NIHDI

Monitoring Of Reimbursement Significant Expenses

Reimbursable drugs

MORSE report - 2024 data

.be

Colophon

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List of acronyms

Acronyms	Definition
AM (French), MO (English)	Arrêté ministériel, Ministerial Order
MB (Dutch)	Ministerieel Besluit
AR (French), RD (English)	Arrêté royal, Royal Decree
KB (Dutch)	Koninklijk Besluit
ARV	Antiretroviral
ATC	Anatomical, Therapeutic and Chemical Classification System for pharmaceutical specialties
BCMA	B-cell maturation antigen
BIC	Bictegravir
BTKI	Bruton's tyrosine kinase inhibitors
CAR-T	Chimeric antigen T cell receptors
CDK4/6	Cyclin-Dependent Kinases 4 and 6
(anti) - CGRP	(anti) - Calcitonin Gene-Related Peptide
CRM (French)	Commission de Remboursement des Médicaments,
CRM (English)	Commission for reimbursement of medecines
CTG (Dutch)	Commissie Tegemoetkoming Geneesmiddelen
CRSwNP	Chronic RhinoSinusitis with Nasal Polyps
DDD	Defined Daily Dose
DLBCL R/R	Diffuse Large B-cell Lymphoma Relapsed/Refractory
EACS	European AIDS Clinical Society
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
FTC	Emtricitabine
GLP-1	Glucagon-like peptide 1
HCV	Hepatitis C Virus
HR+/HER2 -	Hormone Receptor-positive / Human Epidermal growth factor Receptor 2 negative
INAM (French)	Institut National d'Assurance Maladie-Invalidité
NIHDI (English)	National Institute for Health and Disability Insurance
RIZIV (Dutch)	RijksInsitituut voor Ziekte- en Invaliditeit Verzekering
INSTI	Integrase Strand Transfer Inhibitors
KCE	Federal Centre of Health Care Expertise
MEA	Managed Entry Agreement (Convention Article 81/111)
MORSE	Monitoring Of Reimbursement Significant Expenses (Annual reports from the NIHDI on expenditure and consumption of reimbursed medicines in Belgium)
NRTI	Nucleoside Reverse Transcriptase Inhibitors
P4P	Pay for performance
PCSK9	Proprotein convertase subtilisin/kexin type 9
PN	Prurigo Nodularis
PrEP	Pre-Exposure Prophylaxis
RSV	Respiratory Syncital Virus
SGLT2	Sodium-glucose transport 2
T2D	Diabetes mellitus type 2
TAF	Tenofofir Alafenamide
TDF	Tenofovir Dispoproxil
TKI	Tyrosine Kinase Inhibitor
VAT	Value Added Tax
WAIT	Waiting to Access Innovative Therapies

Executive Summary

OVERALL CONTEXT

In 2024, gross expenditures by the National Institute for Health and Disability Insurance (NIHDI) reached €7.9 billion (+9.6% vs. 2023). Growth was particularly pronounced in the hospital sector, which accounts for 54.7% of total spending, mainly due to products under managed entry agreements (Articles 81/111). After clawbacks and taxes, net expenditures amounted to €5.6 billion (+6.6%). In community pharmacies, 8.8 million patients accessed reimbursed medicines (+0.6%), with average spending per patient increasing by €2.1 all sector together. Between 2019 and 2024, patient contributions rose by 10%, while gross and net expenditures grew by 51% and 32%, respectively; the relative share borne by patients declined thanks to measures such as co-payment caps, maximum billing limits, and the shift of expenditures toward hospital care. In parallel, other pharmaceutical services (medical nutrition, care pathways, etc.) represented €258 million in 2024 (+6.7%).

HIGH-IMPACT PHARMACOLOGICAL CLASSES: KEY GROWTH DRIVERS

Expenditures remain highly concentrated: 15 classes out of 164 account for 68% of total spending. Price fluctuations, expanded indications, innovation, and increased volumes for certain classes explain most significant trends:

- L01F – Monoclonal antibodies and conjugates: €1.3 billion (+8.6%), driven by indication extensions (pembrolizumab, daratumumab, ipilimumab) and broader use of next-generation molecules (trastuzumab deruxtecan, teclistamab, tafasitamab).
- L01E – Protein kinase inhibitors: €510 million, slight decrease (–1%) but volumes rising through new indications (zanubrutinib, abemaciclib).
- A10B – Non-insulin antidiabetics: €275 million (+16.5%), tripled over 10 years, fueled by patient growth, expanded indications, and increased use of GLP-1 and SGLT2; control measures introduced in 2025 to address off-label use (weight loss).
- C10A/C10B – Lipid-lowering agents: Strong growth since 2022, driven by PCSK9 inhibitors, inclisiran, and combination regimens (statin + ezetimibe) for high cardiovascular risk patients.
- Other rising classes: Immunoglobulins (J06B), innovative dermatology (dupilumab), anti-CGRP migraine treatments, nervous system drugs (tafamidis), often under temporary reimbursement agreements.
- L04A – Immunosuppressants: Largest category in community pharmacies and second overall (< €1 billion), no in-depth analysis this year due to limited 2024 growth.

CRM ENGAGEMENT AND OVERSIGHT OF MANAGED ENTRY AGREEMENTS

The Commission for Reimbursement of Medicines (CRM) processed 532 unique dossiers in 2024 (+23%), with a growing share of reimbursement modality changes. The Minister followed CRM advice in 89% of cases (99% for positive opinions).

In 2024, 189 agreements covering 149 molecules were in force (+16% agreements; +10% molecules vs. 2023), including 38 new agreements (a record). Reported turnover reached at least €2.9 billion, with €1.8 billion in clawbacks (+18.2%). Between 2015 and 2024, the cumulative clawback rate reached 45.4%; the average net cost per agreement rose from €6.9 million to €8.2 million (2015–2023). Agreements are mainly concentrated in oncology and immunomodulators (~60%).

CONCLUSION

The dynamics of pharmaceutical spending in 2024 confirm a structural trend: rapid innovation, expanded indications, and intensified treatments are shifting the center of gravity toward the hospital sector and a few high-impact classes. While managed entry agreements partially mitigate net costs, their growing weight and the concentration of expenditures on highly innovative classes pose a major challenge for financial sustainability and budgetary pressure.

Introduction

The primary aim of the MORSE report is to ensure financial monitoring of expenditure on reimbursable drugs, in line with the strategic measures taken by the National Institute for Health and Disability Insurance (NIHDI). These measures may concern the reimbursement of new medicines, the introduction of cost-saving policies or other decisions likely to influence budget dynamics. The report presents the trends in expenditure on pharmaceutical specialties dispensed both in public pharmacies and in hospitals, and aims to provide a clear, documented view of the trends observed.

Unless otherwise stated, the expenditure detailed corresponds to amounts charged to the health insurance system, i.e. the budget for pharmaceutical specialties. These amounts, referred to as gross expenditure, do not include income from conventions under articles 81/111, nor the patient's personal share (co-payments). To estimate the actual budgetary burden borne by the health insurance system, or net expenditure, we need to take into account the revenue generated by these conventions, as well as the contributions paid by the pharmaceutical industry to the NIHDI. Some tables in the report therefore incorporate this additional information to provide a more complete picture of budget balances.

The results presented are based on different data sources, chosen according to the nature of the analyses. Expenditure charged to the health insurance system is based on Pharmanet data for public pharmacies and nursing homes, and on consolidated billing data from the DOCPH database for hospitals. These data are complete up to December 2023 for all channels, and information for the year 2024 is fully available for pharmacies. In the hospital sector, the figures for 2024 were extrapolated from data covering the first ten months of the year, representing around 85% of total volume. As a precaution, the tables in question are marked with an asterisk (*). Other data comes from the internal database CTG-CTI, used to manage files with the Commission for Reimbursement of Medicines (CRM). Lastly, data relating to article 81/111 conventions are taken from the budget monitoring system managed by the working group 'contracts'. These figures will likely be adjusted for 2024, as not all company declarations have yet been completed. The values in question appear in square brackets ([xxxx.x €]), indicating that they should be interpreted with caution, and there may still be minor modifications.

In connection with these conventions, it should be recalled that the roadmap for the reform of reimbursement procedures, drawn up by the NIHDI following an extensive consultation process and published at the end of March 2023 on the latter's website (NIHDI, 2023a), provides, in reform n°31, for more transparency as regards conventions, at various levels. In particular, it is stated that (freely translated) *"the annual MORSE report published by the NIHDI on expenditure on medicines will present additional information"*. Since the MORSE 2024 report (NIHDI, 2024), the publication and analysis of this additional information has been an important innovation. These analyses are once again included in this report. The main new sections of this information describe and analyse the following:

- Expenditure and revenue for medicines under convention, broken down by ATC class;
- Estimates of the budget impact of new medicines under convention, compared with actual data;
- The system of advances and adjustments in the context of conventions.

At the same time, the NIHDI has access to more recent data, in particular in the form of technical estimates, which make it possible to continuously monitor expenditure on the basis of billing information provided by the mutual insurance companies. These data are regularly reported to the Insurance Committee and the General Council of the NIHDI. They are therefore not included in this report.

Some of the trends presented in this report may be influenced by exceptional factors, such as the COVID-19 pandemic. The spread of this pandemic from 2020 onwards had a significant impact on the consumption of medicines and, consequently, on overall expenditure on health insurance. This context must be taken into account when interpreting the trends presented.

It should be emphasised that financial monitoring is not an exact science. The analyses are based not only on available data, but also on the expertise of internal staff - evaluators, case managers and members of the Pharmanet team. Previous forecasts are regularly compared with actual expenditure as soon as the information becomes available, to assess whether the estimates were accurate. The NIHDI is also in continual dialogue with a number of actors, including representatives of the pharmaceutical industry, the KCE (Federal Knowledge Centre for Healthcare), the Federal Planning Bureau and other public institutions, with the aim of enhancing our understanding of budgetary trends. The NIHDI set up a network between these actors in 2023, and this was an important step towards more accurate forecasting of future expenditure.

9 - Introduction

The MORSE report is one of several financial monitoring tools produced by the NIHDI, alongside technical estimates, permanent audits, Infospot publications and reports from the data management unit. The aim is to bring together and put into perspective relevant information from these various sources, supplemented where necessary by data from the actuarial department of the NIHDI.

This report is divided into four main sections. The first section provides an overview of historical trends in expenditure and consumption of reimbursed medicines. For hospitals, a distinction is made between outpatients and hospitalised patients, with the latter staying at least one night in hospital, while day hospital patients are included among outpatients. The second section is a detailed analysis of the pharmacological classes (ATC level 3 code) that underwent significant changes in 2024. 13 classes were selected for in-depth study by the scientific committee. The third section presents the figures relating to requests submitted by pharmaceutical companies to the CRM. Finally, the fourth section looks in detail at cases provisionally reimbursed by the NIHDI, also known as "article 111 files" (formerly 81). Finally, a complete list of the cost-saving measures applied in 2024 is also given in Appendix 4. Detailed tables of the analyses produced for this report are also available on the NIHDI website.

The aim of the MORSE reports is to prompt reflection and debate on pharmaceutical expenditure and its evolution. The report will be put on the agenda of the Insurance Committee and the Pharma Budget Analysis Group attached to the Commission for Reimbursement of Medicines. The report will also be published on the website, along with external communication. The NIHDI welcomes all comments and suggestions that could help continuously improve this monitoring system.

1. Overall analysis of expenditure on pharmaceutical specialties

I. General overview

1. Evolution of pharmaceutical expenditure, excluding compensation.

Table 1 shows a steady rise in overall expenditure on medicines. The figure rose by 9.6% in 2024, excluding compensation. By way of comparison, there was growth of between 6% and 7% in 2018 and 2019. In 2020, growth was limited to 5%, before rising to 7.4% in 2021. The subsequent years confirmed this rising trend, with increases of 9.5% in 2022, 11.2% in 2023 and 9.6% in 2024.

NIHDI expenditure x €1,000,000								
Sector	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024***
Pharmacies	2,626.2	2,647.4	2,649.5	2,719.3	2,839.3	3,033.2	3,294.3	3,591.4
Hospitals	1,988.2	2,259.4	2,621.5	2,816.1	3,103.8	3,474.2	3,942.4	4,340.8
Total	4,614.4	4,906.8	5,271.0	5,535.5	5,943.1	6,507.4	7,236.7	7,932.2
Growth in %								
Sector		**2018-2017**	**2019-2018**	**2020-2019**	**2021-2020**	**2022-2021**	**2023-2022**	**2024-2023***
Pharmacies		0.8 %	0.1 %	2.6 %	4.4 %	6.8 %	8.6 %	9.0 %
Hospitals		13.6 %	16.0 %	7.4 %	10.2 %	11.9 %	13.5 %	10.1 %
Total		6.3 %	7.4 %	5.0 %	7.4 %	9.5 %	11.2 %	9.6 %

Source: Pharmanet (Pharmacies) & DocPH (Hospitals)

Table 1: NIHDI annual expenditure (excluding compensation) on reimbursable pharmaceutical specialties, 2017-2024.[1]

Between 2018 and 2019, expenditure on public pharmacies remained virtually stable, while growth in hospital expenditure accounted for the increase in overall expenditure on medicines. From 2020 onwards, this dynamic changed: the rise in overall expenditure was then the result of a combination of increases in hospital expenditure and expenditure on public pharmacies. These rose steadily, from +2.6% in 2020 to +9.0% in 2024. In absolute terms, expenditure on public pharmacies reached €3.6 billion in 2024.

At the same time, hospital expenditure continues to grow steadily, with increases of +11.9% in 2022, +13.5% in 2023 and +10.1% in 2024, for a total of €4.3 billion in 2024.

Overall, the combination of these trends means that expenditure on pharmaceutical specialties rose by +9.6% in 2024, bringing the total to €7.9 billion.

Figure 1 shows the steady rise in the share of hospital expenditure in overall expenditure on pharmaceutical specialties. In 2020, for the first time, hospital expenditure exceeded that of public pharmacies, accounting for 50.9% of the total. This proportion continued to rise, reaching 54.7% in 2024.

It is important to note that the amounts stated in this report do not include compensation linked to article 81/111 conventions (unless explicitly mentioned), nor patient co-payments.

Furthermore, the proportion of expenditure devoted to specialties temporarily included on the list of reimbursable pharmaceutical specialties - those covered by an "art. 81/111" convention between the NIHDI and the company - is growing every year. This trend can be explained by the rise in the number of conventions, the volumes distributed and the prices of the medicines in question.

[1]The NIHDI expenditure (without compensation) for public pharmacies comes from Farmanet data. The NIHDI expenditure (without compensation) for hospitals is based on DocPH data (NIHDI data), where total expenditure = outpatient expenditure + overall expenditure per fixed rate for hospitalisation + expenditure on hospitalised patients accounted for at 100% (excluding fixed rate) + expenditure on hospitalised patients accounted for at 25% (within fixed rate). Since 1 July 2024, total expenditure = outpatient expenditure + total expenditure per fixed rate for hospitalisation + expenditure on hospitalised patients accounted for at 100% (excluding fixed rate).

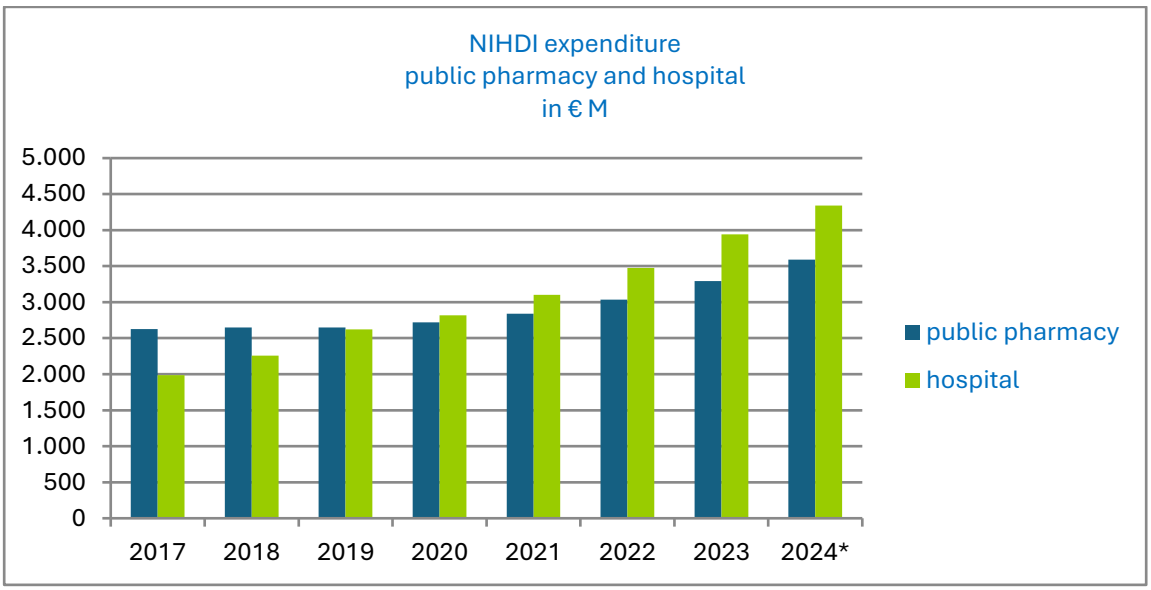

Figure 1: Annual expenditure of the NIHDI (excluding compensation) on reimbursable pharmaceutical specialties, in public pharmacies and in hospitals (2017-2024).

In 2024, pharmaceutical specialties covered by an "art. 81/111" convention accounted for 43% of total expenditure (see Table 2[2]). This figure does not take into account compensation for expenditure incurred under these conventions. In public pharmacies, almost 19% of expenditure is attributed to these medicines, while in hospitals the proportion rises to 64%.

By way of comparison, in 2020, the share of expenditure on medicines under convention was around 35% of the total, with 11% for public pharmacies and 58% for hospital pharmacies. This trend reflects the continuing growth in expenditure related to conventions, which play an increasingly important role in the pharmacy sector (19% in 2024 versus 11% in 2020).

NIHDI expenditure in 2024 (in millions of euros)						
	Pharmacies		Hospitals*		Total	
Pharmaceutical specialties without agreement	2,924.8	81.4%	1,580.3	36.3%	4,505.1	56.7%
Pharmaceutical specialties under convention	666.7	18.6%	2,775.3	63.7%	3,441.9	43.3%
Total	3,591.4	100.0%	4,355.5	100.0%	7,947.0	100.0%

Table 2: Breakdown of NIHDI expenditure in 2024 (excluding compensation) according to whether or not the medicine is covered by an "art. 81/111" convention.

2. Evolution in the actual budget cost of pharmaceutical expenditure, taking into account compensation.

To accurately assess the actual budget cost of pharmaceutical expenditure for the health insurance system, we need to include the compensation that partially neutralises this expenditure. In order to understand the budget compensation linked to the "art. 81/111" conventions - for which it is not possible to make a detailed analysis due to the confidentiality of the mechanisms - we rely on data provided by the Actuarial Department of the NIHDI. Furthermore, we also include compensation from the annual levies imposed on the pharmaceutical industry. Changes in "art. 81/111" compensation and levies are illustrated in the table below.

According to Table 3, gross expenditure of the NIHDI, excluding compensation, rose by 9.5% in 2024, from €7,298.1 million in 2023 to €7,991.0 million in 2024. After deducting compensation, the rise was 8.1%, or €6,198.4 million in 2024 compared with €5,734.6 million in 2023. Finally, if we also take into account levies, growth in the actual budget cost of pharmaceutical expenditure for the health insurance system reached 6.6% in 2024.

[2] Situation as of 01/12/2024 for the breakdown of specialties considered under contract.

	2019	2020	2021	2022	2023	2024
Recorded expenditure (docN) (1)	5,263.3	5,586.2	5,984.2	6,494.4	7,298.1	7,991.0
Compensation art. 81/111 (2)	605.0	754.2	1,019.5	1,257.2	1,563.5	[1,792.6]
(3) = (1) - (2)	4,658.2	4,832.0	4,964.7	5,237.2	5,734.6	6,198.4
Levies (4)	397.4	307.3	333.8	358.1	444.6	557.9
Actual budget cost of the pharmaceutical expenditure for the NIHDI (5) = (3) - (4)	4,260.8	4,524.7	4,630.9	4,879.1	5,290.1	5,640.6
Annual growth rate over previous year	-	6.2%	2.3%	5.4%	8.4%	6.6%

(1) Gross expenditure; to allow a comparison with previous years, specific fees were added to gross expenditure in 2024.
(2) The system of advance payments was introduced in 2017.
(4) Levies relate to all levies imposed on the sector (e.g. turnovers levy, clawback) collected by the NIHDI; reductions in levies for the years 2022 and 2023 were only reimbursed in December 2024 and December 2025.
Source: permanent audit, NIHDI Actuarial Department.

