

Reimbursement of Medicines

5 years experience with CRM procedure

SRBGE Brussels Oct 2007

Philippe Van Wilder

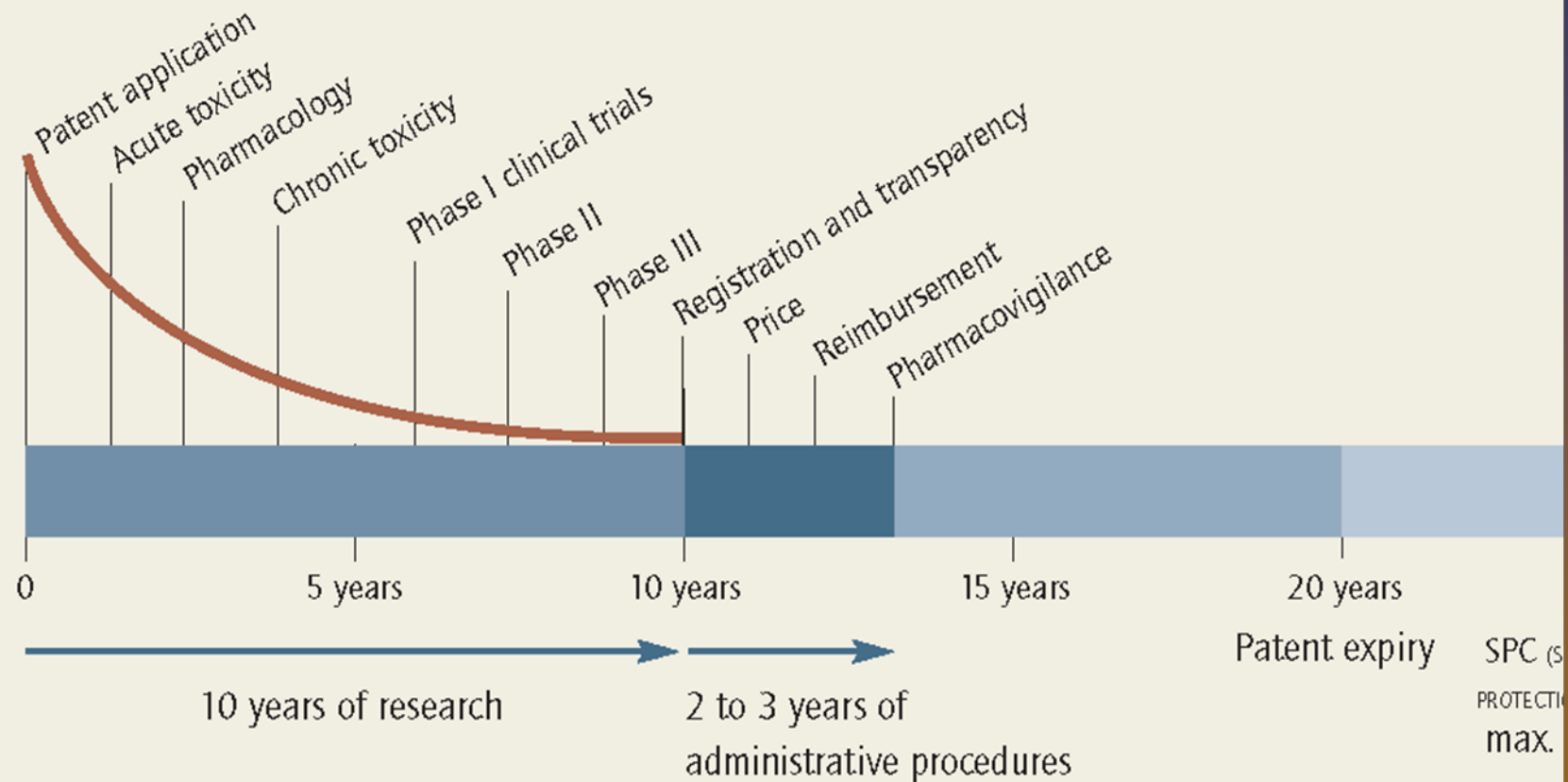
RIZIV - INAMI

Head Reimbursement of Medicines Dept.

Structure

1. Market authorisation versus reimbursement decision
2. Reimbursement procedure
3. Reimbursement facts & figures

Product life-cycle



Source: Recherche & Vie, LIM (AGIM)

1. Marketing Authorization versus Reimbursement Evaluation



Marketing Application
Authorization (MAA) >



Reimbursement
decision >

1. European Centralized or Mutual Recognition
2. Dossier based on
 - Efficacy
 - Safety
 - Pharmaceutical quality
3. Benefit/risk balance of the drug on its own

1. Per member state
2. Dossier goes beyond MAA-elements:
 - + Effectiveness
 - + Convenience
 - + others
3. Relative therapeutic value as compared to alternatives
4. Relative economic value as compared to alternatives

