22**	**5,6%**	**8**	**2,0%**	**396**

Table 46: 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	**9**	**52,9%**	**3**	**17,6%**					**5**	**29,4%**	**17**
positive prop	7	100%									**7**
negative prop	1	20,0%							4	80,0%	**5**
no prop	1	20,0%	3	60,0%					1	20,0%	**5**
class 2	**94**	**86,2%**	**10**	**9,2%**	**1**	**0,9%**	**1**	**0,9%**	**3**	**2,8%**	**109**
positive prop	85	93,4%	4	4,4%	1	1,1%			1	1,1%	**91**
negative prop	2	33,3%	3	50,0%					1	16,7%	**6**
no prop	7	58,3%	3	25,0%			1	8,3%	1	8,3%	**12**
class 3	**149**	**96,8%**	**2**	**1,3%**					**3**	**1,9%**	**154**
positive prop	149	98,0%							3	2,0%	**152**
negative prop			1	100%							**1**
no prop			1	100%							**1**
modification	**169**	**93,9%**	**11**	**6,1%**							**180**
positive prop	163	100%									**163**
negative prop	1	9,1%	10	90,9%							**11**
no prop	5	83,3%	1	16,7%							**6**
orphan	**11**	**73,3%**	**4**	**26,7%**							**15**
positive prop	8	88,9%	1	11,1%							**9**
negative prop	1	33,3%	2	66,7%							**3**
no prop	2	66,7%	1	33,3%							**3**
total	**432**	**90,9%**	**30**	**6,3%**	**1**	**0,2%**	**1**	**0,2%**	**11**	**2,3%**	**475**

Table 47: 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	**100**	**80,6%**	**15**	**12,1%**					**9**	**7,3%**	**124**
positive prop	93	95,9%	2	2,1%					2	2,1%	**97**
negative prop	2	13,3%	7	46,7%					6	40,0%	**15**
no prop	5	41,7%	6	50,0%					1	8,3%	**12**
class 3	**143**	**97,3%**	**4**	**2,7%**							**147**
positive prop	141	100%									**141**
negative prop	2	33,3%	4	66,7%							**6**
no prop											
modification	**87**	**88,8%**	**9**	**9,2%**	**2**	**2,0%**					**98**
positive prop	78	96,3%	1	1,2%	2	2,5%					**81**
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	**343**	**89,6%**	**29**	**7,6%**	**2**	**0,5%**			**9**	**2,3%**	**383**

ATTACHMENT 4

SUMMARY OF THE FIGURES

SUMMARY OF THE TABLES