Table 3: Evolution of expenditure, including compensation for "art. 81/111" conventions and levies, expressed in millions of euros.

In order to make an accurate assessment of the actual budget cost of expenditure relating to "art. 81/111" conventions, we have drawn on the data provided in the section dedicated to these conventions, presented later in this report (see Analysis of ART. 111/112/113 conventions- pp. 72- 96).

	2019	2020	2021	2022	2023	2024
Actual budget cost of the pharmaceutical expenditure for the NIHDI: (5) = (3) - (4)	4,260.8	4,524.7	4,630.9	4,879.1	5,290.1	5,640.6
Actual budget cost of medicines under conventions, after including declared turnovers and corresponding compensation (see Table 49).	934.55	1,133.79	1,067.56	1,225.27	1,338.66	[1,037.63]
Share of actual budget cost of expenditure on pharmaceuticals under convention compared with total actual budget cost on pharmaceuticals.	21.9	25.1	23.1	25.1	25.3	[18.4%]

Table 4: Evolution of the actual budget cost of pharmaceutical expenditure for the health insurance system, both overall and for expenditure linked to "art. 81/111" conventions.

Table 4 shows that the share of pharmaceutical expenditure in the context of conventions, as a proportion of total expenditure on medicines, remains relatively stable when the actual budget cost is taken into account (including expenditure and compensation). One point to bear in mind when interpreting these data is that expenditure and compensation for medicines under convention do not always fall within the same accounting year; the compensation in some cases takes place after the year in which the expenditure was billed. It should also be borne in mind that these data are not yet complete for the year 2024.

3. Evolution of the patient contribution to the reimbursement of pharmaceutical specialties

Patients contribute to the financing of pharmaceutical specialties reimbursed by the NIHDI in ways that depend on both the reimbursement category of the medicine and the patient's status (ordinary patients versus beneficiaries of the increased intervention - BIM/VIPO). The reimbursement categories set out the rules for calculating the personal contribution, as defined in current regulations.

In general, the amount of the co-payment is a combination of a variable part, calculated as a percentage of the reimbursement base, and a fixed part[3], specified by the reimbursement category (NIHDI, 2025a). Moreover, these contributions are capped: certain categories of reimbursement are associated with a maximum amount payable by the patient, above which no additional contribution can be claimed (NIHDI, 2025b). In addition, the system also provides for an annual ceiling via the Maximum to be Charged (MàF in French). This guarantees that above a certain annual level - which varies according to household composition and social status - the NIHDI will pay in full all additional costs that are normally chargeable to the patient. The MàF is therefore an essential financial protection mechanism, limiting the cumulative cost of co-payments over a year (NIHDI, 2025c).

The data available mean that the MàF can be taken into account for expenditure in public pharmacies (Pharmanet), but not for hospitals (DocPH). As a result, only patient contributions for outpatient hospital care are taken into

[3] The fixed part of the co-payment is intended to limit the contribution made by patients if pharmaceutical specialties have a high reimbursement base.

consideration - the fixed daily hospital charge is not included. The patient share of hospital care is therefore underestimated. Nevertheless, it should be emphasised that this underestimate is very limited: the financial contribution made by patients mainly relates to medicines dispensed in public pharmacies.

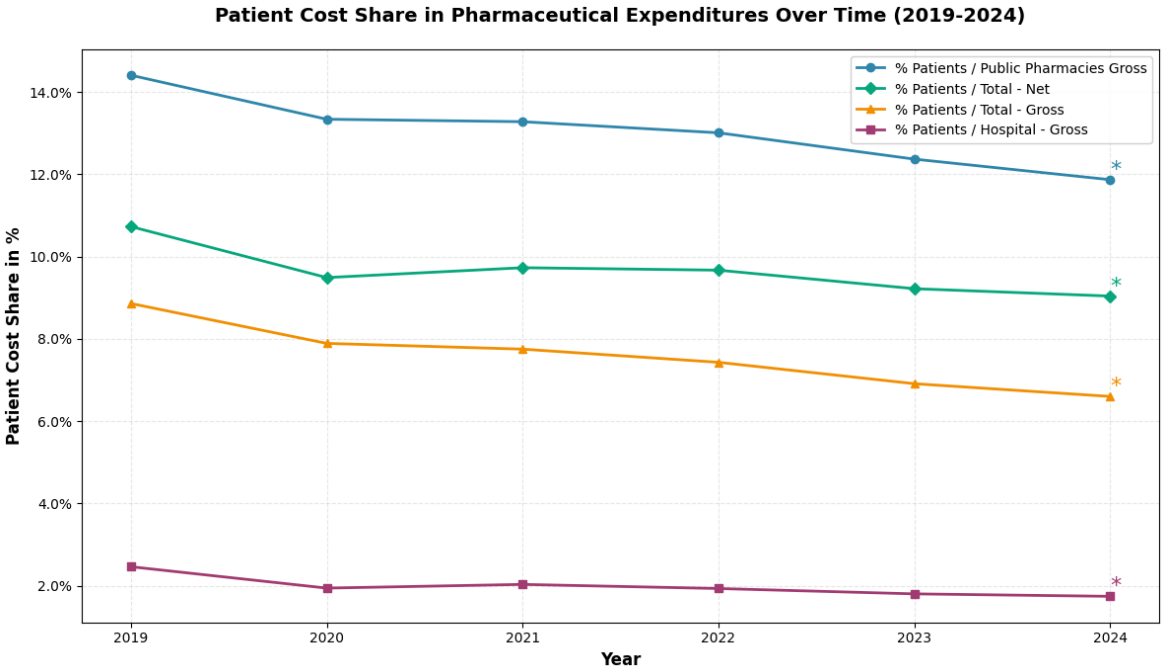

Figure 2: Evolution in the patient share of the budget for reimbursed pharmaceutical specialties between 2019 and 2024.

Figure 2 and Table 5 show the evolution of patient contributions broken down by distribution sector for the period 2019-2024. In absolute terms, the share paid by patients rose from around €512 million in 2019 to €560 million in 2024, an increase of around 10% over the period. However, compared to the total pharmaceutical budget, this nominal growth masks the opposite trend: the proportion represented by these contributions in the gross expenditure of the NIHDI fell from 8.86% in 2019 to 6.60% in 2024. If we consider net expenditure, the decline is also observable, but on a more moderate scale, from 10.73% to 9.04% over the same period. Overall, considering the amount of patient (cf. Table 8), the increase per patient is around € 2.1 all sector together.

		2019	2020	2021	2022	2023	2024*
NIHDI Expenditure	1. Public Pharmacies - Gross (cfr. Table 1)	€2,649.50	€2,719.30	€2,839.30	€3,033.20	€3,294.30	€3,591.40
	2. Hospital - Gross (cfr. Table 1)	€2,621.50	€2,816.10	€3,103.80	€3,474.20	€3,942.40	€4,340.80
	3. Gross (1+2)	€5,271.00	€5,535.40	€5,943.10	€6,507.40	€7,236.70	€7,932.20
	4. Total - Net (cfr. Table 4)	€4,260.80	€4,524.70	€4,630.90	€4,879.10	€5,290.10	€5,640.60
Patient costs	5. Patients - Pharmacies	€445.89	€418.47	€434.91	€453.67	€464.87	€483.72
	6. Patients - Hospital Outpatient Care	€66.24	€55.72	€64.31	€68.54	€72.41	€76.76
	7. Patients - Total (5+6)	€512.13	€474.19	€499.22	€522.21	€537.28	€560.48
Total expenditure	8. Total Public Pharmacies - Gross (1+5)	€3,095.39	€3,137.77	€3,274.21	€3,486.87	€3,759.17	€4,075.12
	9. Total Hospital - Gross (2+6)	€2,687.74	€2,871.82	€3,168.11	€3,542.74	€4,014.81	€4,417.56
	10. Total - Gross (3+7)	€5,783.13	€6,009.59	€6,442.32	€7,029.61	€7,773.98	€8,492.68
	11. Total - Net (4+7)	€4,772.93	€4,998.89	€5,130.12	€5,401.31	€5,827.38	€6,201.08
Patient share	12. % Patients / Pharmacies Gross (5/8)	14.41%	13.34%	13.28%	13.01%	12.37%	11.87%
	13. % Patients / Hospital Gross (6/9)	2.46%	1.94%	2.03%	1.93%	1.80%	1.74%
	14. % Patients / Total - Gross (7/10)	8.86%	7.89%	7.75%	7.43%	6.91%	6.60%
	15. % Patients / Total - Net (7/11)	10.73%	9.49%	9.73%	9.67%	9.22%	9.04%

Table 5: Gross and net expenditure of the NIHDI, patient costs, total expenditure (in millions of euros) and relative share of patients in total expenditure (in %)

These trends simultaneously reflect changes in the overall expenditure of the NIHDI and the impact of financial protection mechanisms that limit the actual cost borne by patients. The observed reduction in patient contributions can be explained by a number of concurrent factors: on the one hand, the rising price of certain pharmaceutical specialties, for which the personal co-payment remains capped; on the other hand, the rise in expenditure in the hospital sector, where the patient's share is structurally lower. Finally, cost-cutting measures applied to standard reimbursements also help reduce the price of certain specialties, which then reduces the financial contribution made by patients.

II. Expenditure on pharmaceutical specialties in public pharmacies

NIHDI expenditure x €1,000,000							
2017	2018	2019	2020	2021	2022	2023	2024
2,626.2	2,647.4	2,649.5	2,719.3	2,839.3	3,033.2	3,294.3	3,591.4
Growth (in %)							
	2018/2017	2019/2018	2020/2019	2021/2020	2022/2021	2023/2022	2024/2023
	0.8	0.1	2.6	4.4	6.8	8.6	9.0

Table 6: Trend in annual NIHDI expenditure on medicines, excluding compensation, for the period 2017-2024.

Table 6 provides a summary of NIHDI expenditure on public pharmacies and nursing homes, as described in the previous section. In 2024, expenditure on reimbursement of medicines in public pharmacies, excluding compensation, rose by 9.0% overall compared with the previous year. However, analysis by pharmacological class reveals significant and contrasting trends, ranging from marked growth to significant decline, or even a reversal of the trend. Later on in the report, we will take a closer look at certain pharmacological classes to better explain the mechanisms behind these variations. The classes concerned are indicated by the symbol †.

ATC3	Name	Growth 2023/2022	Growth 2024/2023	NIHDI expenditure 2024 (in millions)
	Total	**8.6%**	**9.0%**	**3,591.4**
L04A	Immunosuppressants (T)	10.0%	9.5%	634.6
B01A	Antithrombotic Agents (T)	4.0%	-1.7%	313.2
A10B	Blood Glucose Lowering Drugs, Excl. Insulins (T) †	20.2%	16.4%	273.2
C10A	Lipid Modifying Agents, Plain (T) †	27.4%	23.3%	172.6
R03A	Adrenergics, Inhalants	7.1%	8.4%	170.1
J05A	Direct Acting Antivirals †	4.7%	6.4%	162.4
B02B	Vitamin K and Other Haemostatics (T)	5.6%	10.2%	115.2
A02B	Drugs for Peptic Ulcer and Gastro-Oesophageal Reflux Disease (GORD)	5.0%	3.8%	114.1
N06A	Antidepressants	5.4%	6.2%	94.7
R03D	Other Systemic Drugs for Obstructive Airway Diseases	18.3%	19.9%	94.0
A10A	Insulins and Analogues	2.0%	3.8%	89.9
C10B	Lipid Modifying Agents, Combinations (T) †	73.4%	56.0%	82.9
N05A	Antipsychotics	2.6%	-3.8%	78.9
C09D	Angiotensin II Receptor Blockers (ARBs), Combinations	15.1%	13.8%	68.9
N03A	Antiepileptics	-1.2%	6.4%	59.4
N02C	Antimigraine Preparations (T) †	32.4%	14.6%	57.5
N02A	Opioids	1.0%	3.5%	56.9
C09B	ACE Inhibitors, Combinations	6.6%	7.1%	52.4
M05B	Drugs Affecting Bone Structure and Mineralization †	12.6%	11.3%	51.7
D11A	Other Dermatological Preparations (T) †	47.6%	68.9%	48.2
C07A	Beta Blocking Agents	2.6%	4.0%	43.3
J07B	Viral Vaccines	3.7%	3.5%	40.9

(T): This ATC3 class includes one or more specialties temporarily registered under an article 81/111 convention.
† ATC3 class analysed in depth in section 2 of the report.

Table 7: Top 80% of annual NIHDI expenditure (excluding compensation) on medicines sold in public pharmacies

An analysis of expenditure, excluding compensation, and its evolution by ATC3 class (see Table 7) reveals that 22 of the 147 classes account for 80% of expenditure in public pharmacies. ATC3 classes comprising one or more specialties temporarily registered under an agreement provided for in article 81/111 are identified by "(T)". The actual cost to the NIHDI for these classes is generally lower than the amounts shown, due to the financial compensation stipulated in these conventions. In 2024, medicines under contract accounted for 19% of expenditure in public pharmacies (see Table 2). We also refer to the "Medicines" reports of the Efficient Care Department. These reports are available online (NIHDI, 2025d), as is the methodology used to produce them (NIHDI, 2025e).

Figure 2 illustrates the relationship between total expenditure and the number of patients treated. For the period 2021-2024, we see a continued rise in expenditure, while growth in the number of patients treated slowed. In 2022, we saw a 6.8% rise in expenditure, compared with a 3% increase in the number of patients treated. In 2023 and 2024, expenditure rose by 8.6% and 9% respectively, accompanied by a slowdown in growth in the number of patients treated, to 1.6% in 2023 and 0.6% in 2024. These trends result in an increase in average NIHDI expenditure per patient, reaching €409.2 in 2024, compared with €340.7 in 2021 (an increase of 20% over the period 2021-2024). Table 8 shows the evolution of the number of patients treated by ATC3 class.

15 - Overall analysis of expenditure on pharmaceutical specialties

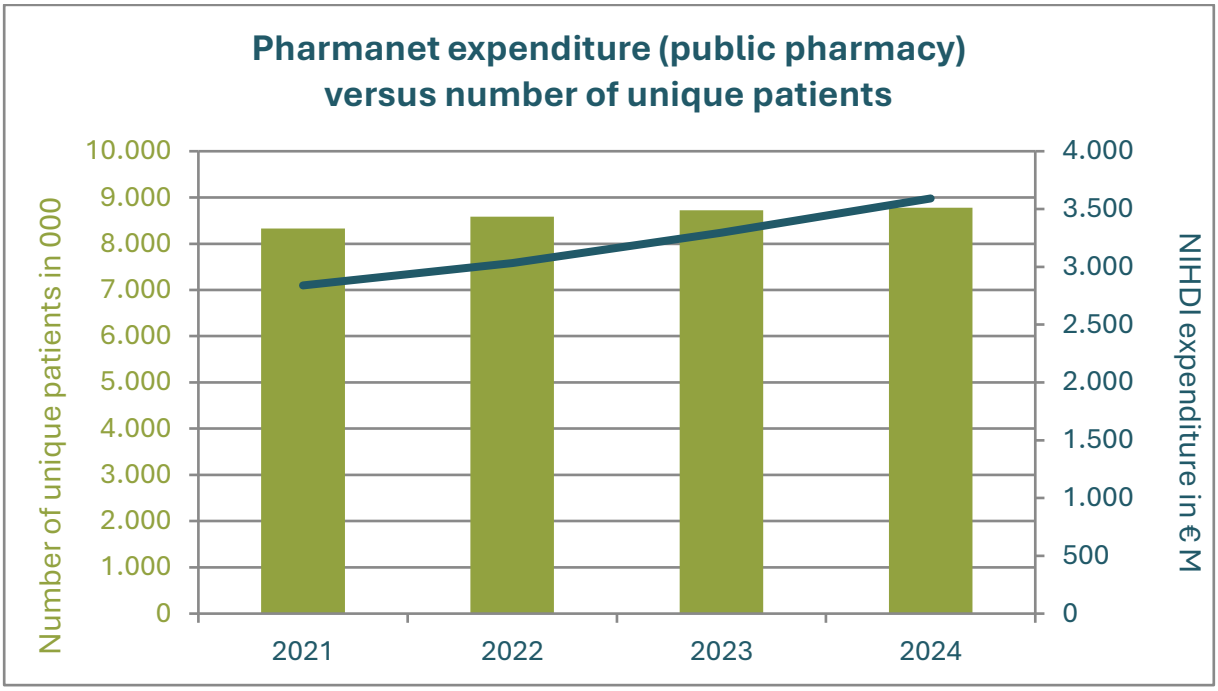

Figure 3: Evolution of NIHDI expenditure (excluding compensation) in public pharmacies, compared with the number of patients treated (unique).

ATC3	Name	Growth 2023/2022	Growth 2024/2023	# patients 2024
	Total	**1.6%**	**0.6%**	**8,775,745**
L04A	Immunosuppressants (T)	6.3%	7.0%	161,506
B01A	Antithrombotic Agents (T)	-0.1%	0.3%	1,569,583
A10B	Blood Glucose Lowering Drugs, Excl. Insulins (T) †	9.1%	8.7%	852,698
C10A	Lipid Modifying Agents, Plain (T) †	3.6%	1.9%	1,773,084
R03A	Adrenergics, Inhalants	3.3%	2.7%	1,475,320
J05A	Direct Acting Antivirals †	8.1%	177.9%	136,429
B02B	Vitamin K and Other Haemostatics (T)	2.9%	11.2%	476
A02B	Drugs for Peptic Ulcer and Gastro-Oesophageal Reflux Disease (GORD)	2.1%	1.5%	2,416,346
N06A	Antidepressants	2.2%	2.3%	1,368,481
R03D	Other Systemic Drugs for Obstructive Airway Diseases	-4.2%	-5.3%	112,676
A10A	Insulins and Analogues	1.7%	2.7%	175,418
C10B	Lipid Modifying Agents, Combinations (T) †	54.1%	42.9%	546,462
N05A	Antipsychotics	0.2%	1.3%	380,097
C09D	Angiotensin II Receptor Blockers (ARBs), Combinations	6.0%	5.8%	406,916
N03A	Antiepileptics	0.7%	0.2%	177,543
N02C	Antimigraine Preparations (T) †	10.3%	11.8%	44,221
N02A	Opioids	0.4%	0.9%	1,140,274
C09B	ACE Inhibitors, Combinations	4.0%	4.2%	567,570
M05B	Drugs Affecting Bone Structure and Mineralization †	4.6%	4.4%	155,637
D11A	Other Dermatological Preparations (T) †	15.5%	19.1%	36,896
C07A	Beta Blocking Agents	-0.2%	-0.2%	1,283,847
J07B	Viral Vaccines	-0.9%	-2.0%	1,922,139

(T): This ATC3 class includes one or more specialties temporarily registered under an article 81/111 convention.
† ATC3 class analysed in depth in section 2 of the report.

Table 8: Trend in the number of unique patients treated in public pharmacies (in thousands), broken down by ATC3 class.

Compared with overall expenditure trends (see Table 6), there are significant differences in both percentages and proportions. These differences indicate significant changes in NIHDI expenditure per patient, as shown in Table 9.

ATC3	Name	Growth 2023/2022	Growth 2024/2023	NIHDI expenditure per patient 2024
	Total	**6.9%**	**8.4%**	**409.2**
L04A	Immunosuppressants (T)	3.4%	2.3%	3,929.5
B01A	Antithrombotic Agents (T)	4.0%	-2.0%	199.6
A10B	Blood Glucose Lowering Drugs, Excl. Insulins (T) †	10.2%	7.1%	320.4
C10A	Lipid Modifying Agents, Plain (T) †	23.0%	21.0%	97.4
R03A	Adrenergics, Inhalants	3.7%	5.5%	115.3
J05A	Direct Acting Antivirals †	-3.1%	-61.7%	1,190.6
B02B	Vitamin K and Other Haemostatics (T)	2.7%	-0.9%	242,064.3[4]
A02B	Drugs for Peptic Ulcer and Gastro-Oesophageal Reflux Disease (GORD)	2.8%	2.3%	47.2
N06A	Antidepressants	3.1%	3.8%	69.2
R03D	Other Systemic Drugs for Obstructive Airway Diseases	23.5%	26.6%	834.2
A10A	Insulins and Analogues	0.3%	1.0%	512.7
C10B	Lipid Modifying Agents, Combinations (T) †	12.5%	9.2%	151.8
N05A	Antipsychotics	2.3%	-5.0%	207.5
C09D	Angiotensin II Receptor Blockers (ARBs), Combinations	8.6%	7.5%	169.3
N03A	Antiepileptics	-1.9%	6.1%	334.6
N02C	Antimigraine Preparations (T) †	20.0%	2.5%	1,300.2
N02A	Opioids	0.6%	2.6%	49.9
C09B	ACE Inhibitors, Combinations	2.5%	2.7%	92.4
M05B	Drugs Affecting Bone Structure and Mineralization †	7.7%	6.6%	332.3
D11A	Other Dermatological Preparations (T) †	27.8%	41.8%	1,305.6
C07A	Beta Blocking Agents	2.8%	4.3%	33.7
J07B	Viral Vaccines	4.6%	5.6%	21.3

(T): This ATC3 class includes one or more specialties temporarily registered under an article 81/111 convention.
† ATC3 class analysed in depth in section 2 of the report.