$$\Delta C / \Delta E$$

HealthCast 2020: Creating a Sustainable Future*

PricewaterhouseCoopers' Health Research Institute



*connectedthinking

Executive Summary

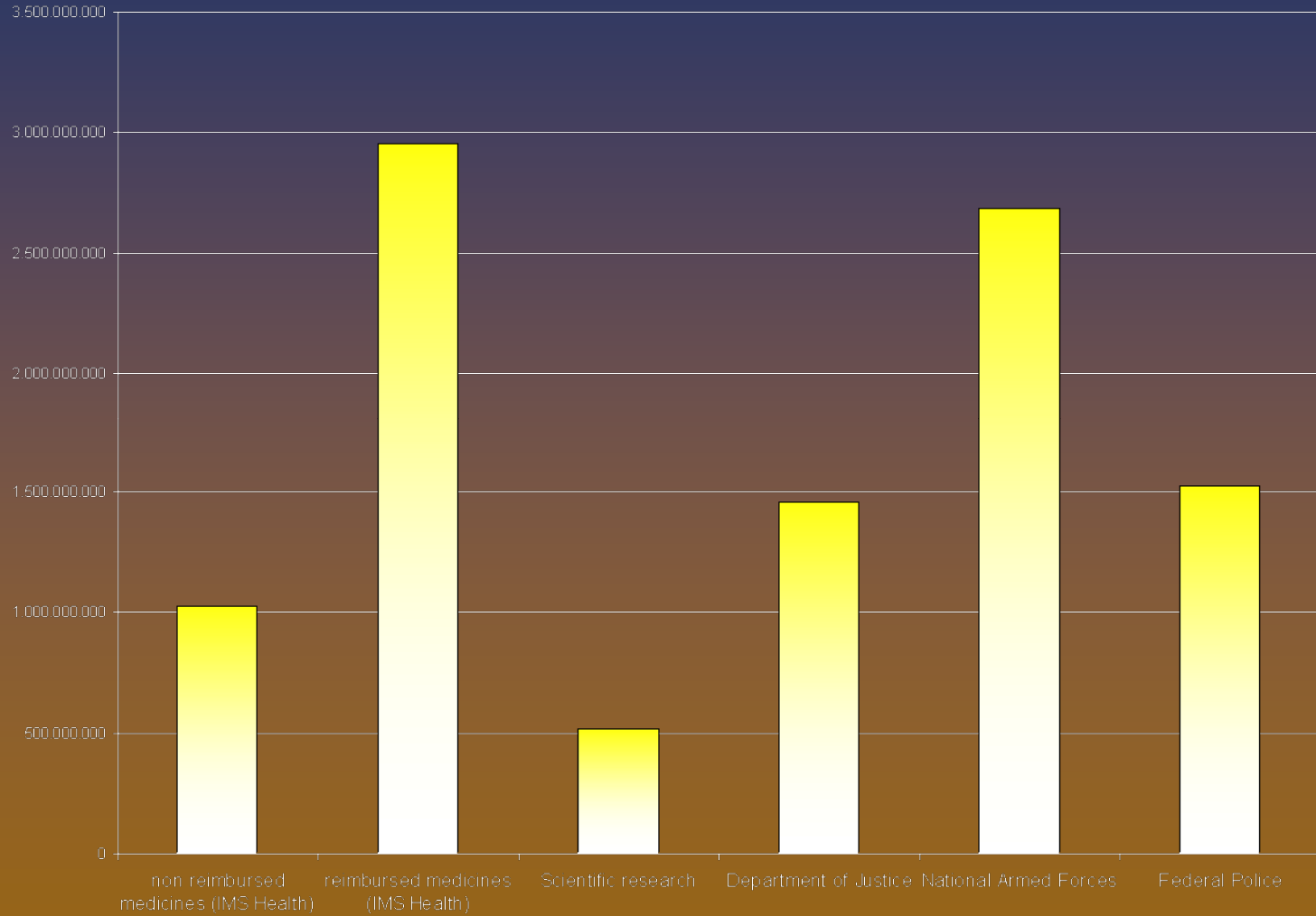
Look out. Better yet, look outward.

There is growing evidence that the current health systems of nations around the world will be unsustainable if unchanged over the next 15 years. Globally, healthcare is threatened by a confluence of powerful trends – increasing demand, rising costs, uneven quality, misaligned incentives. If ignored, they will overwhelm health systems, creating massive financial burdens for individual countries and devastating health problems for the individuals who live in them.

Expected to go bankrupt according to this report:

- US Medicare Trust Fund by 2019
- French healthcare system by 2020

Budget 2006 (in EURO)

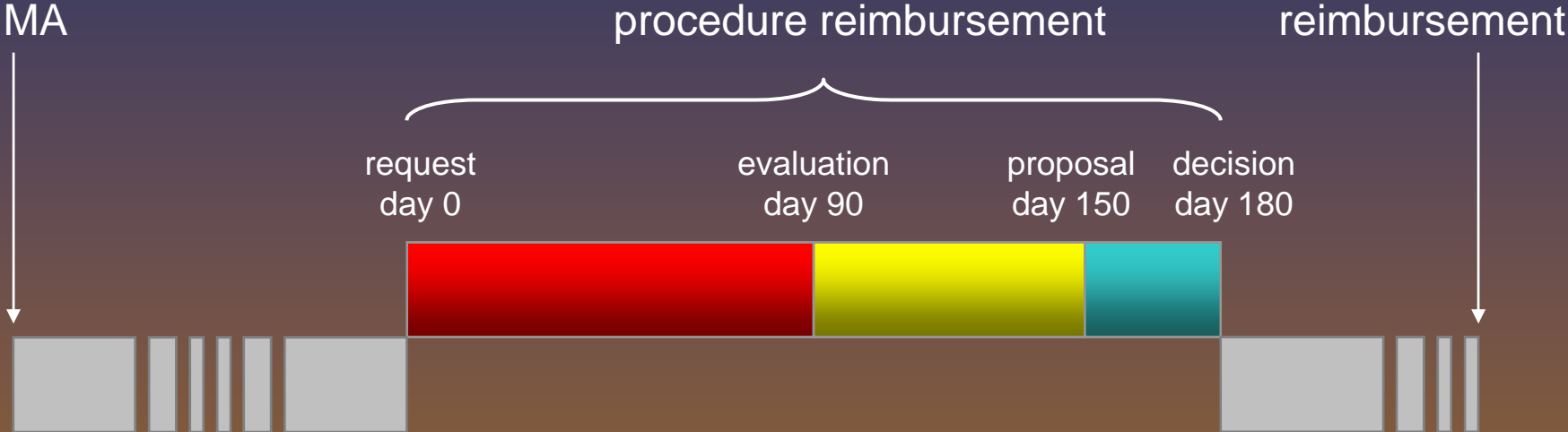


2. Reimbursement procedure

Reimbursement Key Features



- Positive list based on dossier submitted by applicant
- Claiming added (class 1 price premium) or similar value (class 2)
- Reimbursement granted within SPC
- Reimbursement may be limited to specific subgroups
- Different reimbursement categories (A B C Cs Cx D)
- 2 phases in reimbursement procedure:
 - Evaluation of scientific evidence
 - Concrete Reimbursement proposal
- Conditional listing in case of cl I >>> Review! (18-36m)