Table 9: Evolution in average NIHDI expenditure per patient in public pharmacies, by ATC3 class (excluding compensation)

III. Expenditure on pharmaceutical specialties in hospitals

1. Overall analysis

Table 10 shows a summary of NIHDI expenditure in hospitals. In hospitals, around 64% of expenditure is allocated to medicines under convention (see Table 2).

NIHDI expenditure x €1,000,000							
2017	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024***
1,988.2	2,259.4	2,621.5	2,816.1	3,103.8	3,474.2	3,942.4	4,340.8
Growth in %							
	2018/2017	**2019/2018**	**2020/2019**	**2021/2020**	**2022/2021**	**2023/2022**	**2024/2023**
	13.6	16.0	7.4	10.2	11.9	13.5	10.1

Table 10: Annual expenditure by the NIHDI on medicines (excluding compensation), period 2017–2024 (DocPH).

An analysis of (virtual) expenditure and growth by ATC3 class reveals that 10 of the 163 classes account for 80% of expenditure on pharmaceutical specialties in hospitals. ATC3 classes comprising one or more specialties temporarily registered under a convention provided for in articles 81/111 are highlighted in Table 11 by "(T)". The actual cost to the NIHDI for these ATC3 classes is generally lower than the amounts indicated, due to the financial compensation defined in articles 81/111 conventions.

In 2024, as in previous years, the class of monoclonal antibodies and antibody-drug conjugates (L01F) were at the top of the list, with expenditure amounting to €1.3 billion, or 30% of total hospital expenditure on medicines. In second place were protein kinase inhibitors (L01E), with expenditure of €510 million, followed by other nervous system drugs (N07X). At €353 million, immunosuppressants (L04A) are no longer in the top three classes in terms of hospital expenditure.

[4]Pharmacological class B02B - which will not be analysed in depth in this report - groups together antihaemorrhagic agents, in particular blood coagulation factors in class B02BD (blood coagulation factors VII, VIII, IX, X, vWF, etc.) used in the treatment of haemophilia and severe coagulation disorders. Class B02BB01 includes fibrinogen for the treatment of hypofibrinogenemia or afibrinogenemia. They have a very high unit cost in most cases, and the dosage is often substantial, which explains the particularly high cost per patient.

17 - Overall analysis of expenditure on pharmaceutical specialties

Ranking			Fixed rate	ATC3	Name	Growth (%)		Total x € 1,000,000[5]
2022	2023	2024				2023-2022	2024-2023	2024*
1	1	1	No	L01F	Monoclonal Antibodies and Antibody Drug Conjugates (T) †	19.0%	8.6%	1,298.5
2	2	2	No	L01E	Protein Kinase Inhibitors (T) †	14.2%	-1.0%	510.1
4	4	3	Mix	N07X	Other Nervous System Drugs (T) †	56.9%	44.3%	368.2
3	3	4	Mix	L04A	Immunosuppressants (T)	-8.4%	-2.5%	352.6
6	6	5	No	J06B	Immunoglobulins (T) †	17.1%	36.9%	205.0
8	8	6	No	L01X	Other Antineoplastic Agents (T) †	12.8%	52.5%	181.9
5	7	7	No	L02B	Hormone Antagonists and Related Agents (T)	-6.2%	25.9%	177.5
9	5	8	No	R07A	Other Respiratory System Products (T)	77.2%	0.7%	175.5
7	9	9	No	S01L	Ocular Vascular Disorder Agents (T)	3.5%	12.7%	128.6
10	10	10	No	B02B	Vitamin K and Other Haemostatics (T)	12.3%	13.6%	97.9

(T): This ATC3 class includes one or more specialties registered temporarily in the context of an article 81/111 convention.
† ATC3 class analysed in depth in section 2 of the report.

Table 11: Evolution in annual NIHDI expenditure on drugs (excluding compensation) - 80% of the most expensive classes in hospitals.

2. Breakdown of expenditure by patient type

For this analysis, we use DocPH data, which includes consolidated billings of NIHDI expenditure, broken down by specialty and type of patient (hospitalised patient or outpatient). The DocPH data refer to the period when the medicines were dispensed. They have a time lag, as the information relating to a given year is extracted from registrations recorded over an 18-month period (the year in question and the following 6 months).

a. Note on the fixed rate

Since 1 July 2006, a fixed rate system for hospitalised patient medicines has been in force in acute hospitals. In principle, all medicines are included in this fixed rate reimbursement system, with the exception of those on a specific list (based on the code ATC5). An ATC code may be added to this list when the active substance concerned is essential for medical practice, and its cost may mean that it is not administered to hospitalised patients on a fixed rate basis. Certain medicines are automatically excluded (e.g. orphan drugs, cytostatics, cf. art. 127 § 3 of the Royal Decree of 01/02/2018) or on the proposal of the "permanent working group on the flat rate prices of specialties".

Until 30 June 2024, the regulations stipulate that, for specialties included in the flat rate, 25% of the reimbursement base is charged per specialty, with the balance covered by a flat rate per admission. Since 1 July 2024, all costs have been charged to the flat rate charge for hospital admissions, while the medicines taken are still recorded ("charging at 0%"). This measure is intended to encourage optimal use of medicines subject to fixed-rate charges in hospitals.

Each year, the average national cost per APR-DRG and per degree of severity is calculated by combining medical and financial data (MKG-AZV - Minimum Clinical Data - Anonymous Hospital Stays) for hospital stays completed for a reference year. Only standard hospitalisations, including at least one overnight stay, are taken into account. Based on national averages by APR-DRG and severity level, and the casemix declared by the hospital (number of stays by APR-DRG and degree of severity during the reference year), the individual envelope for each hospital is calculated. This envelope is paid as a fixed rate amount per admission.

b. Analysis

The breakdown of annual data by patient type is shown in Table 12 and Figure 4[6]. For hospitalised patients, expenditure fell by 10.9% in 2020, the year the COVID-19 pandemic broke out. In 2021, they started to rise again (+8.9%), but did not reach the level of 2019 (-3.0% vs. 2019). Expenditure only slightly exceeded that of 2019 (+1.8%)

[5] NIHDI expenditure by ATC-3 class is based on DocPH data, where total expenditure = outpatient expenditure (A) + expenditure recorded at 100% (excluding fixed rate) (B) + a calculated theoretical amount (C) for medicines included in the fixed rate (until 30/6/2024 calculated on the basis charging 25% of the amount, from 01/07/2024 calculated on the basis of "charging 0% of the amount"). Given that the amount (C) is not an absolute expenditure but a theoretical amount, the expenditure per ATC3 class does not represent absolute expenditure but virtual expenditure, making it possible to draw up a ranking.

[6] In order to accurately visualise the variations, the expenditure data have been divided into two separate vertical axes. Without this separation, expenditure related to hospitalisations would have remained concentrated in the lower part of the chart, making it difficult to compare one year with another. The vertical axis on the left represents the scale of expenditure for hospital outpatient and total expenditure, while the vertical axis on the right corresponds to the scale used for the different series of hospitalised patient expenditure.

in 2022, with a growth of 4.9%. In 2023 and 2024, the rises were 4.8% and 13.0% respectively. In 2024, expenditure for hospitalised patients reached €506 million.

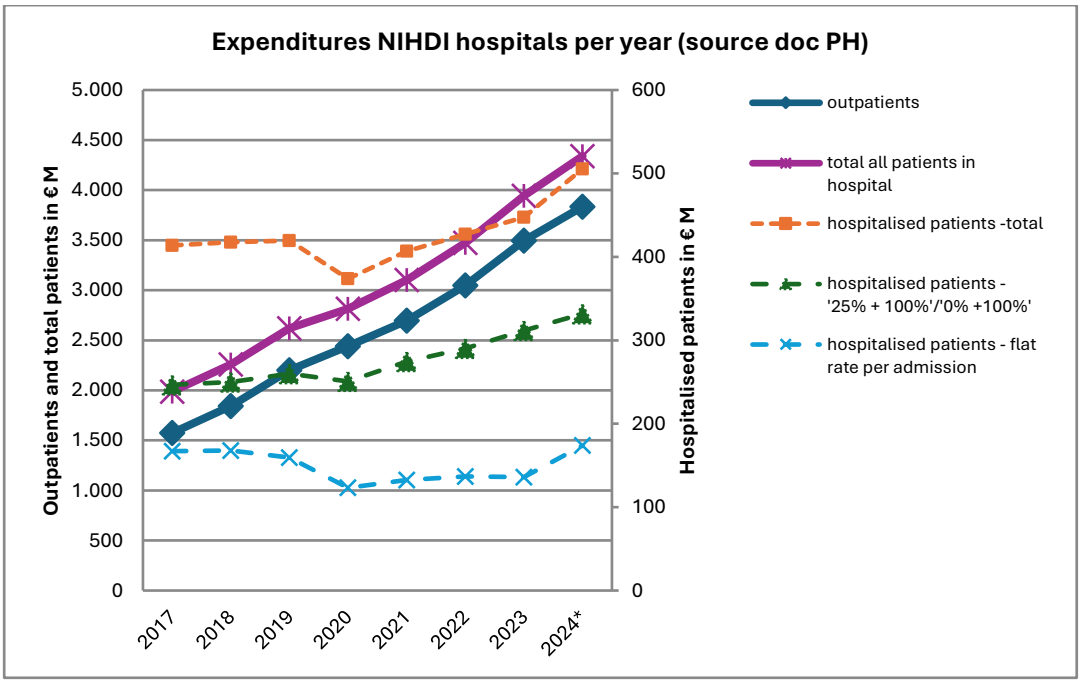

Figure 4: NIHDI expenditure in hospitals by patient type (outpatient [left axis]/hospitalised [right axis]) and taking into account the application of the fixed rate (without taking into account conventions) for the period 2017-2024.

There are two significant evolutions in expenditure linked to the fixed rate per admission: a 22.8% fall in 2020, due to the sharp drop in hospital admissions caused by the COVID-19 pandemic, followed by a 27.9% rise in 2024. This rise is due to the revision of the national budget for the fixed rate for medicines after 1 July 2024, which must now cover all costs, as explained above. Expenditure on outpatients continues to rise. After sustained growth in 2017, 2018 and 2019 (+21.6%, +17.0% and +19.6%), the rise was less pronounced between 2020 and 2024. In 2020 and 2021, the rise was limited to 10.9% and 10.4% respectively. After 2022, growth accelerated (+13.0% in 2022 and +14.7% in 2023), before slowing slightly in 2024 (+9.7%), bringing expenditure for outpatients to €3.8 billion. Total hospital expenditure reached €4.3 billion in 2024, a rise of 10.1% compared to 2023. Following strong annual growth of 14% to 17% between 2017 and 2019, the increase slowed in 2020 (+7.4%) due to the pandemic, then accelerated again between 2021 and 2023 (+10.2%, +11.9% and +13.5%).

Table 13 shows that the proportion of expenditure on outpatients in total expenditure on pharmaceutical specialties within hospitals rose leading up to 2023, although this growth slowed from 2020 onwards. In 2024, this proportion appeared to stabilise at 88.4%, a slight 0.2% decrease compared to 2023. Expenditure on hospitalised patients accounted for just 11.6% of total expenditure on medicines within hospitals in 2024, compared with 20.8% in 2017.

19 - Overall analysis of expenditure on pharmaceutical specialties

NIHDI expenditure x €1,000,000								
	2017	2018	2019	2020	2021	2022	2023	2024*
Outpatients[7]	1,574.5	1,841.7	2,202.0	2,442.4	2,696.9	3,047.2	3,494.9	3,835.2
Hospitalised patients – total	413.7	417.7	419.4	373.7	407.0	427.0	447.5	505.6
Excluding fixed rate[8]+fixed rate[9]	246.7	249.8	259.8	250.5	274.5	290.1	311.6	331.7
Fixed rate per admission[10]	167.0	168.0	159.6	123.2	132.5	136.9	135.9	173.9
Total Hospital	1,988.2	2,259.4	2,621.5	2,816.1	3,103.8	3,474.2	3,942.4	4,340.8
Growth in %								
		2018/2017	2019/2018	2020/2019	2021/2020	2022/2021	2023/2022	2024*/2023
Outpatients [7]		17.0	19.6	10.9	10.4	13.0	14.7	9.7
Hospitalised patients – total		1.0	0.4	-10.9	8.9	4.9	4.8	13.0
Excluding fixed rate + fixed rate		1.3	4.0	-3.6	9.6	5.7	7.4	6.5
Fixed rate per admission		0.5	-5.0	-22.8	7.6	3.3	-0.7	27.9
Total Hospital		13.6	16.0	7.4	10.2	11.9	13.5	10.1

Table 12: NIHDI expenditure and evolutions in costs for the period 2017-2024 (excluding compensation), expressed in millions of euros, with a detailed breakdown of hospital expenditure.

The national budget set aside for fixed rate medicines, i.e. charging based on an amount per admission, is calculated annually by the General Council. This budget is based on open envelopes. Each hospital receives a fixed payment for each admission, based on the declared casemix - including the number of stays by APR-DRG and by degree of severity during the reference year.

	2017	2018	2019	2020	2021	2022	2023	2024*
Share of outpatient expenditure / total hospital expenditure	79.2%	81.5%	84.0%	86.7%	86.9%	87.7%	88.6%	88.4%

Table 13: Outpatient expenditure as a proportion of total expenditure on pharmaceutical specialties in hospitals for the period 2017-2024 (in %) (excluding compensation).

Table 14 shows the amounts allocated to the national budget for fixed rate medicines. This mechanism has been in force since 1 July 2006. For the first year of application (1 July 2006 to 30 June 2007), the national budget was €258.86 million. This amount has gradually decreased over the years, falling to €142.831 million in the 18th year of the fixed rate system (from 1 July 2023 to 30 June 2024). For the 19th year (1 July 2024 to 30 June 2025), the national budget rose again to €194.364 million, to cover 100% of costs after 1 July 2024, compared with 75% previously.

Period	National budget (in € millions)	Overall budget set at
1/07/2016 - 30/06/2017	167.159	75%
1/07/2017 - 30/06/2018	169,612	75%
1/07/2018 - 30/06/2019	168,100	75%
1/07/2019 - 30/06/2020	154,010	75%
1/07/2020 - 30/06/2021	148,825	75%
1/07/2021 - 30/06/2022	150,159	75%
1/07/2022 - 30/06/2023	147,372	75%
1/07/2023 - 30/06/2024	142,831	75%
1/07/2024 - 30/06/2025	194,364	100%

Source: Actuarial data - NIHDI.

Table 14: Amounts set for the national budget for the fixed amount per admission for the period from July 2016 to June 2024 (i.e. NOT per calendar year).

After 1 January 2014, the price per admission was reduced to 82% of the amount for a readmission of the same patient to the same hospital within 10 days of a previous admission. This measure was expected to generate an annual return of €1.9 million. The system changed on 1 July 2024: the amount covered by the fixed rate hospital charge

[7]Outpatients: medicines dispensed in the hospital, systematically excluding fixed rate medicines, with a reimbursement base set at 100% and an intervention determined according to the reimbursement category.

[8]Hospitalised patients - 100% (excluding fixed rate): medicines not included in the fixed rate dispensed to hospitalised patients, either because they are on the list of exceptions, or because they were administered to a patient admitted before 1 July 2006, when the fixed price for drugs came into force, or admitted to a non-acute hospital. The reimbursement base is set at 100%, with intervention determined according to reimbursement category.

[9]Hospitalised patients - 25/0% fixed rate: medicines dispensed to patients admitted to an acute hospital after 1 July 2006, for a drug included in the fixed rate. Until 30 June 2024, the intervention was 25% of the reimbursement base, with the remaining 75% covered by a fixed rate per admission, with the intervention waived depending on the reimbursement category. Since 1 July 2024, the intervention has been set at 0% of the reimbursement base, and 100% of costs are covered via the fixed rate amount per admission.

[10]Fixed rate per admission: This is a fixed rate amount paid to the hospital for each admission. This amount, revised every year, is based on the casemix (MZG) declared by the hospital. Until 30 June 2024, the fixed rate amount covered 75% of the costs. Since 1 July 2024, it has covered 100% of costs.

increased from 75% of the cost of the medicines, with medicines being charged at 25% of the reimbursement base, to full cover (100%) and a purely administrative charge (registration) of 0% of the reimbursement base.

Until 2019, there were between 1.7 and 1.8 million admissions each year. The COVID-19 pandemic led to a significant decrease in 2020 and 2021: in 2020, the number of admissions fell from 1.78 million to 1.56 million, a 12% decrease on 2019. In 2021 and 2022, this figure again exceeded 1.60 million per year, rising to over 1.7 million in 2023 and 2024. The evolution of the average amount per admission over the period 2019-2024 is illustrated in Table 15. The average cost per admission to cover the expenditure on medicines under the fixed rate system fell from €89.97 in 2019 to €79.30 in 2023. Since 1 July 2024, the fixed rate amount per admission has covered 100% of the cost, instead of 75%, and the average cost rose to €87.35 per admission in 2024.

	2019	2020	2021	2022	2023	2024
Fixed rate amount	160,298,295	129,974,496	130,208,687	134,981,444	137,062,299	151,754,324
Number of admissions	1,781,763	1,564,852	1,603,404	1,662,939	1,728,480	1,737,248
Amount per admission	89.97	83.06	81.21	81.17	79.30	87.35

Source: Actuarial data - NIHDI.

Table 15: Evolution of the average amount per admission (2019 - 2024 expressed in calendar years)

IV. Total expenditure on pharmaceutical specialties, irrespective of where dispensed

ATC3	Name	Share of hospital budget	Share of budget for public pharmacies	Share of total budget	NIHDI expenditure 2024 in millions	% cumulative	Growth 2023/2022	Growth 2024/2023
L01F	Monoclonal Antibodies and Antibody Drug Conjugates (T) †	29.8%	0.0%	16.3%	1,298.46	16%	19.0%	8.6%
L04A	Immunosuppressants (T)	8.1%	17.7%	12.4%	987.21	28%	2.1%	4.9%
L01E	Protein Kinase Inhibitors (T) †	11.7%	0.2%	6.5%	517.35	35%	13.9%	-1.0%
N07X	Other Nervous System Drugs (T) †	8.5%	0.1%	4.7%	370.99	40%	55.9%	43.8%
B01A	Antithrombotic Agents (T)	0.8%	8.7%	4.4%	346.44	44%	2.7%	-1.9%
A10B	Blood Glucose Lowering Drugs, Excl. Insulins (T) †	0.0%	7.6%	3.5%	275.33	47%	20.3%	16.5%
J06B	Immunoglobulins (T) †	4.7%	0.4%	2.8%	218.64	50%	12.3%	44.7%
B02B	Vitamin K and Other Haemostatics (T)	2.2%	3.2%	2.7%	213.16	53%	8.5%	11.7%
J05A	Direct Acting Antivirals †	1.1%	4.5%	2.7%	210.56	56%	5.2%	7.2%
L02B	Hormone Antagonists and Related Agents (T)	4.1%	0.6%	2.5%	198.38	58%	-5.4%	23.3%
L01X	Other Antineoplastic Agents (T) †	4.2%	0.1%	2.3%	185.49	60%	12.7%	51.6%
R03A	Adrenergics, Inhalants	0.1%	4.7%	2.2%	175.91	62%	7.0%	8.6%
R07A	Other Respiratory System Products (T)	4.0%	0.0%	2.2%	175.48	64%	77.2%	0.7%
C10A	Lipid Modifying Agents, Plain (T) †	0.0%	4.8%	2.2%	173.87	66%	27.5%	23.2%
S01L	Ocular Vascular Disorder Agents (T)	3.0%	0.0%	1.6%	128.61	68%	-3.9%	10.7%

(T): This ATC3 class includes one or more specialties registered temporarily in the context of an article 81/111 convention.
† ATC3 class analysed in depth in section 2 of the report.

Table 16: Top 15 overall annual NIHDI expenditure (excluding compensation) on medicines, regardless of place where dispensed: public pharmacies and hospital pharmacies - share and evolution of expenditure by ATC3 class within the budget for medicines.

Table 16 shows the 15 most expensive drug classes, based on the combined expenditure of public pharmacies and hospitals. The top three classes are monoclonal antibodies and antibody-drug conjugates (L01F), immunosuppressants (L04A) and protein kinase inhibitors (L01E). In 2024, expenditure on these classes amounted to €1.3 billion, €1.0 billion and €0.5 billion respectively. Together, these three classes accounted for just over a third (35%) of the total budget for medicines.

V. Overview of expenditure on other pharmaceutical services in public pharmacies

Table 17: Evolution of annual NIHDI expenditure, excluding compensation, relating to reimbursable pharmaceutical specialties and other pharmaceutical services in public pharmacies, for the period 2021-2024 (in millions of euros).

21 - Overall analysis of expenditure on pharmaceutical specialties

Most of the expenditure on reimbursable pharmaceutical services goes on pharmaceutical specialties. In 2024, expenditure in public pharmacies for these specialties amounted to €3,591.4 million (93%), compared with €258.1 million (7%) for other reimbursable pharmaceutical services (see Table 17).

In addition to dispensing reimbursable pharmaceutical specialties, the health insurance system also covers a range of other services, such as magistral preparations, specific fees (out-of-hours fees for public pharmacists, fees for dispensing methadone, oxygen, etc.), medical nutrition, as well as services linked to diabetes and care for chronic renal failure (strips and lancets, glucometers, blood pressure monitors, etc.). The Pharmanet database contains information on the reimbursable pharmaceutical services provided by public pharmacies. An analysis of NIHDI expenditure for 2024, ranked in descending order, shows that the ten categories listed in Table 18 alone account for 97% of expenditure on other pharmaceutical services.

Rank	Category	2021	2022	2023	2024	*Cumulative proportion of total expenditure*
	Total	**203.9**	**240.2**	**241.9**	**258.1**	**100**
1	Magistral preparations	65.6	67.7	76.8	85.7	33
2	Fees for the "referring pharmacist" role	36.6	42.6	51.5	59.0	56
3	Self-catheterisation	22.3	23.5	24.7	26.2	66
4	Specific intervention for contraceptives	15.8	16.5	16.9	17.3	73
5	Fees and packages for oxygen	14.4	14.7	14.5	14.2	78
6	Preparation / administration of COVID vaccine	0.0	3.7	13.3	11.1	83
7	Health food	10.0	10.4	10.2	10.6	87
8	Diabetes care pathway	8.3	8.4	8.9	9.2	90
9	Storage and availability fees	*6.6*	*7.3*	*7.9*	*8.1*	94
10	Administration of the flu vaccine	0.0	0.0	4.4	7.8	97
	Growth in %					
			2022/201	**2023/2022**	**2024/2023**	
	Total		**17.8**	**0.7**	**6.7**	
1	Magistral preparations		3.3	13.4	11.6	
2	Fees for the "referring pharmacist" role		16.4	21.0	14.4	
3	Self-catheterisation		5.5	4.9	6.2	
4	Specific intervention for contraceptives		4.7	2.5	1.9	
5	Fees and packages for oxygen		1.6	-1.3	-1.5	
6	Preparation / administration of COVID vaccine			255.3	-16.2	
7	Health food		4.3	-2.1	4.6	
8	Diabetes care pathway		1.2	5.8	3.2	
9	Storage and availability fees		7.3	7.9	8.1	
10	Administration of the flu vaccine				77.0	

Source: Pharmanet

Table 18: Evolution in annual NIHDI expenditure on other pharmaceutical services in public pharmacies, top 10 expenditure items (2021-2024; in millions of euros)

In addition to the section devoted to expenditure relating to magistral preparations, a fixed rate allowance is envisaged for the fractional dispensing of methadone-based substitution treatments by pharmacists. The evolution in this expenditure is shown in the table below.

	2021	2022	2023	2024
Recorded expenditure	3.3	3.3	3.5	3.4
Growth %		0.5%	5.8%	-2.9%

Source: Actuarial data

Table 19: Evolution in annual NIHDI expenditure for the fractional dispensing of methadone-based substitution treatments (2021-2024, in millions of euros)

2. Detailed analysis of different pharmacological classes

13 pharmacological classes were selected by the scientific expertise coordinator of the Pharmaceutical Policy Department of the NIHDI for in-depth analysis. This choice is based on significant changes observed in 2024, whether in terms of a significant rise in healthcare insurance expenditure, significant variations in consumption volumes, or even structural transformations in the market - such as changes in reimbursement conditions or the introduction of new specialties. The data on which the analyses are based are available on the NIHDI website (NIHDI, 2025f).

Additional figures and indicators not included in the body of this section are presented in Appendix 1 to ensure full transparency of results. Certain graphs show evolutions by molecule within the pharmacological class. For ease of reading, the figures will only show data for the 20 largest molecules in the cluster. These will be labelled with the full ATC code. A list of ATC codes and their corresponding molecules will be presented at the start of each analysis of a class.

I. Class A10B - Drugs used in diabetes

Chemical Substance
A10BA02 metformin - GLUCOPHAGE a.o. (+ generic)
A10BB01 glibenclamide - DAONIL
A10BB07 glipizide - GLIBENESE a.o.
A10BB08 gliquidone - GLURENORM
A10BB09 gliclazide - UNI DIAMICRON (+ generic)
A10BB12 glimepiride - AMARYLLE (+ generic)
A10BD07 metformin and sitagliptin - JANUMET (+ generic)
A10BD08 metformin and vildagliptin - EUCREAS
A10BD10 metformin and saxagliptin - KOMBOGLYZE
A10BD11 metformin and linagliptin - JENTADUETO
A10BD13 metformin and alogliptin - VIPDOMET
A10BD15 metformin and dapagliflozin - XIGDUO
A10BD16 metformin and canagliflozin - VOKANAMET
A10BD20 metformin and empagliflozin - SYNJARDY
A10BD23 metformin and ertugliflozin - SEGLUROMET
A10BD24 sitagliptin and ertugliflozin - STEGLUJAN
A10BG03 pioglitazone - ACTOS
A10BH01 sitagliptin - JANUVIA (+ generic)
A10BH02 vildagliptin - GALVUS
A10BH03 saxagliptin - ONGLYZA
A10BH04 alogliptin - VIPIDIA
A10BH05 linagliptin - TRAJENTA
A10BJ01 exenatide - BYETTA a.o.
A10BJ02 liraglutide - VICTOZA
A10BJ03 lixisenatide - LYXUMIA
A10BJ05 dulaglutide - TRULICITY
A10BJ06 semaglutide - OZEMPIC a.o.
A10BK01 dapagliflozin - FORXIGA
A10BK02 canagliflozin - INVOKANA
A10BK03 empagliflozin - JARDIANCE
A10BK04 ertugliflozin - STEGLATRO
A10BX02 repaglinide - NOVONORM (+ generic)

Table20: List of reimbursed molecules in pharmacological class A10B.

The upward trend in expenditure on antidiabetic medicines (excluding insulin), which could already be observed in previous years, remained unchanged. This trend can be seen in both public pharmacies (see Figure 5) and hospital pharmacies (see Figure 6), with, as expected for these medicines, much higher turnover via public pharmacies. In 2015, total NIHDI expenditure (public pharmacies and hospital pharmacies combined) on antidiabetic medicines (excluding insulin) was €88.77 million; in 2024, this expenditure was €275.33 million. This represents a threefold increase in annual expenditure compared to 10 years ago. In 2024, 99.2% of the NIHDI expenditure on antidiabetic medicines (excluding insulin) was via public pharmacies.

The upward trend in expenditure can be explained by three factors:

- An annual absolute increase (prevalence) in the number of diabetes patients in Belgium,

- The recent arrival on the market of antidiabetic medicines that are much more expensive than older antidiabetic medicines, and which patients are using more, and
- The extension of reimbursement not approved by the NIHDI for the indication of obesity without diabetes (for Ozempic, this is an EMA off-label indication).

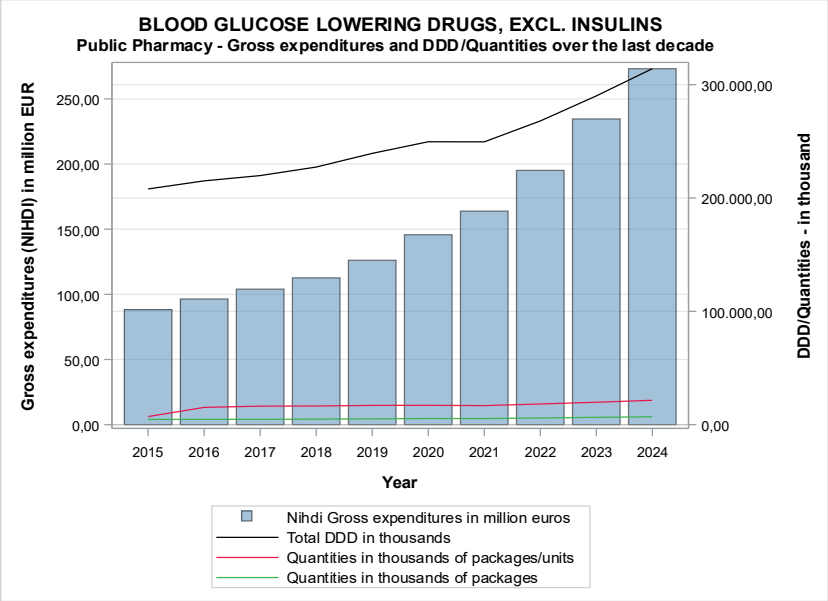

Figure 5: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class A10B.

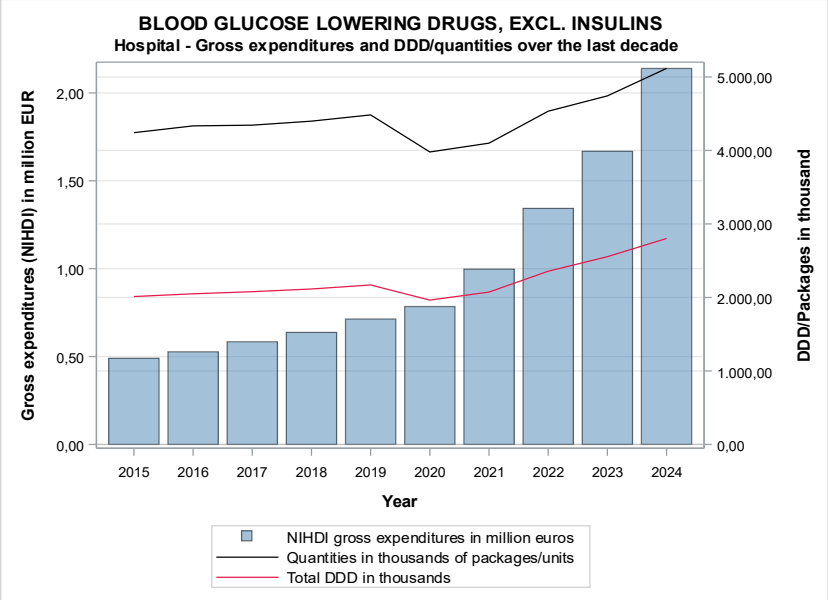

Figure 6: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class A10B.

The number of patients receiving antidiabetic medicines (excluding insulin) through public pharmacies rose from 673,080 in 2021 to 852,698 in 2025, representing a 26.7% increase in the number of patients over four years (see Figure 7).

A major impact on the rising expenditure on antidiabetic medicines is explained by more use of the two most expensive classes: the class of incretins (GLP-1 receptor agonists) and the class of gliflozins (SGLT2 inhibitors).

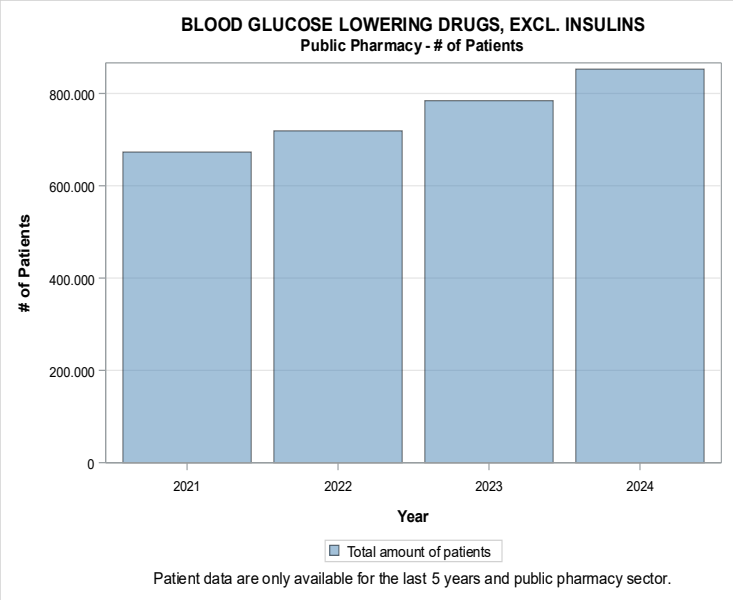

Figure 7: Annual evolution in the number of patients using specialties from pharmacological class A10B reimbursed in public pharmacies and nursing homes.

Among the incretins (ATC: A10BJ), the impact of Ozempic (semaglutide - ACT code: A10BJ06), which has been reimbursed since May 2019, is significant. Figure 8 shows that in January 2020, metformin (ACT code: A10BA02) was still the antidiabetic medicine with the highest turnover in public pharmacies, namely €2.257 million (19.3% of the total turnover of antidiabetic medicines (excluding insulin) in public pharmacies). Five years later, in December 2024, semaglutide had the highest turnover in public pharmacies, namely €3.024 million (11.9% of the total turnover of antidiabetic medicines (excluding insulin) in public pharmacies). In the space of four years, between December 2020 and December 2024, monthly turnovers of Ozempic tripled, and the Figure shows that this upward trend in monthly expenditure is still observable. Non-compliant use of Ozempic in patients without type 2 diabetes mellitus (T2D) may explain part of the significant expenditure on Ozempic. The NIHDI took measures to combat this abuse in 2025. Turnover of the incretin insulin Trulicity, which has been available on the market for some time (dulaglutide - ACT code: A10BJ05), has since fallen. This is likely due to the popularity of Ozempic, which has a better positive effect on controlling obesity associated with T2D than Trulicity, with Ozempic taking over part of Trulicity's market share.

The impact of the group review of diabetes in 2019, which resulted in a 10% price reduction for incretins, is not visible as it is offset by increased use caused by the same group review, which relaxed the reimbursement criteria.

Gliflozins (ATC: A10BK) have been reimbursed for T2D for about 10 years now. A sharp increase in expenditure in this class was observable from 2022 onwards, when the indication for reimbursement of Forxiga (dapagliflozin - ACT code: A10BK01) and Jardiance (empagliflozin - ACT code: A10BK03) was extended to indications other than T2D, namely chronic heart failure and chronic renal insufficiency (cf. Figure 8 & Figure 10). Note: gliflozins are the only antidiabetic drugs that are reimbursed through an agreement between the manufacturer and the NIHDI. The actual gross expenditure is therefore lower than shown in the graph.

25 - Detailed analysis of different pharmacological classes

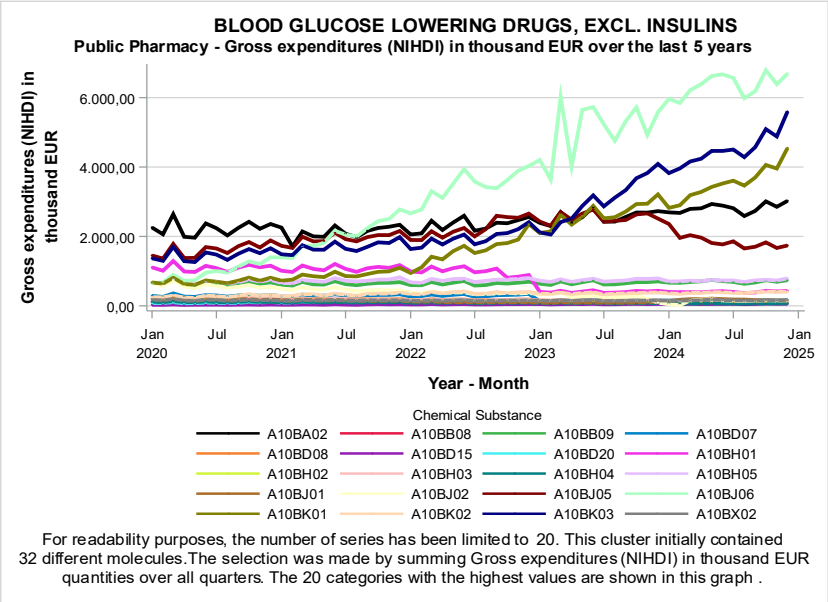

Figure 8: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class A10B.

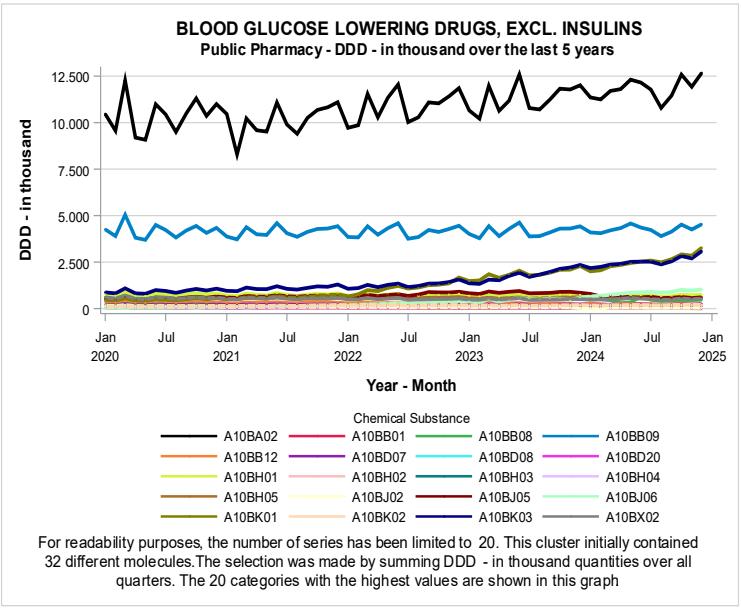

Figure 9: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class A10B.

Metformin (ACT code: A10BA02) and sulphonylurea derivatives (ACT code: A10BB09) are still the most commonly used molecules. Consumption of these medicines (see Figure 9) and turnover (see Figure 8) has been fairly stable for 10 years now. Despite the much higher expenditure, the use of Ozempic (semaglutide), Forxiga (dapagliflozin) and Jardiance (empagliflozin) is much lower compared to the use of metformin and sulphonylurea derivatives, but we can observe a rising trend in the use of these three molecules (see Figure 9). The graphs show that the significant expenditure on semaglutide and gliflozins currently goes on a minority of treated patients.

In summary, expenditure on antidiabetic medicines (excluding insulin) is currently dominated by expenditure on Ozempic (semaglutide), Forxiga (dapagliflozin) and Jardiance (empagliflozin), and this expenditure continues to show a rising trend. Expenditure on Trulicity (dulaglutide) shows a downward trend, while expenditure on other pharmaceutical specialties remains fairly stable (see Figure 8). The same trends can be observed with regard to consumption (see Figure 9), but here consumption is still dominated by the older antidiabetic medicines, namely metformin and sulphonylurea derivatives. This observation shows that the cost of treatment with an incretin or gliflozin is many times higher than the cost of treatment with metformin or a sulphonylurea derivative.

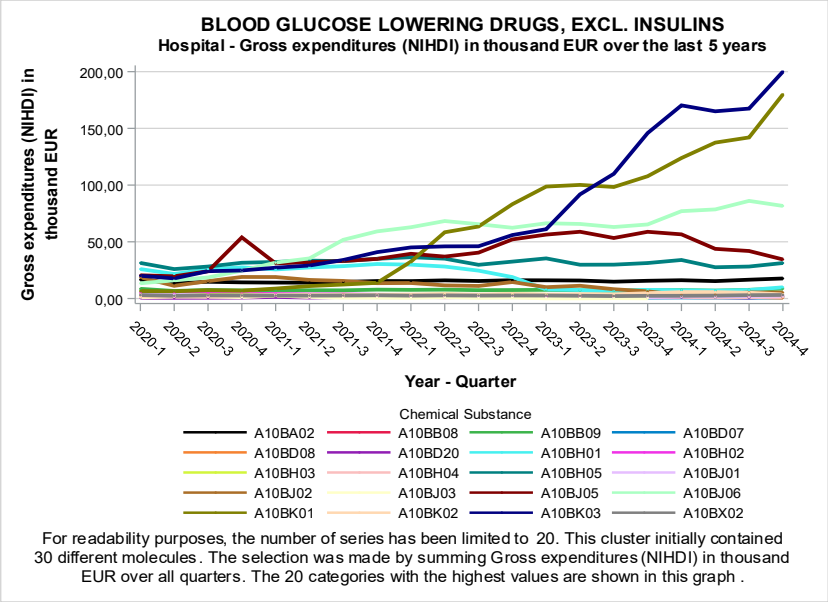

Figure 10: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class A10B.