Composition of the CRM/CTG



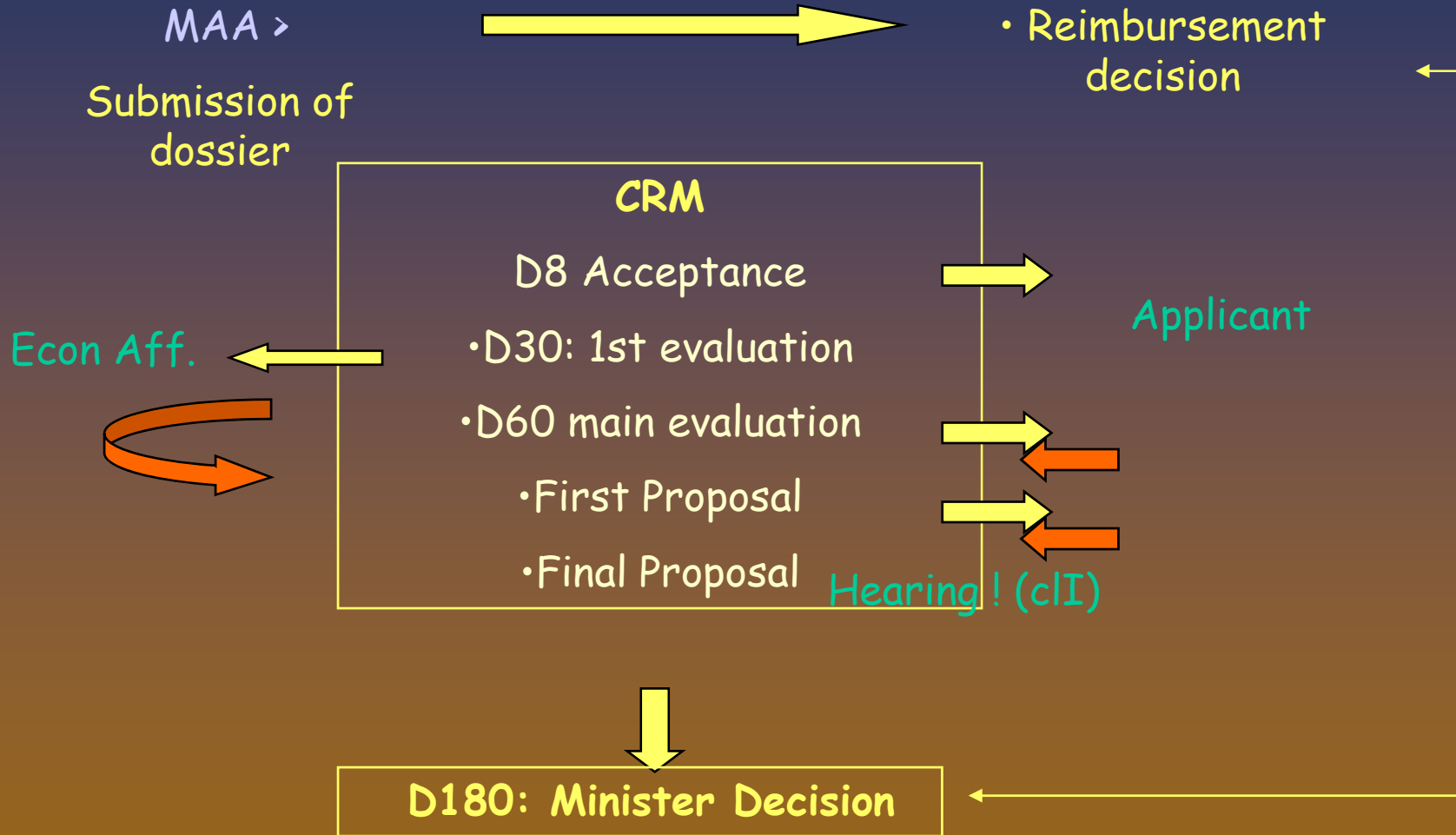
30 members

- 22 voting members :
 - 7 academics
 - 8 sick funds
 - 4 physicians association
 - 3 pharmacists association
- 8 non voting members :
 - 4 ministry rep.
 - 1 INAMI/RIZIV
 - 2 Pharma.be
 - 1 Febelgen



- academics
- sick funds
- physician's assoc
- pharmacists assoc
- non voting members

Reimbursement Evaluation Process : Belgium



Evaluation criteria

- Therapeutic value
- Price and proposed reimbursement level ← CI III
- Position of the drug in medical practice (therapeutic and social needs) ← CI III
- Budgetary impact to National Insurance Agency ←
- **class I** only: Efficiency (cost / therapeutic value)

Therapeutic value



- Efficacy
- Safety
- Effectiveness
- Applicability
- Convenience

= sum of elements

As determined by :

- Morbidity
- Mortality
- Quality of life

- > class I added value
- > class II comparable value
- class III copy/generic

R.D Dec.21st, 2001 via: www.inami.be

Questions addressed by reimbursement procedure:

- Clinical data (RCT)
- Epidemiological data
- Real Life data
- Health economics data
- Budget impact data



Efficacy

= Can it work ?

controlled setting

Effectiveness

= Does it work ?

daily practice

Efficiency

= Is it worthwhile ?

cost-effective

Submission for reimbursement in Belgium, France and the Netherlands

Source:

Reimbursement agencies:

MAA

Elements included in (A)TV:

	B RIZIV	FR HAS	NL CVZ	EMEA
Efficacy	✓	✓	✓	✓
Safety	✓	✓	✓	✓
Effectiveness	✓	✓	✓	
Applicability	✓	✓	✓	
Convenience	✓	✓	✓	
Disease severity		✓		
Other:				
Experience:			✓	
Conditional:	✓	✓	✓	
<u>Added value:</u>	✓	✓	✓	

Class I - medicines: Conditional reimbursement / review procedure

R.D. of Dec 21st 2001 : Art.16, 62, & 63

- Elements & timelines > specified in CRM proposition
- Timelines: within 18m to 36m
- Aim = Confirmation y/n of assumptions at initial approval

- Criteria :
 - Those applicable to therapeutic value assessment but special emphasis on : effectiveness, PE in daily practice
 - Sales volume
 - Reimbursement modalities in European Member States

- Additional elements:
 - Recent documents/guidelines from CRM
 - Scientific studies (peer reviewed)
 - Yearly cost evolution within therapeutical class
 - Prescribed daily dose
 - Other elements relating to applicability and effectiveness
 - Consensus reports

3. Reimbursement facts & figures

Belgium, CRM procedure, 2002 - 2006 data

Number of unique* finished submissions in the period 2002-2006

* unique = same DCI same day0 same decision

Year of submission	Type of submission							Total
	cl 1	cl 2	cl 3	orphan	Change in reimburse.	other	Revision cl 1	
2002	24	94	123	1	64	60	0	366
2003	21	99	118	3	64	53	0	358
2004	20	68	141	2	59	65	2	357
2005	18	85	115	8	65	70	6	367
2006	17	62	80	7	39	25	9	239
Total	100	408	577	21	291	273	17	1687

Note: 2006 is an underestimate because only finished files are considered

Crosstabulation
Minister Decision split per type of submission

Minister Decision	N (%)	Type of submission							Total
		cl 1	cl 2	cl 3	orphan	chng reim	other	rev cl 1	
pos	Count	63	310	528	15	188	194	12	1310
	% column	63,0%	76,0%	91,5%	71,4%	64,6%	71,1%	70,6%	77,7%
neg	Count	32	62	14	4	67	42	1	222
	% column	32,0%	15,2%	2,4%	19,0%	23,0%	15,4%	5,9%	13,2%
no dec	Count	2	22	25	0	16	36	0	101
	% column	2,0%	5,4%	4,3%	,0%	5,5%	13,2%	,0%	6,0%
closed	Count	0	0	0	0	2	0	0	2
	% column	,0%	,0%	,0%	,0%	,7%	,0%	,0%	,1%
missing	Count	3	14	10	2	18	1	4	52
	% column	3,0%	3,4%	1,7%	9,5%	6,2%	,4%	23,5%	3,1%
Total	Count	Count	408	577	21	291	273	17	1687
	% row	% column	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%



INCENTIVES FOR BREAKTHROUGH DRUGS

William B. Schultz



ZUCKERMAN SPAEDER LLP

HOW SUCCESSFUL HAVE WE BEEN IN STIMULATING INNOVATION?

■ Prescription Drug Spending

- 1980 - \$40 billion
- 2005 - \$250 billion

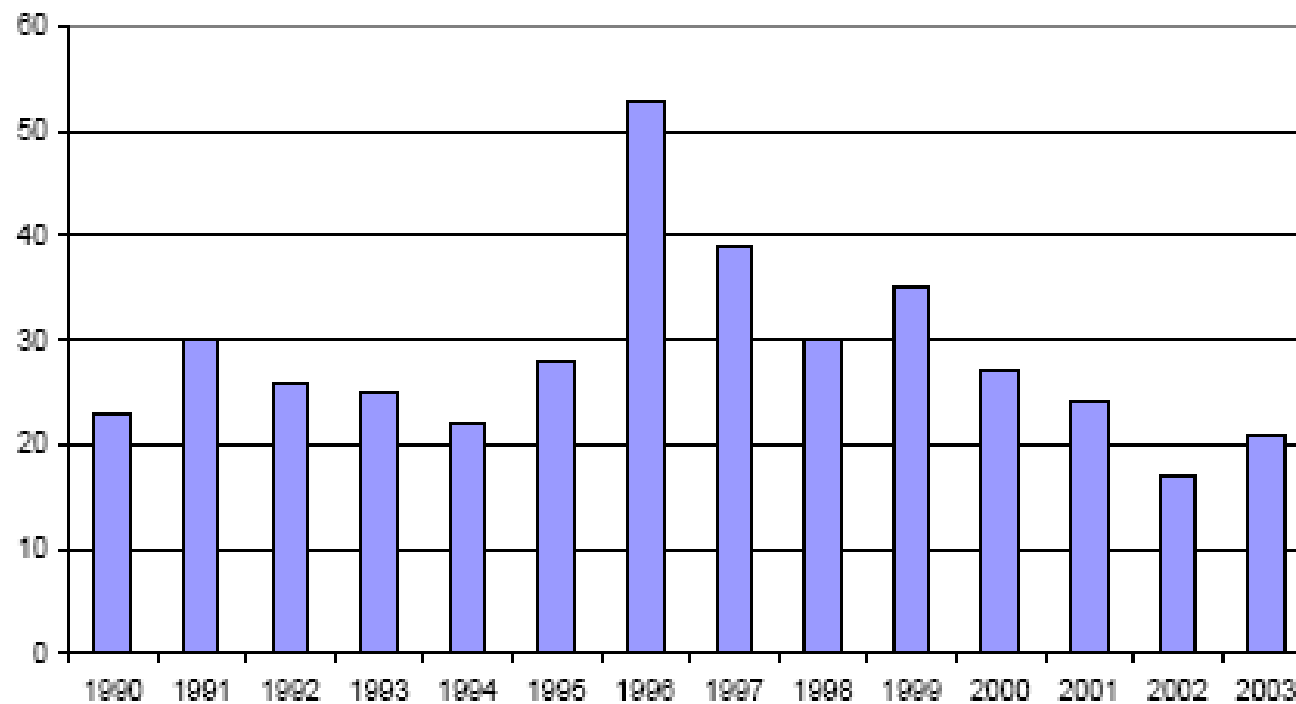
■ Has the money been spent on developing important drugs? In her book, *The Truth about the Drug Companies*, Marcia Angel compiled figures for 1998 - 2002