The reimbursement of new indications for gliflozins, the continued use of Ozempic and the reimbursement of Mounjaro (tirzepatide) since July 2025 for T2D mean that expenditure will continue to rise in the coming years.

II. Class C01E - Serum lipid-lowering agents

Chemical Substance
C01EA01 alprostadil - PROSTIN
C01EA01 adenosine - ADENOCOR
C01EB17 ivabradine - PROCORALAN (+ generic)
C01EA01 macvacamten - CAMZYOS

Table 21: List of reimbursed molecules in pharmacological class C01E.

There are four active substances within ATC class C01E: alprostadil; adenosine; ivabradine; and mavacamten. These correspond to the pharmaceutical specialties PROSTIN, ADENOCOR, PROCORALAN and CAMZYOS. The first three medicines have been reimbursed for quite some time now. CAMZYOS, on the other hand, only became reimbursable in 2024 via a Managed Entry Agreement (MEA). Mavacamten is a selective inhibitor of myosin in heart muscle cells.

Over the past few years, both consumption volume and expenditure within class C01E have been stable, with the exception of 2024 in hospital pharmacies. This discrepancy is explained by the introduction of CAMZYOS into the reimbursement system, specifically for the indication of obstructive hypertrophic cardiomyopathy. Reimbursements started on 1 September 2024, after which an immediate rise was observed in the use of class C01E in hospitals during the third and fourth quarters of that year. Both consumption, expressed in Defined Daily Doses (DDD), and the associated expenditure rose as a result of the availability of CAMZYOS, when comparing the calendar year 2024 with previous years.

For the first year of reimbursement, the Commission for Reimbursement of Medicines (CRM) estimated an additional gross expenditure of €25.4 million for CAMZYOS. By way of comparison, annual expenditure for the entire C01E class in hospitals averaged approximately €0.5 million in previous years. These initial expenditure figures clearly illustrate a break in the trend following the introduction of CAMZYOS.

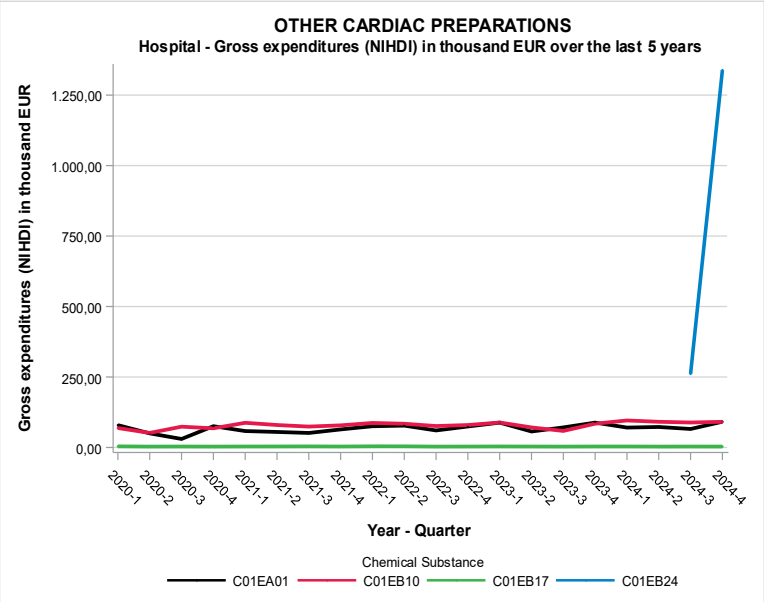

Figure 11: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class C01E.

III. Class C10A – Serum-lipid reducing agents, not combined

Chemical Substance
C10AA01 simvastatin - ZOCOR (+ generic)
C10AA03 pravastatin - PRAREDUCT (+ generic)
C10AA04 fluvastatin - LESCOL
C10AA05 atorvastatin - LIPITOR (+ generic)
C10AA07 rosuvastatin - CRESTOR (+ generic)
C10AB02 bezafibrate - CEDUR a.o.
C10AB05 fenofibrate - LIPANTHYL a.o. (+ generic)
C10AB08 ciprofibrate - HYPERLIPEN
C10AC01 colestyramine - QUESTRAN
C10AC02 colestipol - COLESTID
C10AD06 acipimox - OLBETAM
C10AX09 ezetimibe - EZETROL (+ generic)
C10AX13 evolocumab - REPATHA
C10AX14 alirocumab - PRALUENT
C10AX15 bempedoic acid - NILEMDO
C10AX16 inclisiran - LEQVIO

Table 22: List of reimbursed molecules in pharmacological class C10A.

Figure 12 shows the evolution of expenditure and use of serum-lipid reducing agents in public pharmacies over the period 2015 to 2024. In the early years, expenditure exceeded €150 million due to the widespread use of drugs that were still under patent. From 2018 onwards, expenditure fell due to the arrival of cheap generics, while consumption (DDD) continued to rise. After 2022, expenditure rose sharply again, to over €160 million in 2024, due to the introduction of innovative, expensive therapies for high-risk patients. These medicines are reimbursed through confidential contracts, whereby the NIHDI recovers part of the costs through refunds. The figures shown therefore overestimate the actual budget impact.

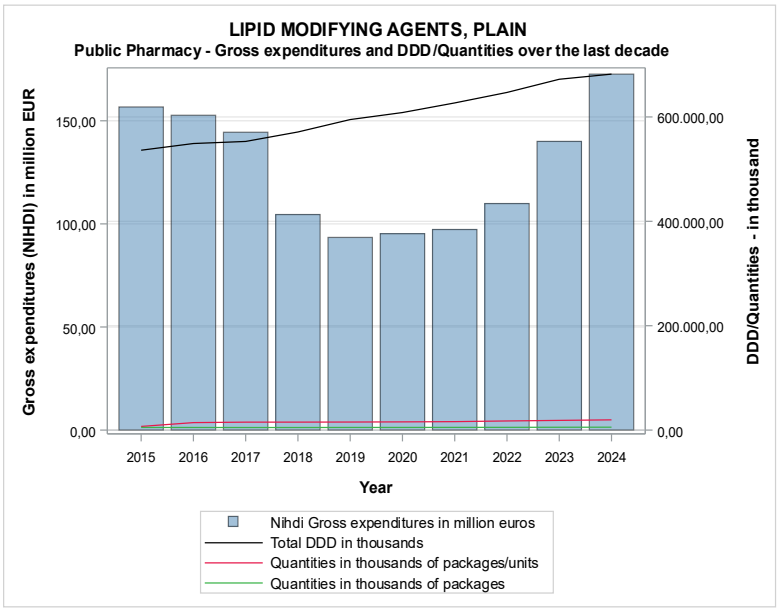

Figure 12: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class C10A.

Consumption, expressed in DDD, rises steadily throughout the period, reflecting both the growth in the number of patients treated and stricter treatment targets. The number of packages remains relatively stable, indicating more intensive therapies per patient.

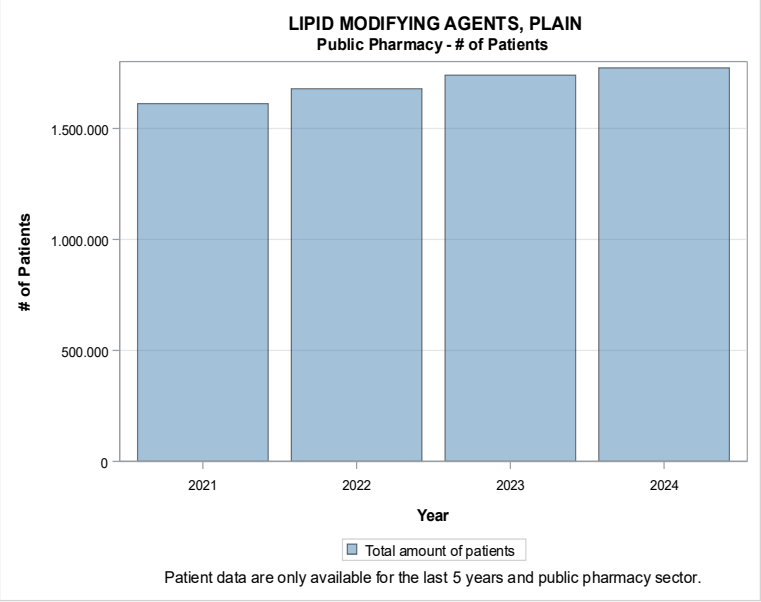

Figure 13: Annual evolution in the number of patients using specialties from pharmacological class C10A reimbursed in public pharmacies and nursing homes.

The number of patients using cholesterol-lowering drugs has remained high in recent years and gradually increased (from 1.6 to 1.8 million patients). This trend is consistent with what we saw in Figure 13: the stronger rise in DDD and the recent increase in expenditure is not really due to more patients, but mainly by more intensive therapies and the introduction of more expensive new medicines.

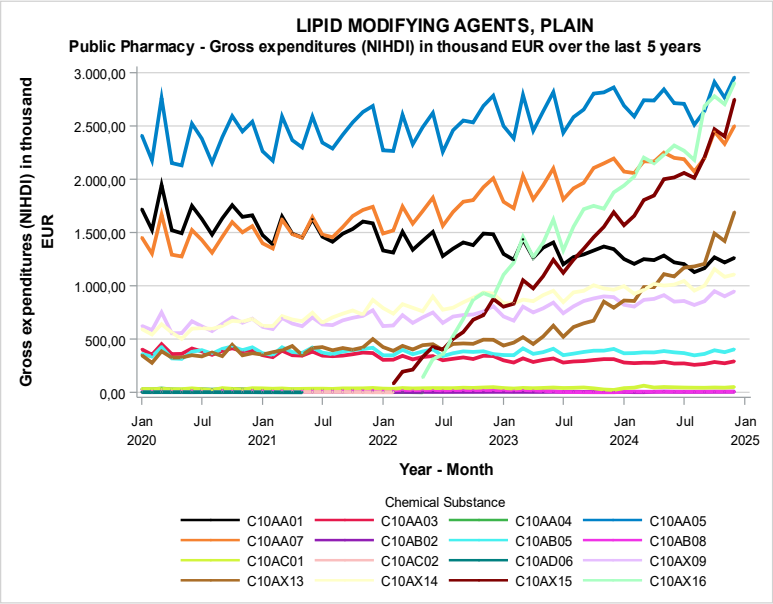

Figure 14: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class C10A.

Expenditure on traditional statins such as atorvastatin and rosuvastatin remains relatively stable due to the widespread availability of inexpensive generics (See Figure 14). For older drugs such as simvastatin, there is even a noticeable downward trend. However, there was a striking rise in expenditure from 2022 onwards due to the introduction of new lipid-lowering therapies, including PCSK9 inhibitors (alirocumab, evolocumab), inclisiran and bempedoic acid. As a result, the expenditure pattern is shifting increasingly towards innovative therapies, while conventional treatments are still under control from a budget perspective. The figures shown overestimate the actual budget impact, as these products are reimbursed through confidential contracts.

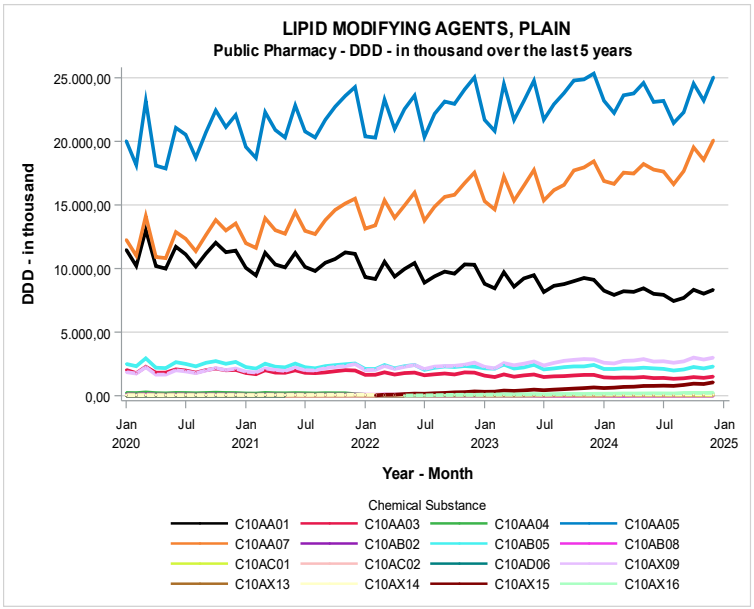

Figure 15: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class C10A.

Figure 15 clearly shows that the use of conventional statins (atorvastatin and rosuvastatin) is still dominant and is even increasing, while older drugs such as simvastatin continue to lose ground. In addition, the use of complementary therapies such as ezetimibe is slowly increasing, especially in combination therapy. The most striking element is the emergence of new drugs (PCSK9 inhibitors, inclisiran and bempedoic acid), which, despite their relatively limited use, are already having a strong impact on total expenditure.

IV. Class C10B - Lipid Modifying Agents, Combinations[11]

Chemical Substance
C10BA02 simvastatin and ezetimibe - INEGY (+ generic)
C10BA03 pravastatin and fenofibrate - PRAVAFENIX
C10BA05 atorvastatin and ezetimibe - ATOZET a.o. (+ generic)
C10BA06 rosuvastatin and ezetimibe - MYROSOR a.o.
C10BA10 bempedoic acid and ezetimibe - NUSTENDI
C10BX06 atorvastatin, acetylsalicylic acid and ramipril - TRINOMIA
C10BX11 atorvastatin, amlodipine and perindopril - LIPERTANCE
C10BX15 atorvastatin and perindopril - LIPERCOSYL

Table 23: List of reimbursed molecules in pharmacological class C10B.

Figure 16 shows that expenditure in public pharmacies on combination therapies of lipid-lowering agents remained relatively stable for a long time, at around €20 to €25 million per year. However, from 2021 onwards, a sharp increase can be seen, with a threefold increase in 2024. This is accompanied by a significant rise in DDDs, indicating increasing consumption in practice. The growth can be explained by the increased focus on treatment targets in cardiovascular risk patients and the increasing use of combination preparations of statins with other agents (such as ezetimibe).

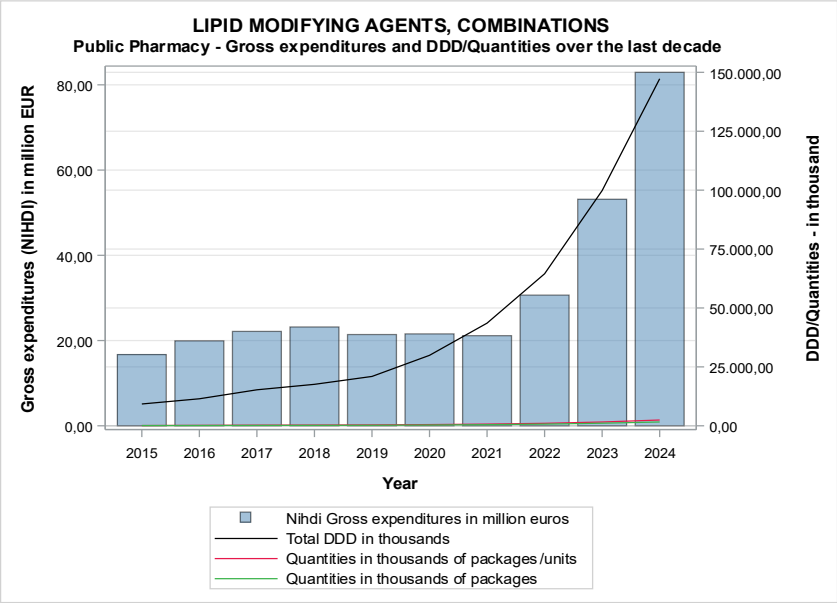

Figure 16: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class C10B.

The number of patients receiving combination therapy has risen sharply in recent years, from around 160,000 in 2021 to more than half a million in 2024 (see Figure 17). This clearly shows that combination therapies are increasingly being used in patients who do not achieve their treatment targets with monotherapy alone. The increase in patient numbers largely explains the sharp rise in expenditure.

Within combination therapies, Figure 18 shows that expenditure is mainly driven by a few dominant subgroups: rosuvastatin + ezetimibe, atorvastatin + ezetimibe and bempedoic acid + ezetimibe. These figures reflect the fact that combinations with ezetimibe and newer drugs are preferred in practice and have a bigger budget impact. For combination preparations with atorvastatin + ezetimibe, the expenditure graph shows a striking decline in 2021 as a result of the structural measures (reference price system, patent cliff, etc.) that were applied. There was then another upward trend in expenditure on this molecule. The start of reimbursement for the combination of bempedoic acid + ezetimibe since 2022 also shows an increase in expenditure. The figures shown may overestimate the actual budget impact, as this speciality is reimbursed through a confidential contract.

[11] The difference between the C10A class previously analysed and the C10B class presented in this section is that the former groups together medicines used as monotherapy to reduce blood lipids, such as statins or fibrates, while the latter concerns polytherapies combining a lipid-lowering agent with another active ingredient, such as ezetimibe or an antihypertensive. As such, C10A corresponds to treatments targeted exclusively at dyslipidemia, while C10B includes combinations aimed at a broader therapeutic management.

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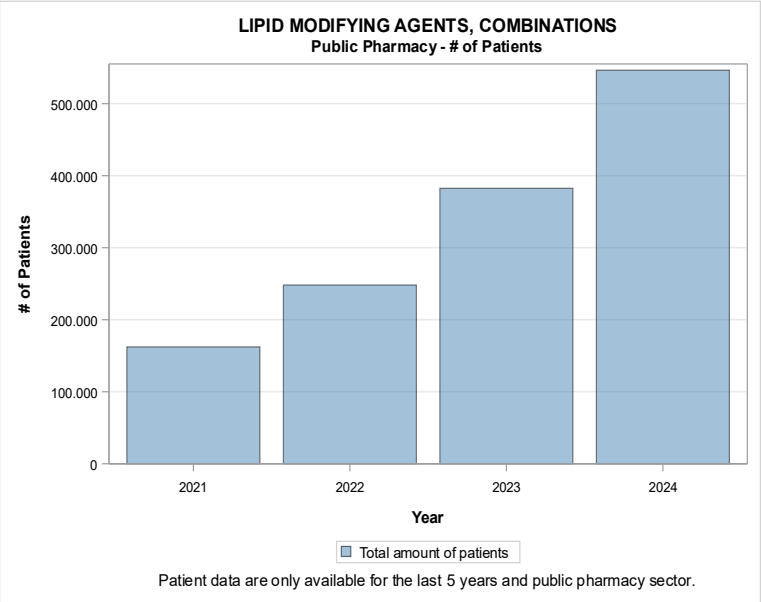

Figure 17: Annual evolution in the number of patients using specialties from pharmacological class C10B reimbursed in public pharmacies and nursing homes.

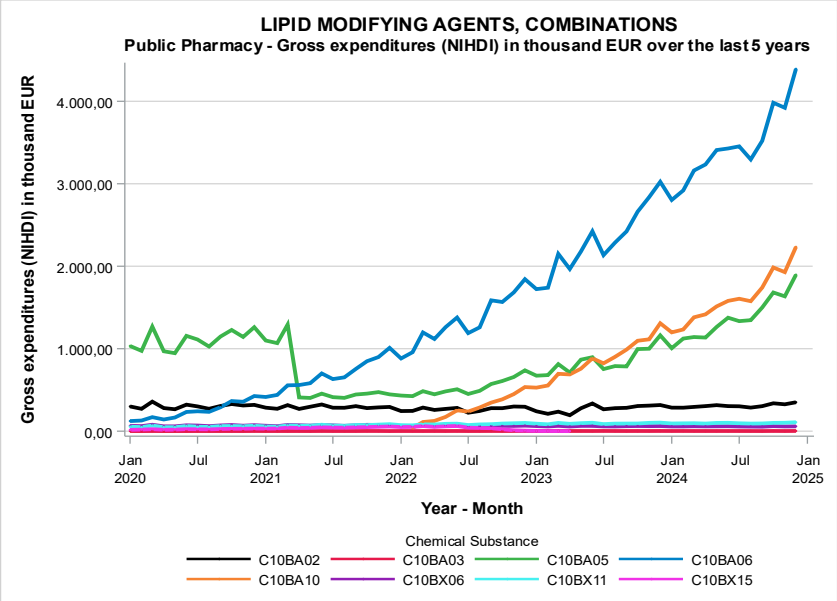

Figure 18: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class C10B.

In terms of consumption (DDD), the same subgroups are dominant (seeFigure 19). Rosuvastatin + ezetimibe in particular has seen an explosive increase in consumption, confirming its key role in the current treatment of hypercholesterolaemia. Consumption of atorvastatin + ezetimibe and bempedoic acid + ezetimibe is also increasing, while older combinations such as simvastatin + ezetimibe and pravastatin + fenofibrate remain stable or limited in use. The clear shift towards modern combinations confirms the trend towards more intensive and personalised lipid-lowering treatment.

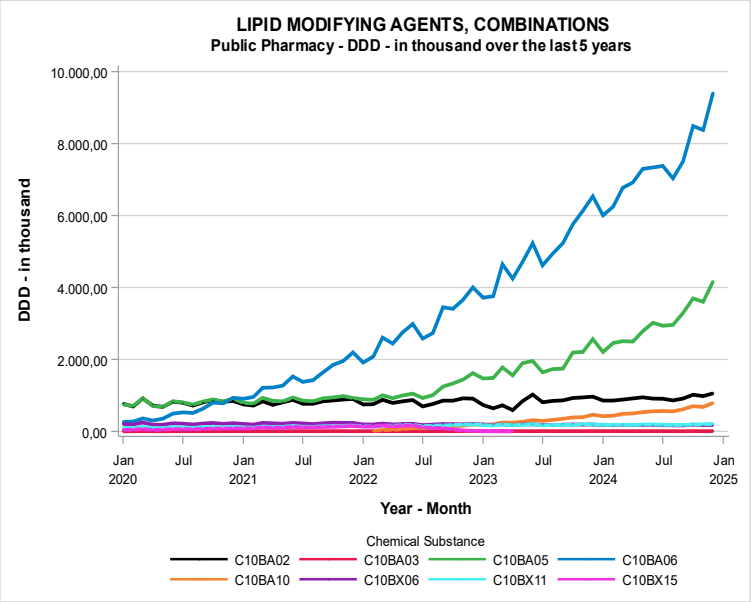

Figure 19: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class C10B.

Expenditure on combination therapies in hospitals remained relatively stable until 2021, but increased significantly after 2022 (see Figure 20). This increase coincides with a sharp rise in the number of DDDs, indicating a wider use of combination therapies in hospitalised patients. Although total expenditure remains low at around €0.25 million compared to community pharmacies, the recent growth is striking and reflects the increasing role of combinations in acute and specialised treatment.

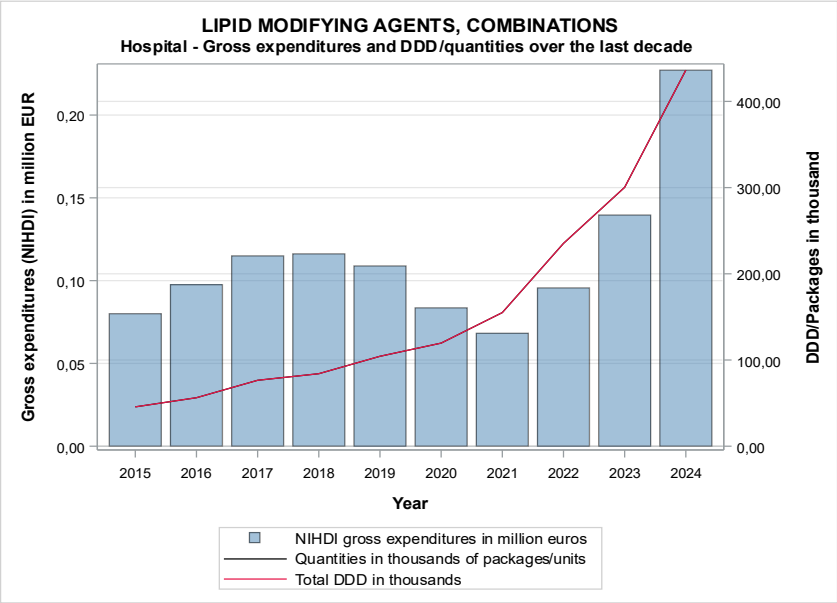

Figure 20: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class C10B.

Within hospital pharmacies (see Figure 21), rosuvastatin + ezetimibe and atorvastatin + ezetimibe primarily account for the sharp rise in expenditure. Their share has increased significantly in recent years, while older combinations such as simvastatin + ezetimibe are stable or slightly declining. It is striking that bempedoic acid + ezetimibe has also recently made a significant contribution to the rising costs. This shows that modern combinations are being used more and more prominently in hospitals, at the expense of older and cheaper alternatives. The figures shown may overestimate the actual budget impact, as this combination is reimbursed through a confidential contract.

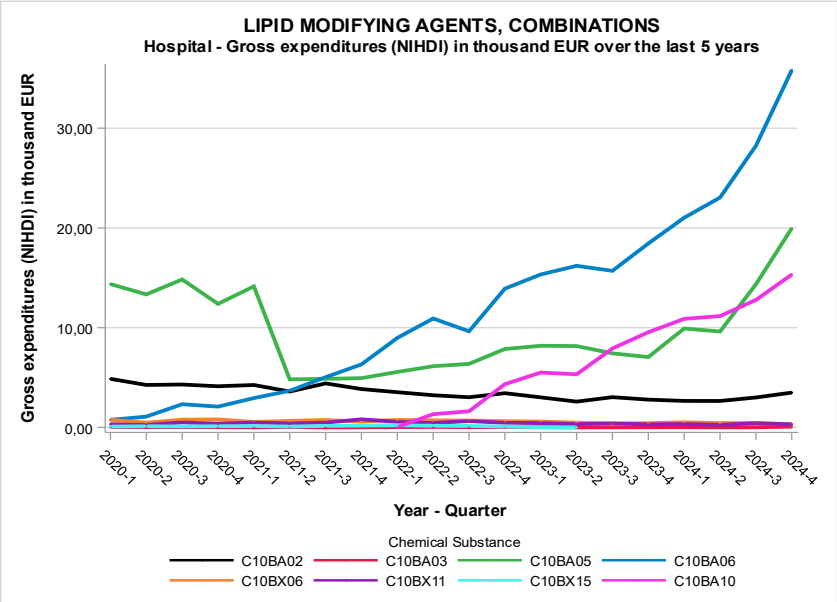

Figure 21: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class C10B.

The consumption trend (DDD) shown in Figure 22 follows the same evolution as expenditure. Rosuvastatin + ezetimibe is by far the fastest growing combination and is being used more and more frequently. In addition, we also see a steady rise in atorvastatin + ezetimibe and bempedoic acid + ezetimibe, while conventional combinations such as simvastatin + ezetimibe remain stable or are declining. This confirms that the growth in hospital expenditure is not only due to higher prices but also to a real increase in the use of modern combination therapies.

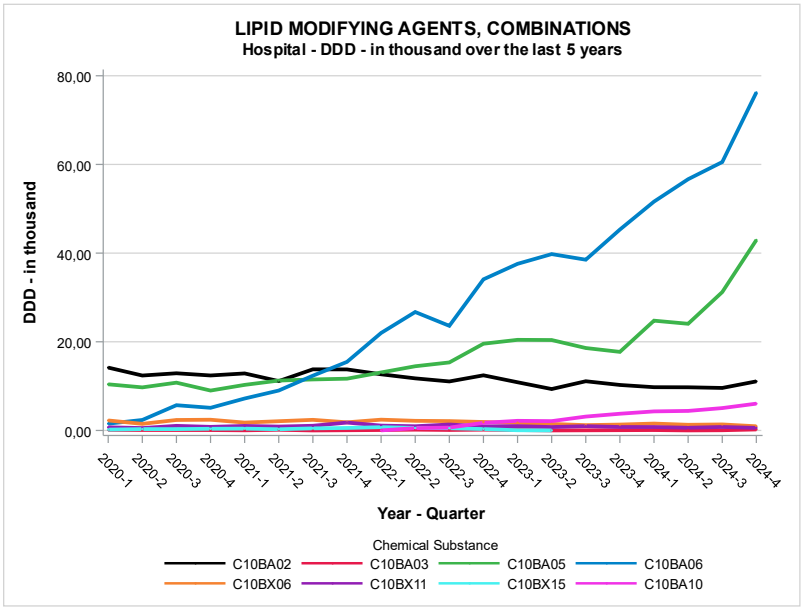

Figure 22: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class C10B.

V. Class D11A - Other dermatological preparations

Chemical Substance
D11AH01 tacrolimus - PROTOPIC (+ generic)
D11AH02 pimecrolimus - ELIDEL
D11AH05 dupilumab - DUPIXENT
D11AH07 tralokinumab - ADTRALZA
D11AH08 abrocitinib - CIBINQO

Table 24: List of reimbursed molecules in pharmacological class D11A.

Since 2020, there has been a sustained rise in expenditure in public pharmacies for this group of medicines (see Figure 23). Consumption, measured in DDD, shows a similar upward trend. However, the total number of packages has hardly increased, indicating that the growth in DDD is likely due to higher dosages and/or longer treatment duration per patient.

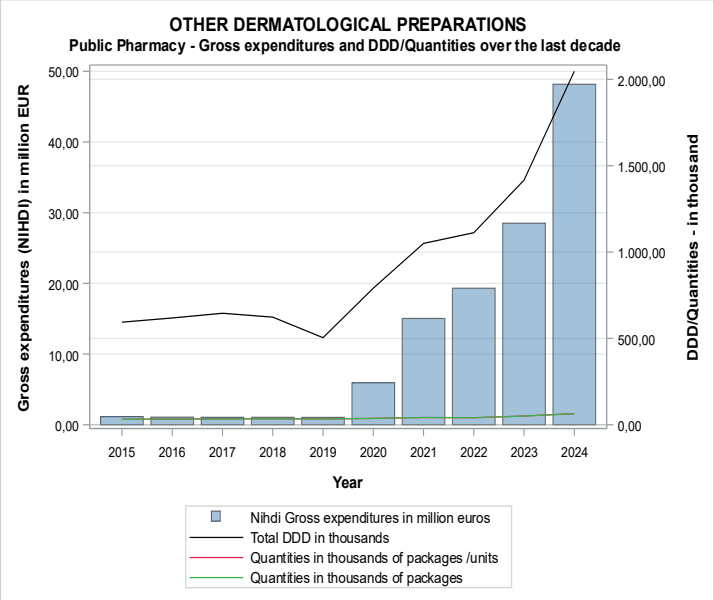

Figure 23: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class D11A.

The number of patients treated with other dermatological preparations has only increased slightly in recent years, from approximately 28,000 to approximately 37,000, as shown in Figure 24. This confirms that the increase in expenditure is mainly due to more intensive consumption per patient and more expensive treatments, and not to an increase in the number of patients. This observation is backed up by the data in the accompanying graph.

Pimecrolimus (Elidel®) and tacrolimus (Protopic®) are anti-inflammatory drugs that inhibit the release of mediators such as calcineurin. Since 2003 and 2004, respectively, these drugs have been reimbursed for the treatment of moderate to severe atopic dermatitis, both for short-term symptom relief and for intermittent long-term use. Figure 25 shows that expenditure on these products has remained limited and stable over the years.

Dupilumab (Dupixent®), an interleukin (IL-4/IL-13) inhibitor, has been temporarily reimbursed since 1 June 2020 through a confidential agreement for the indication of severe atopic dermatitis in adults. The graph shows that this speciality is currently the main cost driver and has had a direct impact on gross expenditure since the start of temporary reimbursement in 2020. Since then, reimbursement has been repeatedly extended, which explains the continuing upward trend in expenditure after 2020:

- From 1 March 2023, reimbursement for Dupilumab (Dupixent®) was extended to the treatment of corticosteroid-dependent severe asthma with type 2 inflammation.
- Since 1 August 2023, children between the ages of 6 and 12 have also been eligible for reimbursement. This indication is a definitive listing.
- Since 1 March 2024, reimbursement has been extended to include severe chronic rhinosinusitis with nasal polyps (CRSwNP) via a definitive listing.
- Since 1 August 2023, Dupixent has been reimbursed for the additional treatment of corticosteroid-independent severe asthma with type 2 inflammation. This indication is also a definitive listing in the reimbursement scheme.
- The indication for severe atopic dermatitis was extended to children on 1 June 2024.
- On 1 August 2024, the indication was extended to include severe prurigo nodularis (PN) via a temporary listing, and the indication for active eosinophilic oesophagitis followed on 1 November 2024, a permanent listing.

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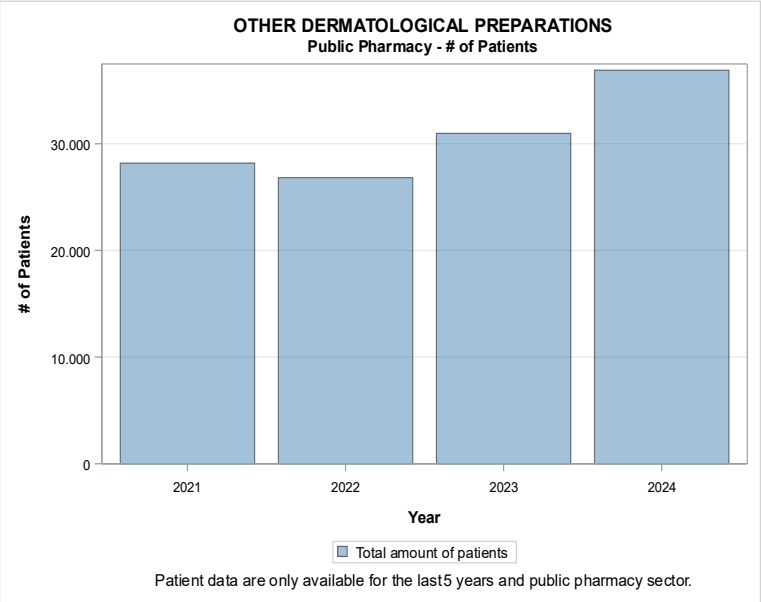

Figure 24: Annual evolution in the number of patients using specialties from pharmacological class D11A reimbursed in public pharmacies and nursing homes.

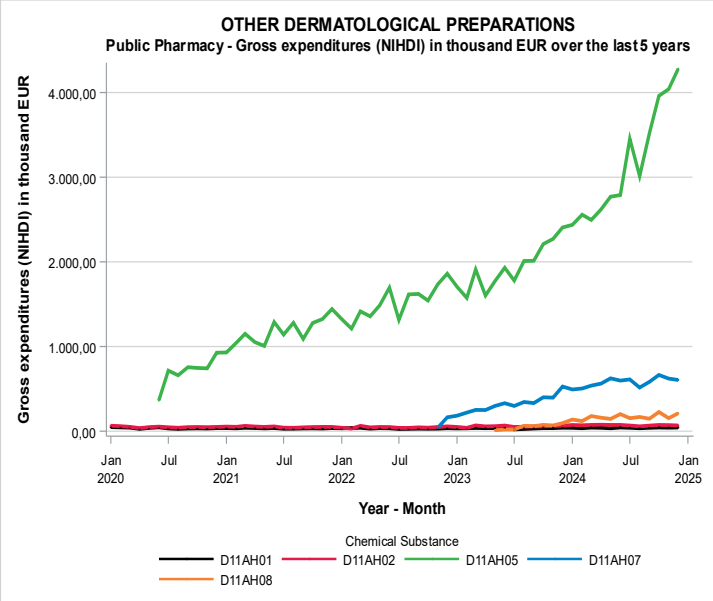

Figure 25: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class D11A.

Tralokinumab (Adtralza®), an interleukin (IL-13) inhibitor, has only been temporarily reimbursed since the end of 2022 for the treatment of severe atopic dermatitis in adults, via a confidential agreement. Since 1 November 2023, this reimbursement has been extended to children. Expenditure in public pharmacies has been rising steadily since its listing in the reimbursement scheme, but is still limited.

Abrocitinib (Cibinqo®) is an inhibitor of protein kinases of the Janus kinase (JAK) family. JAKs are intra-cellular enzymes that transmit signals from cytokines or growth factors involved in a wide range of cellular processes, including inflammatory responses. Cibinqo® has only been temporarily reimbursed since May 2023 for the treatment of severe atopic dermatitis in adults, via a confidential agreement. Expenditure on this speciality is still also very limited.

We see the same pattern recurring in Figure 26 as regards consumption volume (DDD). While pimecrolimus (Elidel®) and tacrolimus (9rotopic®) show a stable trend, and tralokinumab (Adtralza®) and abrocitinib (Cibinqo®) show only a slight upward trend, dupilumab (Dupixent) is also dominant here.

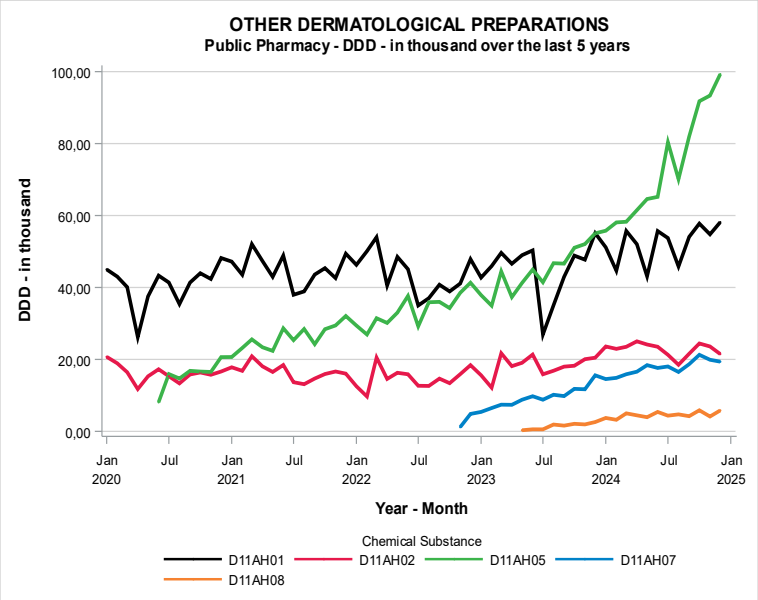

Figure 26: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class D11A.

In hospitals (see Figure 27-Figure 29), a significant increase in gross expenditure was only observed from 2023 onwards. This is due to the fact that Dupilumab (Dupixent) was reimbursed for the treatment of severe asthma with type 2 inflammation.

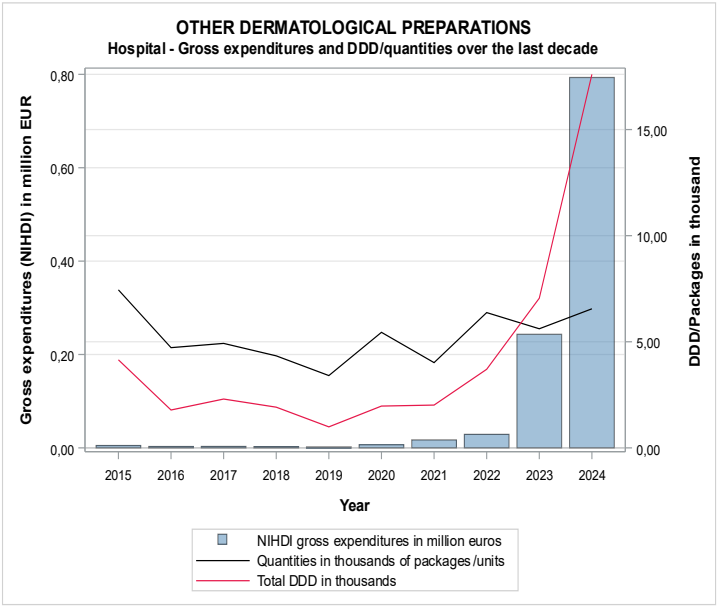

Figure 27: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class D11A.

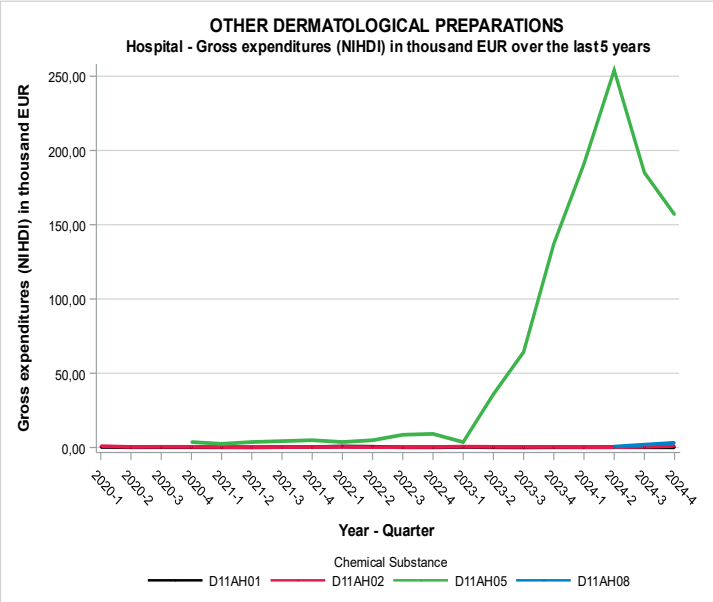

Figure 28: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class D11A.