- 415 drugs approved
- 133 (32%) new molecular entities (the rest were variations on old drugs)
- 58 (14%) deemed by FDA to be a significant therapeutic advance
- 12 drugs a year with a significant therapeutic advance; only 2-3 breakthrough drugs per year

Conclusion

- During the past 20 years, Congress has been very generous with patent incentives and other exclusivities
- Incentives have blocked less expensive generic drugs, raised drug prices and made brand companies profitable
- Impact of the patent extensions and exclusivities have been modest
 - The six month pediatric exclusivity stimulated research on pediatric indications
 - Orphan Drug provisions have stimulated research on some drugs for rare diseases
 - Have led to development of products and innovations that offer no additional therapeutic benefit
 - Creative research by attorneys
- Less clear that these expensive incentives have actually stimulated innovation leading to more important, breakthrough drugs

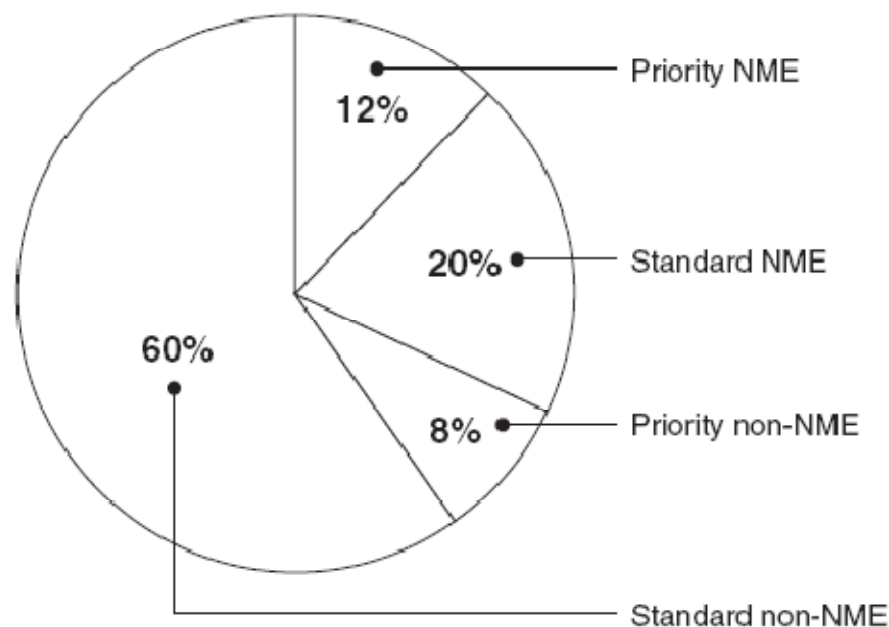
Figure 15: NMEs approved



Source: FDA <http://www.fda.gov/cder/rdmt/>

Based on how FDA classified the 1,264 NDAs submitted from 1993 through 2004, we determined the proportion of NDAs submitted by each of the four classifications. As figure 5 shows, 68 percent of the NDAs were classified as non-NMEs—those representing modifications to existing drugs, while the remaining 32 percent of the NDAs submitted were NMEs. The figure also shows that 12 percent of NDA submissions were for drugs in the priority NME classification—those representing the highest potential level of innovation.

Figure 5: Proportion of 1,264 NDAs Submitted by Innovation Potential, 1993-2004



Source: GAO analysis of FDA data.



http://www.has-sante.fr/portail/upload/docs/application/pdf/rapport_activite_has_2005_2006_09_1 - Microsoft Internet Explorer

Address: http://www.has-sante.fr/portail/upload/docs/application/pdf/rapport_activite_has_2005_2006_09_12_16_25_40_866.pdf

Voir site H.A.S.

Répartition des SMR attribués en 2005

Importance	Ins*	EI**
Important	108	32
Moderé	9	5
Faible	5	0
Insuffisant	6	2

Répartition des ASMR attribuées en 2005

Catégorie	Ins*	EI**
I	3	2
II	6	4
III	12	9
IV	12	6
V	75	18
Commentaires	16	1
non précisé ou sans objet	5	0

*Ins : Première inscription
**EI : Extension d'indication

16,54 x 11,69 in | 11 (10 of 36) | 16:30

Extrait du Rapport INAMI 2006

Tableau 9 - Prescription de spécialités pharmaceutiques - Répartition selon les grandes classes ATC - Evolution 2001 - 2005