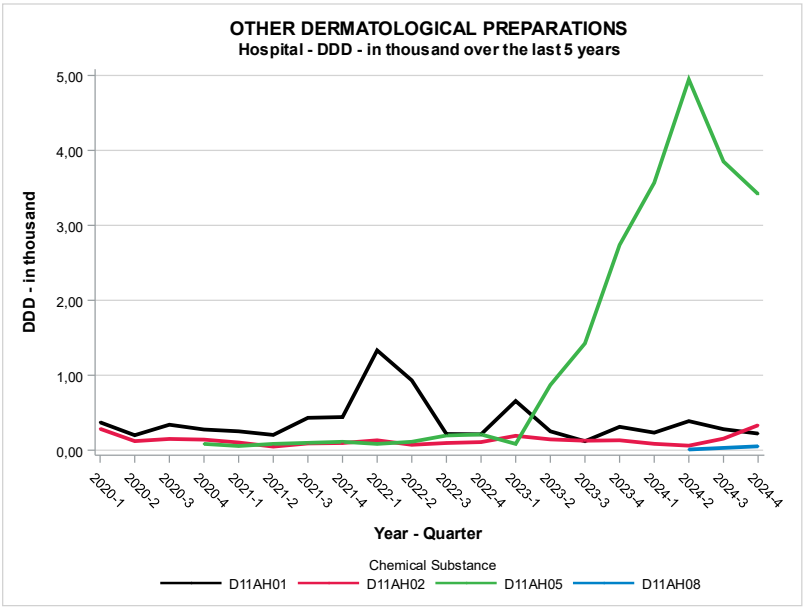

Figure 29: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class D11A.

VI. Class J05A - Direct-Acting Antivirals

Chemical Substance
J05AB01 aciclovir - ACICLOVIR GSK (+ generic)
J05AB01 aciclovir - ACICLOVIR GSK a.o. (+ generic)
J05AB06 ganciclovir - CYMEVENE
J05AB11 valaciclovir - ZELITREX (+ generic)
J05AB14 valganciclovir - VALCYTE (+ generic)
J05AB16 remdesivir - VEKLURY
J05AE01 saquinavir - INVIRASE
J05AE03 ritonavir - NORVIR
J05AE07 fosamprenavir - TELZIR
J05AE08 atazanavir - REYATAZ (+ generic)
J05AE09 tipranavir - APTIVUS
J05AE10 darunavir - PREZISTA (+ generic)
J05AE30 nirmatrelvir and ritonavir - PAXLOVID

J05AF01 zidovudine - RETROVIR
J05AF05 lamivudine - EPIVIR a.o.
J05AF06 abacavir - ZIAGEN
J05AF07 tenofovir disoproxil - VIREAD (+ generic)
J05AF08 adefovir dipivoxil - HEPSERA
J05AF09 emtricitabine - EMTRIVA
J05AF10 entecavir - BARACLUDE
J05AF10 entecavir - BARACLUDE a.o. (+ generic)
J05AF13 tenofovir alafenamide - VEMLIDY
J05AG01 nevirapine - VIRAMUNE (+ generic)
J05AG03 efavirenz - STOCRIN (+ generic)
J05AG04 etravirine - INTELENCE
J05AG05 rilpivirine - EDURANT a.o.
J05AG06 doravirine - PIFELTRO
J05AJ01 raltegravir - ISENTRESS
J05AJ03 dolutegravir - TIVICAY
J05AJ04 cabotegravir - VOCABRIA
J05AP01 ribavirin - COPEGUS
J05AP01 ribavirin - COPEGUS a.o.
J05AP08 sofosbuvir - SOVALDI
J05AP51 sofosbuvir and ledipasvir - HARVONI
J05AP54 elbasvir and grazoprevir - ZEPATIER
J05AP55 sofosbuvir and velpatasvir - EPCLUSA
J05AP56 sofosbuvir, velpatasvir and voxilaprevir - VOSEVI
J05AP57 glecaprevir and pibrentasvir - MAVIRET
J05AR01 zidovudine and lamivudine - COMBIVIR (+ generic)
J05AR02 lamivudine and abacavir - KIVEXA (+ generic)
J05AR03 tenofovir disoproxil and emtricitabine - TRUVADA (+ generic)
J05AR04 zidovudine, lamivudine and abacavir - TRIZIVIR
J05AR06 emtricitabine, tenofovir disoproxil and efavirenz (+ generic)
J05AR06 emtricitabine, tenofovir disoproxil and efavirenz - generic
J05AR08 emtricitabine, tenofovir disoproxil and rilpivirine - EVIPLERA
J05AR09 emtricitabine, tenofovir disoproxil, elvitegravir and cobicistat - STRIBILD
J05AR10 lopinavir and ritonavir - KALETRA
J05AR13 lamivudine, abacavir and dolutegravir - TRIUMEQ
J05AR14 darunavir and cobicistat - REZOLSTA
J05AR18 emtricitabine, tenofovir alafenamide, elvitegravir and cobicistat - GENVOYA
J05AR19 emtricitabine, tenofovir alafenamide and rilpivirine - ODEFSEY
J05AR20 emtricitabine, tenofovir alafenamide and bictegravir - BIKTARVY
J05AR21 dolutegravir and rilpivirine - JULUCA
J05AR22 emtricitabine, tenofovir alafenamide, darunavir and cobicistat - SYMTUZA
J05AR24 lamivudine, tenofovir disoproxil and doravirine - DELSTRIGO
J05AR25 lamivudine and dolutegravir - DOVATO
J05AX05 inosine pranobex - ISOPRINOSINE
J05AX09 maraviroc - CELSENTRI
J05AX10 maribavir - LIVTENCITY
J05AX18 letermovir - PREVYMIS
J05AX29 fostemsavir - RUKOBIA

Table 25: List of reimbursed molecules in pharmacological class J05A.

Expenditure on medicines in the ATC code J05A group showed a slight increase between 2015 and 2018, peaking in 2018 at around €150 million in public pharmacies (see Figure 30). Expenditure then fell slightly, but a gradual increase was noticeable again after 2022. The total number of DDDs follows the same trend as expenditure and also rose slightly after 2022.

In contrast, the number of packages remained relatively stable, suggesting that the increase in DDD and expenditure is not due to an increase in the number of packages, but rather to longer or more intensive treatments per patient.

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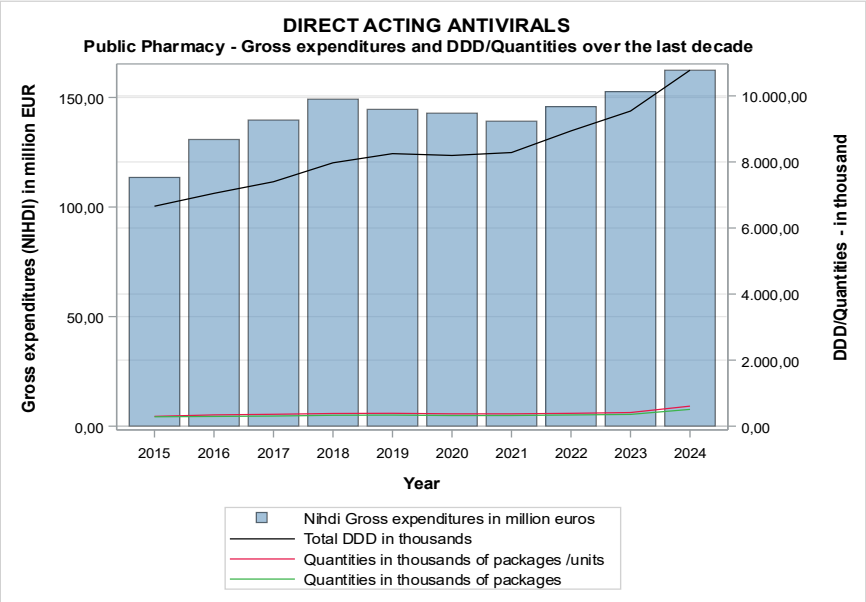

Figure 30: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class J05A.

The number of patients remained stable in the first years of the past five years, at between 40,000 and 50,000. However, in 2024 there was a sharp increase to approximately 135,000 patients, as shown in Figure 31. This increase also explains the rise in expenditure in 2024.

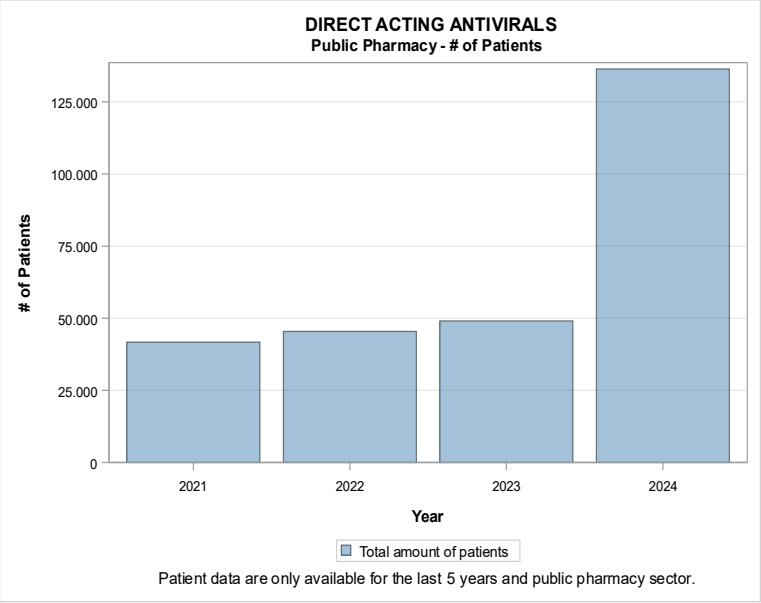

Figure 31: Annual evolution in the number of patients using specialties from pharmacological class J05A reimbursed in public pharmacies and nursing homes.

Over the past five years, most expenditure and the highest total DDD values within this group have been concentrated on 20 of the 47 medicines (see Figure 322 & Figure 33).

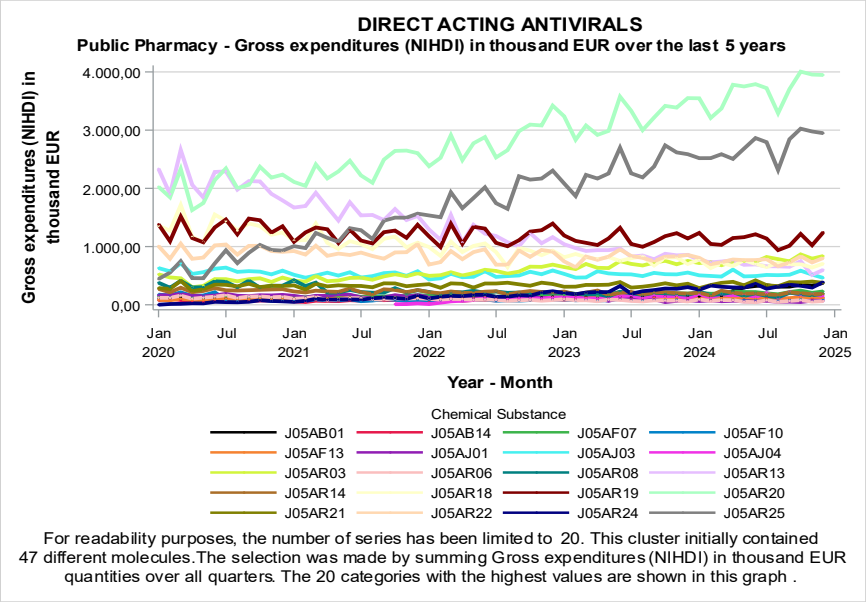

Figure 32: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class J05A.

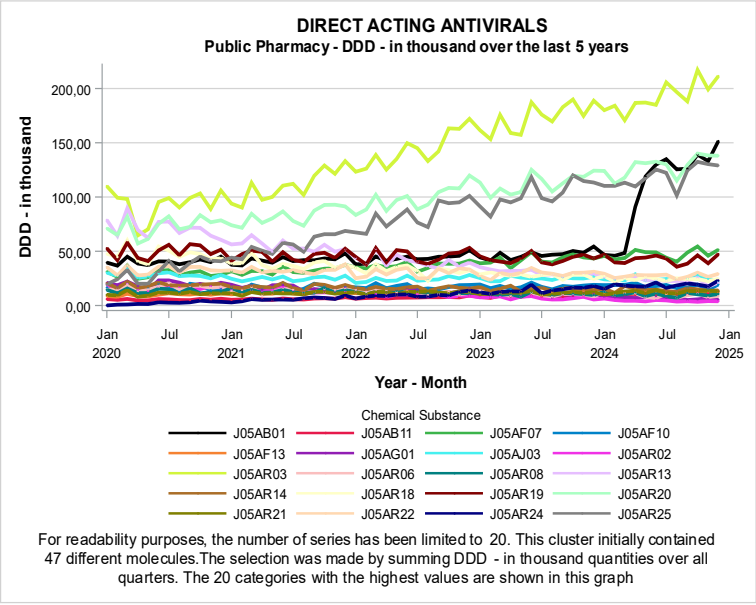

Figure 33: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class J05A.

- **J05AR20 / J05AR25:**

Over the period 2020 to 2025, a sharp increase was observed in consumption of two first-line ARV drugs, namely ATC code J05AR20 for the combination bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF, a combination of two NRTIs and one INSTI, reimbursable since 2019) and ATC code J05AR25 for the combination of dolutegravir and lamivudine (DGT/3TC, a combination of one NRTI and one INSTI, reimbursable since 2019).

This represents a significant and continuous increase, observable for both DDD and gross NIHDI costs for both specialties. The use of these two combination therapy specialties is in line with the most recent EACS guidelines.

- **J05AR03:**

The increase in DDD for ATC code J05AR3 relates to the combination therapy emtricitabine/tenofovir disoproxil (FTC/TDF), which is mainly used in the context of PrEP in accordance with the provisions of §8750000.

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- **J05AB01:**

The specialties of ATC code J05AB01 (aciclovir) show a very sudden and sharp increase in the number of DDD equivalents over the period 2024 to 2025. This is a consequence of the CTG procedure in 2024 and the positive decision by the Minister to transfer all aciclovir specialties from Chapter IV to Chapter I as of 1 May 2024.

This also explains the sharp rise in the number of patients in 2024-2025 who were reimbursed for a prescribed aciclovir speciality.

Expenditure on Direct Acting Antivirals in hospitals (see Figure 34) shows clear peaks in 2015, 2017 and 2019, with amounts ranging from €90 million to almost €120 million. Since 2019, there has been a visible decline in gross expenditure and DDD volume.

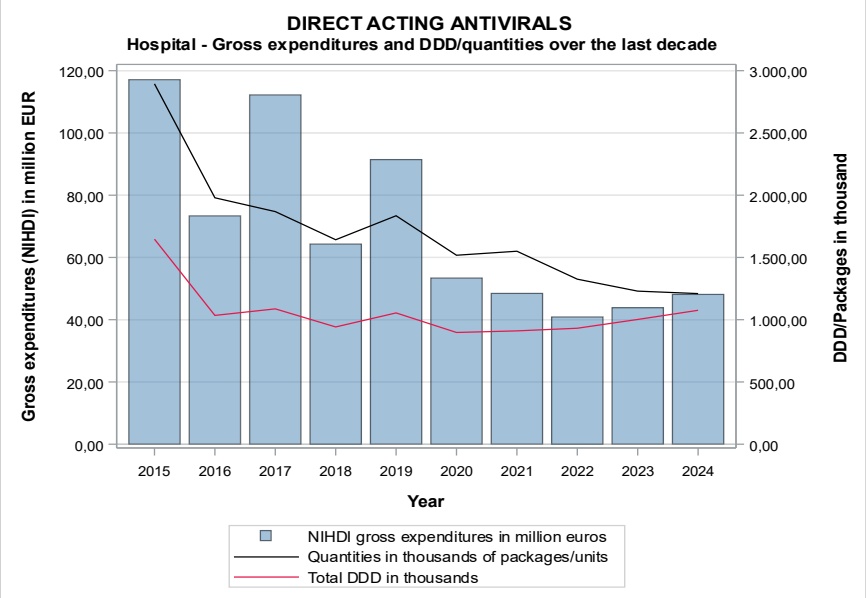

Figure 34: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class J05A.

- **J05AP57 and J05AP55**

As shown in Figure 35, there was a notable peak in expenditure at the start of 2020 for J05AP57 (glecaprevir/pibrentasvir) and J05AP55 (sofosbuvir/velpatasvir) for these two new therapeutic options for the treatment of HCV (since 2018 and 2017 respectively), but with expenditure stabilising in 2023 and 2021 respectively for these specialties.

- **J05AG05 and J05AJ04:**

In terms of DDD (see Figure 36), we have seen a significant increase in the use of molecules in ATC class J05AG05 (rilpivirine) and ATC class J05AJ04 (cabotegravir) since 2021. This is explained by the reimbursement of the intramuscular ARV specialties cabotegravir and rilpivirine since the end of 2021.

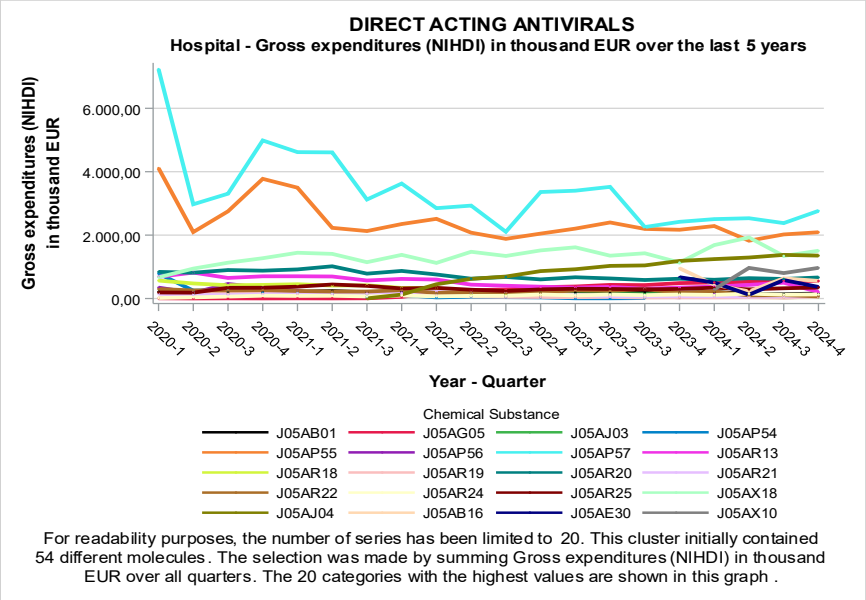

Figure 35: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class J05A.

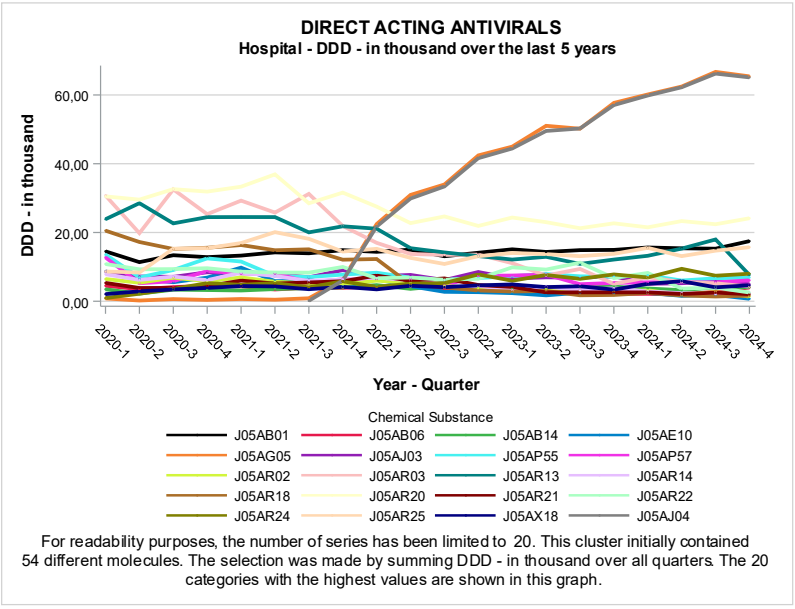

Figure 36: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class J05A.

VII. Class J06B - Immune sera and immunoglobulins

Chemical Substance
J06BA01 immunoglobulins, normal human, for extravascular adm. - GAMMANORM a.o.
J06BA02 immunoglobulins, normal human, for intravascular adm. - SANDOGLOBULINE a.o.
J06BB01 anti-D (rh) immunoglobulin - RhoGAM
J06BB04 hepatitis B immunoglobulin - NEOHEPATECT a.o.
J06BB04 hepatitis B immunoglobulin - ZUTECTRA
J06BB05 rabies immunoglobulin - BERIRAB
J06BB09 cytomegalovirus immunoglobulin - IVEGAM-CMV a.o.
J06BD01 palivizumab - SYNAGIS J06BD08 nirsevimab - BEYFORTUS

Table 26: List of reimbursed molecules in pharmacological class J06B.