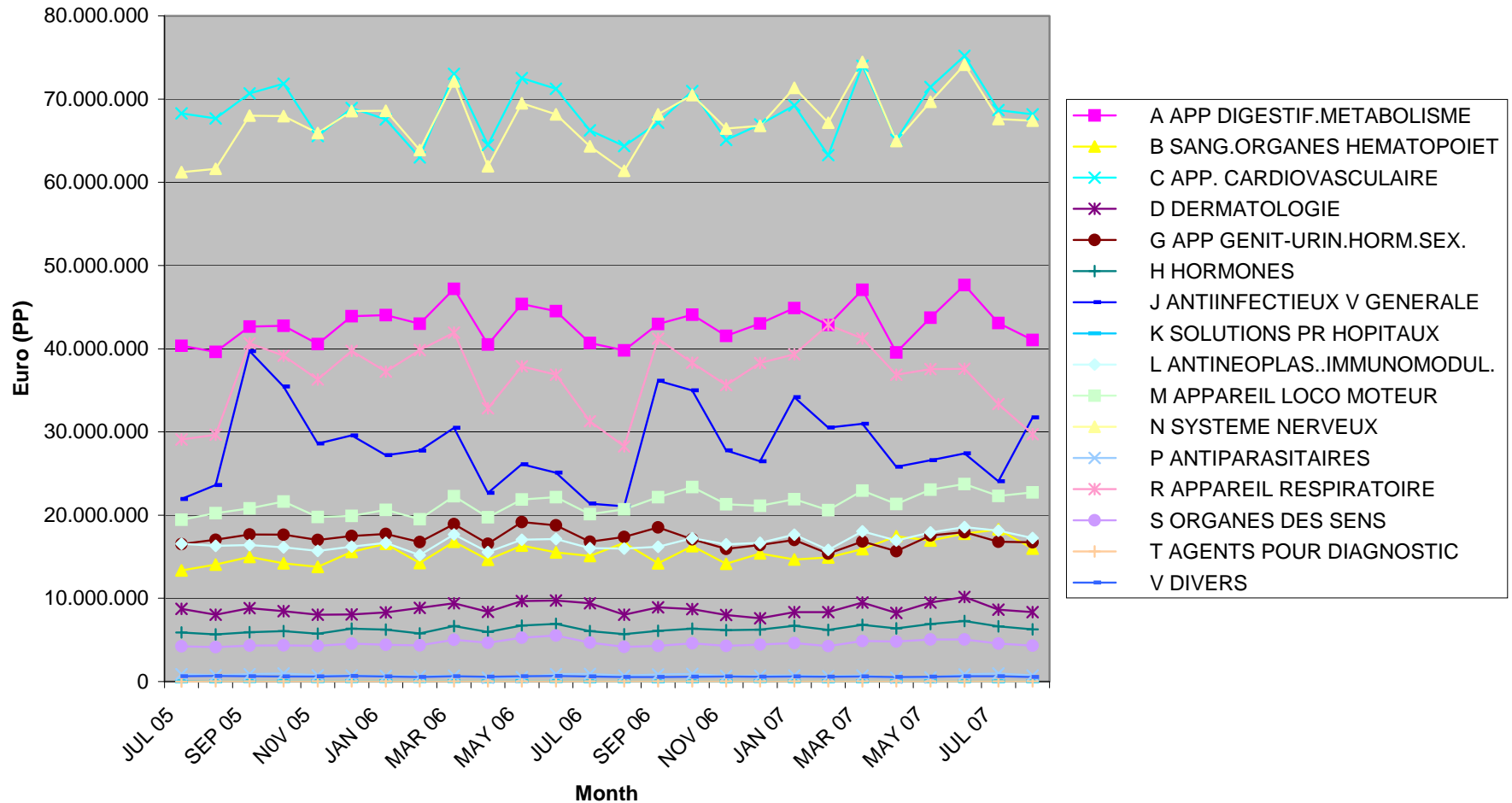
	Montants remboursés par l'assurance	2001	2002	2003	2004	2005
A	Tractus gastro-intestinal et métabolisme	211 083 632	222 200 578	237 595 860	253 876 559	243 276 126
B	Sang et système hématopoïétique	60 537 845	81 412 787	97 428 052	112 167 361	125 008 403
C	Système cardio-vasculaire	529 406 517	554 882 205	562 180 648	590 932 295	559 165 708
D	Préparations dermatologiques	30 279 338	31 401 010	31 292 064	33 677 900	33 397 601
G	Système uro-génital et hormones sexuelles	45 179 638	50 903 398	53 091 220	56 413 861	48 818 718
H	Hormones systémiques, sauf les hormones sexuelles	51 589 295	52 819 902	55 374 849	56 108 006	58 761 908
J	Anti-infectieux à usage systémique	214 755 275	210 549 127	214 232 399	205 026 584	204 962 869
L	Cytostatiques, agents immunomodulateurs	121 376 101	133 654 141	162 709 856	195 560 554	222 583 554
M	Système squelettique et musculaire	84 013 101	97 248 419	108 003 036	114 198 870	103 619 018
N	Système nerveux central	258 812 648	290 157 750	327 853 710	361 895 061	363 631 098
P	Antiparasitaires	687 538	686 571	696 394	695 192	636 208
R	Système respiratoire	160 381 060	167 529 494	170 359 938	182 158 168	190 105 233
S	Organes sensoriels	19 659 294	20 626 811	24 291 842	26 305 913	27 714 284
V	Divers	3 965 157	7 514 319	18 168 008	21 530 997	24 145 926
	Total	1 791 726 438	1 921 586 511	2 063 277 874	2 210 547 321	2 205 826 653

Extrait du Rapport INAMI 2006

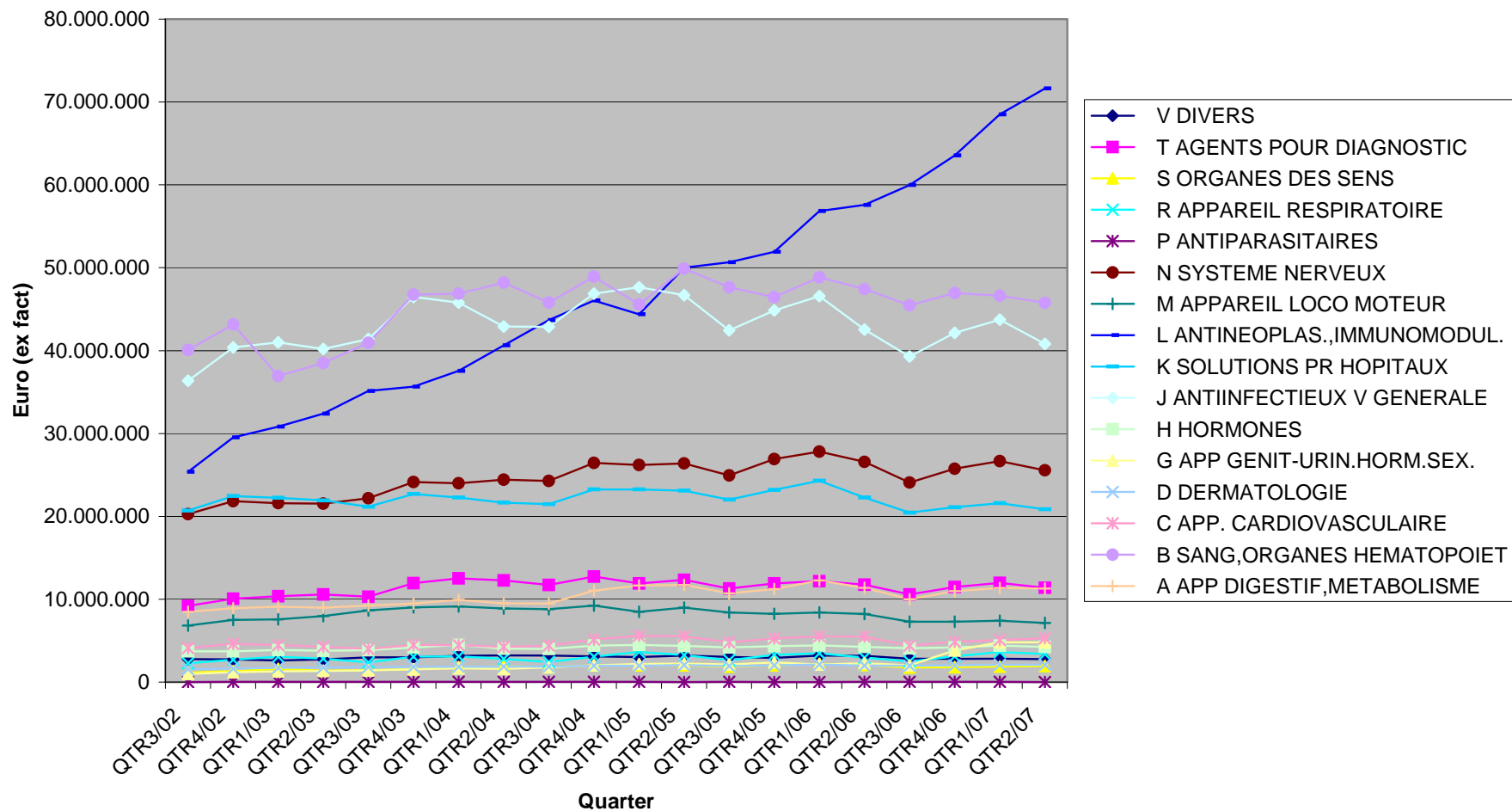
	Coût moyen (Montants remboursés/DDD)	2001	2002	2003	2004	2005
A	Tractus gastro-intestinal et métabolisme	0,82	0,79	0,76	0,72	0,66
B	Sang et système hématopoïétique	1,01	1,57	1,60	1,63	1,67
C	Système cardio-vasculaire	0,45	0,44	0,41	0,39	0,35
D	Préparations dermatologiques	1,22	1,25	1,26	1,31	1,31
G	Système uro-génital et hormones sexuelles	0,12	0,14	0,15	0,16	0,25
H	Hormones systémiques, sauf les hormones sexuelles	0,48	0,47	0,47	0,46	0,48
J	Anti-infectieux à usage systémique	2,17	2,11	2,10	2,09	1,96
L	Cytostatiques, agents Immunomodulateurs	4,53	4,62	5,13	5,67	6,30
M	Système squelettique et musculaire	0,48	0,50	0,51	0,52	0,49
N	Système nerveux central	0,93	0,96	1,01	1,03	1,01
P	Antiparasitaires	0,55	0,55	0,54	0,52	0,47
R	Système respiratoire	0,53	0,54	0,54	0,58	0,58
S	Organes sensoriels	0,29	0,31	0,34	0,37	0,39
V	Divers	13,65	15,87	18,20	17,84	17,88

Source: INAMI - Service des soins de santé - Section Pharmanet

IMS Health LMPB per ATC main class



IMS Health BHA: sales per ATC main class



Officine ouverte: dépenses INAMI



Dépenses ATC-3 (top 80%)	2.005	2.006	cum % 2006	gr_0504	gr_0605
C10A	192.635.720	177.632.318	8,2%	-4,8%	-7,8%
N06A	145.441.503	133.414.435	14,4%	-7,6%	-8,3%
A02B	134.625.561	115.704.285	19,8%	-9,3%	-14,1%
L04A	81.336.572	93.962.281	24,2%	33,2%	15,5%
B01A	91.160.765	92.713.509	28,5%	7,4%	1,7%
R03A	95.712.874	92.130.224	32,8%	1,4%	-3,7%
N05A	73.682.990	82.019.434	36,6%	13,1%	11,3%
L03A	55.825.131	57.716.400	39,2%	9,6%	3,4%
A10A	51.111.799	55.699.997	41,8%	6,9%	9,0%
C07A	56.571.504	54.890.793	44,4%	-5,2%	-3,0%
C09C	54.321.089	54.104.346	46,9%	1,0%	-0,4%
N02A	53.870.831	53.291.681	49,4%	2,2%	-1,1%
C09A	56.050.156	51.842.227	51,8%	-3,1%	-7,5%
M01A	55.640.311	46.578.839	53,9%	-19,8%	-16,3%
J05A	43.802.626	46.527.275	56,1%	6,9%	6,2%
M05B	41.162.082	43.368.491	58,1%	8,8%	5,4%
A10B	40.527.849	42.851.706	60,1%	3,4%	5,7%
N03A	38.290.600	42.144.355	62,1%	-4,9%	10,1%
R03B	41.916.373	41.525.528	64,0%	15,3%	-0,9%
C08C	45.900.233	41.278.518	65,9%	-24,9%	-10,1%
J01C	42.218.684	40.657.860	67,8%	4,7%	-3,7%
C01D	42.206.577	39.541.492	69,6%	-3,7%	-6,3%
B02B	32.157.061	37.310.474	71,4%	24,3%	16,0%
C09D	27.810.545	31.877.353	72,8%	15,6%	14,6%
L02A	30.062.062	29.265.756	74,2%	-5,0%	-2,6%
L02B	32.768.333	28.837.165	75,5%	2,2%	-12,0%
J02A	30.062.866	24.223.918	76,7%	-10,8%	-19,4%
V03A	23.202.502	23.525.530	77,7%	13,8%	1,4%
N06D	20.257.966	23.407.172	78,8%	23,7%	15,5%
J01M	25.349.002	23.000.354	79,9%	-2,2%	-9,3%
N04B	21.622.035	22.176.984	80,9%	5,7%	2,6%

Officine hospitalière: ventes IMS



IMS BHA ex fact	yr_06	cum_06	pct_06	gr_0403	gr_0504	gr_0605
L01 ANTINEOPLASIQUES	164.133.773	164.133.773	16,4%	20,0%	18,3%	24,0%
J01 ANTIBACTERIENS SYSTEMIQ.	105.413.504	269.547.277	27,0%	-0,6%	1,5%	-11,6%
B03 ANTIANEMIQUES	92.044.175	361.591.452	36,2%	13,9%	-3,7%	-3,3%
L04 AGENTS IMMUNOSUPPRES.	49.776.545	411.367.997	41,2%	45,7%	27,1%	21,3%
K01 SOL INTRAVENEUSES	59.510.837	470.878.834	47,2%	0,6%	3,7%	-3,8%
B01 THROMBOLYTIQUES	49.003.966	519.882.800	52,1%	18,8%	-1,6%	-2,4%
T01 DIAGNOSTIC PAR IMAGERIE	44.978.799	564.861.599	56,6%	13,7%	-4,0%	-3,3%
B02 ANTIHEMORRAG ET HEMOSTAT	47.629.113	612.490.711	61,4%	19,5%	10,6%	7,7%
N01 ANESTHESIQUES	43.791.381	656.282.092	65,8%	7,4%	-0,4%	-2,3%
J06 SERUMS ET Y GLOBULINES	33.112.026	689.394.118	69,1%	22,2%	2,4%	3,4%
N05 PSYCHOLEPTIQUES	27.402.312	716.796.430	71,8%	16,8%	18,4%	8,4%
L03 AGENTS IMMUNOSTIMULANTS	22.876.342	739.672.771	74,1%	30,2%	-0,4%	2,8%
N02 ANALGESIQUES	20.717.548	760.390.320	76,2%	21,8%	6,9%	-1,3%
M05 AUTR PRDT PR APP LOC-MOT	21.359.982	781.750.302	78,3%	8,5%	-7,1%	-12,8%
J02 ANTIMYCOTIQUES V.GENERALE	16.444.361	798.194.663	80,0%	18,3%	-1,0%	8,2%
J05 ANTIVIRAUX SYSTEMIQUES	12.538.351	810.733.014	81,2%	17,1%	3,7%	4,5%
K04 SOL INJ/ADDI.PERF.<100ML	12.530.957	823.263.971	82,5%	1,0%	4,8%	0,8%
A04 ANTIEMETIQUES,ANTINAUSEE	13.774.661	837.038.632	83,9%	11,8%	-1,9%	-8,1%
A16 DIVERS APP.DIGESTIF	9.987.651	847.026.283	84,9%	92,1%	148,9%	11,2%
G03 HORM.SEX.INDUCT APP GENIT	2.604.418	849.630.701	85,1%	23,3%	2,8%	202,8%
R03 ANTIASSTM & COPD PRDTS	9.146.461	858.777.163	86,0%	3,4%	13,2%	-4,8%
V03 MEDICAMENTS DIVERS	11.791.528	870.568.690	87,2%	10,5%	-5,0%	-0,7%
H02 CORTICOIDES VOIE GENERALE	10.117.191	880.685.881	88,2%	-0,9%	1,1%	-0,6%
K03 SUBSTITUTS SANG ET PLASMA	10.811.450	891.497.331	89,3%	1,4%	-0,6%	-7,6%
A02 A-ACID.A-FLATUL.A-ULCER.	8.684.804	900.182.135	90,2%	-4,6%	-3,3%	-6,3%

Thank you !

Philippe Van Wilder

RIZIV - Reimbursement of Medicines