The sharp increase shown in Figure 37, Figure 38, Figure 39 in the number of patients, DDD and gross NIHDI cost for ATC class J06B specialties in 2024 in public pharmacies is entirely due to the recent reimbursement (since 01-

08-2024) of the J06BD08 speciality nirsevimab for the prevention of RSV infection in neonates, with periodic use during the current RSV season (typically from October to March).

Figure 40 and Figure 41 show the evolution of gross expenditure and quarterly DDD consumption in hospitals, respectively. For polyvalent human immunoglobulins for subcutaneous (J06BA01) and intravenous use (J06BA02), we still see an annual increase in gross NIHDI expenditure.

Here too, we see a clear rise in expenditure in 2024 for the J06BD08 speciality nirsevimab as passive immunisation for the prevention of RSV infection in neonates.

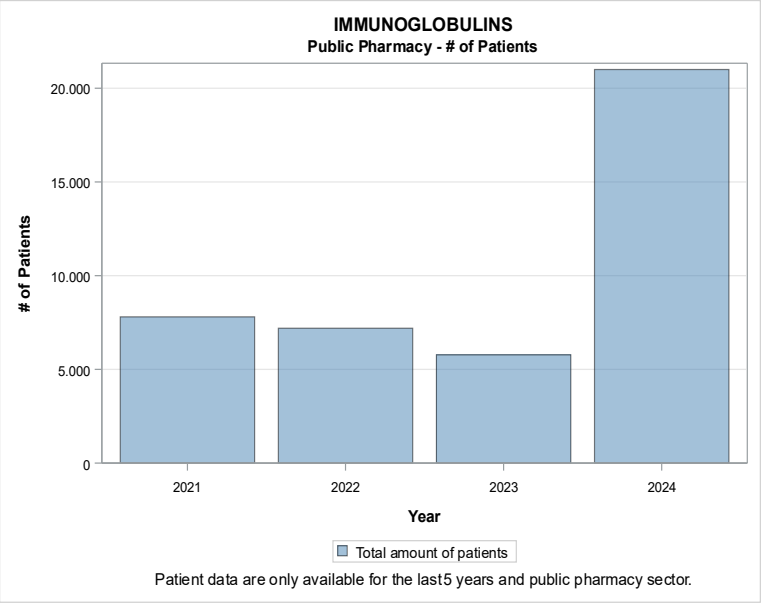

Figure 37: Annual evolution in the number of patients using specialties from pharmacological class J06B reimbursed in public pharmacies and nursing homes.

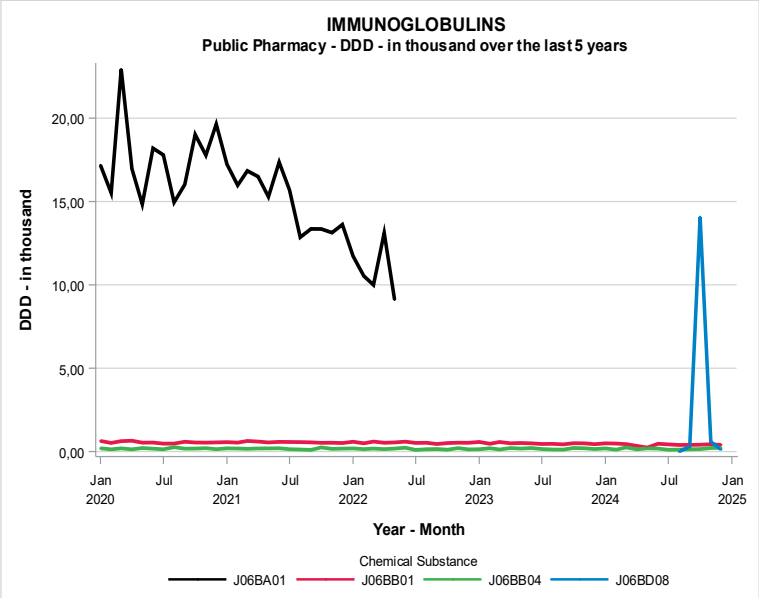

Figure 38: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class J06B.

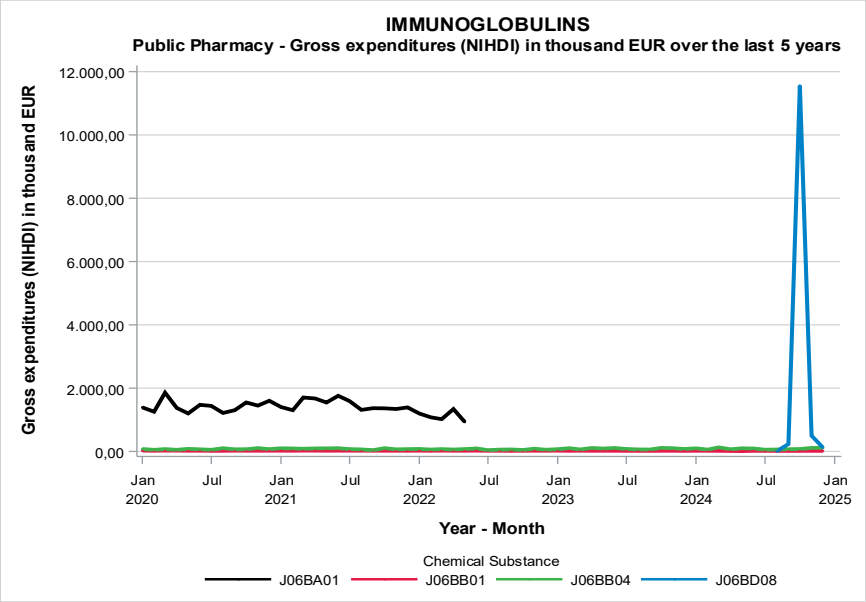

Figure 39: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class J06B.

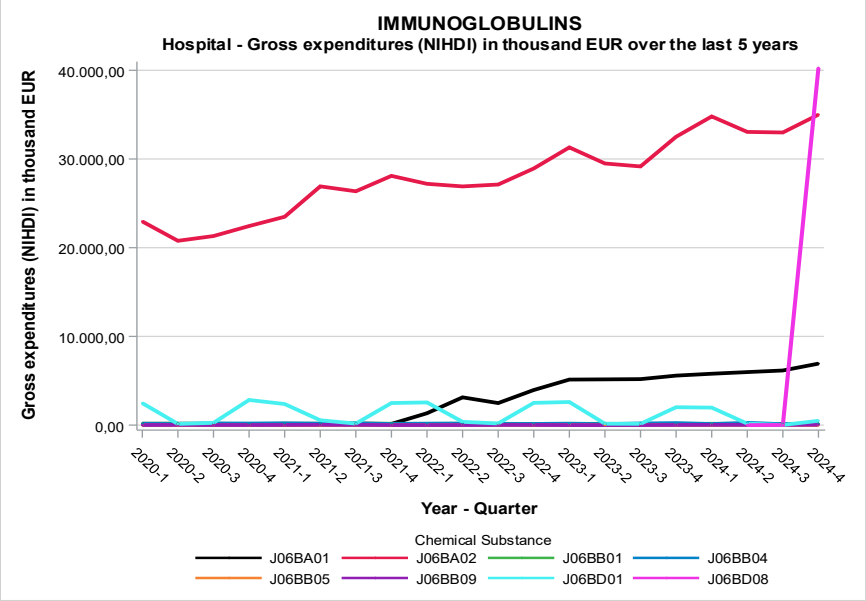

Figure 40: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class J06B.

45 - Detailed analysis of different pharmacological classes

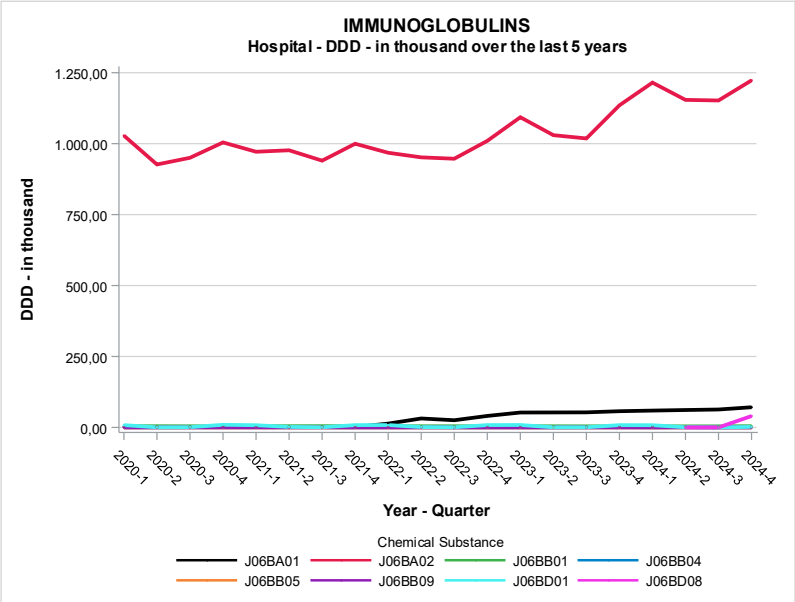

Figure 41: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class J06B.

VIII. Class L01E - Protein kinase inhibitors

Chemical Substance
L01EA01 imatinib - GLIVEC (+ generic)
L01EA02 dasatinib - SPRYCEL (+ generic)
L01EA03 nilotinib - TASIGNA
L01EA04 bosutinib - BOSULIF (+ generic)
L01EA05 ponatinib - ICLUSIG
L01EA06 asciminib - SCEMBLIX
L01EB01 gefitinib (+ generic)
L01EB02 erlotinib - TARCEVA (+ generic)
L01EB03 afatinib - GIOTRIF
L01EB04 osimertinib - TAGRISSO
L01EC01 vemurafenib - ZELBORAF
L01EC02 dabrafenib - TAFINLAR
L01EC03 encorafenib - BRAFTOVI
L01ED01 crizotinib - XALKORI
L01ED02 ceritinib - ZYKADIA
L01ED03 alectinib - ALECENSA
L01ED04 brigatinib - ALUNBRIG
L01ED05 lorlatinib - LORVIQUA
L01EE01 trametinib - MEKINIST
L01EE02 cobimetinib - COTELLIC
L01EE03 binimetinib - MEKTOVI
L01EF01 palbociclib - IBRANCE
L01EF02 ribociclib - KISQALI
L01EF03 abemaciclib - VERZENIOS
L01EG01 temsirolimus - TORISEL
L01EG02 everolimus - AFINITOR a.o. (+ generic)
L01EH01 lapatinib - TYVERB
L01EH03 tucatinib - TUKYSA
L01EJ01 ruxolitinib - JAKAVI
L01EJ02 fedratinib - INREBIC
L01EK01 axitinib - INLYTA
L01EL01 ibrutinib - IMBRUVICA
L01EL02 acalabrutinib - CALQUENCE
L01EL03 zanubrutinib - BRUKINSA
L01EM01 idelalisib - ZYDELIG
L01EN02 pemigatinib - PEMAZYRE
L01EX01 sunitinib - SUTENT (+ generic)
L01EX02 sorafenib - NEXAVAR (+ generic)
L01EX03 pazopanib - VOTRIENT
L01EX04 vandetanib - CAPRELSA
L01EX05 regorafenib - STIVARGA
L01EX07 cabozantinib - CABOMETYX
L01EX08 lenvatinib - LENVIMA a.o.
L01EX09 nintedanib - OFEV a.o.
L01EX10 midostaurin - RYDAPT
L01EX12 larotrectinib - VITRAKVI
L01EX13 gilteritinib - XOSPATA
L01EX14 entrectinib - ROZLYTREK
L01EX22 selpercatinib - RETSEVMO

Table 27: List of reimbursed molecules in pharmacological class L01E.

The dynamics in class L01E are driven almost exclusively by the hospital sector, with rapid, sustained growth in volumes (DDD) and gross expenditure, which appears to have stabilised between 2023 and 2024. These evolutions are shown in the three figures below.

Between 2015 and 2024, DDD rose from around 0.89 million to 3.73 million (x4.2), representing an annual growth rate of around ~+17%. Gross NIHDI expenditure rose from ~€108 million to ~€510 million (x4.7). This trend accelerated from 2018, then continued up until 2023, with a decrease between 2023 and 2024 for gross expenditure and a steady rise for DDD.

47 - Detailed analysis of different pharmacological classes

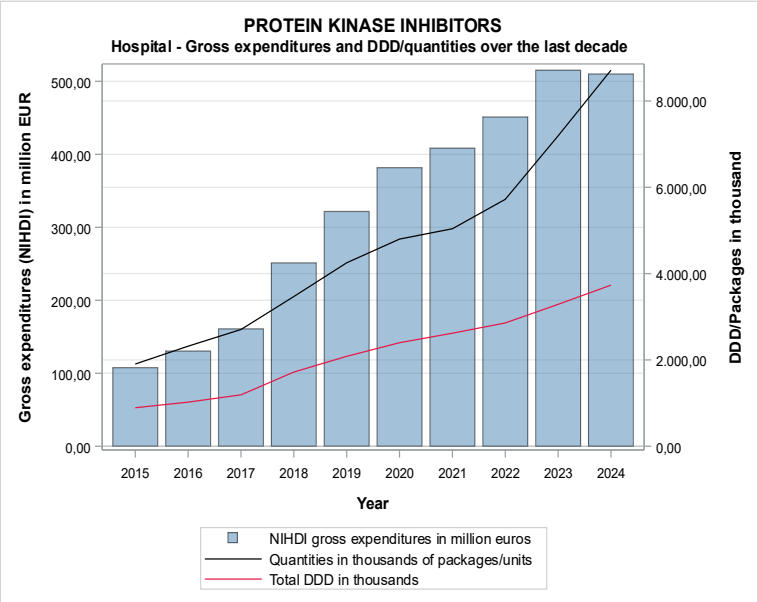

Figure 42: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class L01E.

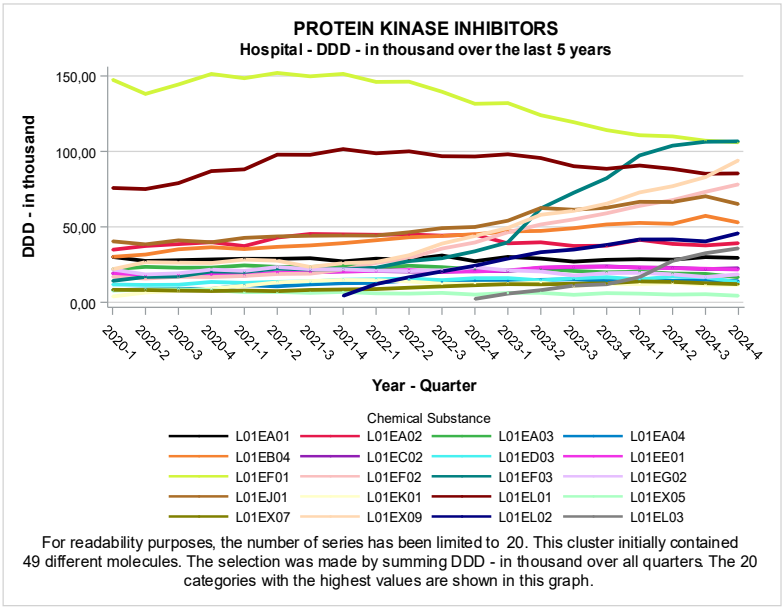

Figure 43: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class L01E.

In 2024, DDD rose by a further +13.5% (from ~3.29 M to ~3.73 M), while gross expenditure fell slightly to -1.0% (from ~€515.2 million to ~€510.1 million). This discrepancy in expenditure/volume suggests a favourable price effect for the NIHDI (lower prices, adjustments to conventions) or consumption of more economical molecules, without acting as a brake on clinical use.

Between 2023 and 2024, the inhibitors with the highest increase in expenditure were:

- Brukinsa® (zanubrutinib) L01EL03 (+203%). In 2023 and 2024, several new indications were added to the list of reimbursable pharmaceutical specialties.
- Verzenios® (abemaciclib) L01EF03 (+61%). In 2023, a new indication (neo-adjuvant treatment) was added to the list of reimbursable medicines.
- Xospata® (giltertinib) L01EX13 (+100%).

In 2023, three new molecules were added to the list of reimbursable medicines, which still witnessed a sharp increase in expenditure:

- Inrebic® (fedratinib) L01EJ02 (+117%).
- Scemblix® (asciminib) L01EA06 (+64%).
- Tukysa ® (tucatinib) L01EH03; reimbursed under convention.

Specialties in decline or stagnation are the older multi-target TKIs such as vandetanib, sunitinib, sorafenib, etc., which are reducing their relative share of the market, reflecting the decline in consumption of these drugs and the move towards earlier lines of new-generation TKIs.

Expenditure on the CDK4/6 inhibitors Ibrance® (palbociclib) Verzenios® (abemaciclib) and Kisqali® (ribociclib) has fluctuated sharply since reimbursement started. The specialty Ibrance® (palbociclib) has seen a sharp drop in expenditure, but also a drop in DDDs, since 2021. At the end of 2023, there was a sharp drop in expenditure on Kisqali® and Ibrance® following definitive post-contract registration in the treatment of HR+/HER2- advanced breast cancer. Ibrance has disappeared from the top 5. For Verzenios, we saw a sharp rise in expenditure at the start of 2023, when Verzenios was included in (neo)adjuvant therapy. However, at the end of 2023, we also saw a decrease in expenditure, following its definitive listing in the treatment of HR+/HER2- advanced breast cancer.

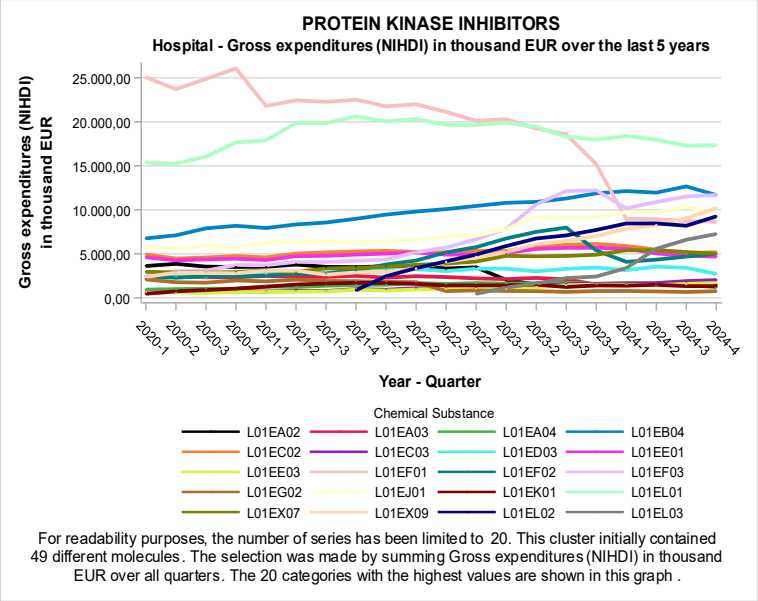

Figure 44: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class L01E.

Imbruvica® (ibrutinib), the first BTKI, is therefore now the specialty with the highest level of expenditure. However, the expenditure is showing a downward trend, following the arrival of 2nd and 3rd generation BTKIs (Brukinsa® and Calquence®).

Tagrisso® (osimertinib) still completes the top three in terms of expenditure. This is the first targeted treatment, initially reimbursed as 2nd, then 1st line in non-small cell lung cancer.

Lastly, we have seen a doubling in expenditure and DDDs for Ofev® (nintedanib) since the end of 2022. This may be due to the fact that the indication (PF-ILD non-IPF) was extended in July 2022, and the new reimbursement conditions for Esbriet® (pirfenidone) were changed at the end of 2022.

These specialties are temporarily reimbursed under a convention between the company concerned and the NIHDI. It is important to emphasise that the costs mentioned here are based on the face value price of these medicines. The actual costs for the NIHDI are confidential and must be calculated on the basis of compensation recorded in a convention between the pharmaceutical company concerned and the NIHDI.

IX. Class L01F - Monoclonal Antibodies and Antibody Drug Conjugates

Chemical Substance
L01FA01 rituximab - MABTHERA a.o. (+ biosimilar)
L01FA03 obinutuzumab - GAZYVARO
L01FB01 inotuzumab ozogamicin - BESPONSA
L01FC01 daratumumab - DARZALEX
L01FC02 isatuximab - SARCLISA
L01FD01 trastuzumab - HERCEPTIN a.o. (+ biosimilar)
L01FD02 pertuzumab - PERJETA
L01FD03 trastuzumab emtansine - KADCYLA
L01FD04 trastuzumab deruxtecan - ENHERTU
L01FE01 cetuximab - ERBITUX
L01FE02 panitumumab - VECTIBIX
L01FF01 nivolumab - OPDIVO
L01FF02 pembrolizumab - KEYTRUDA
L01FF03 durvalumab - IMFINZI
L01FF04 avelumab - BAVENCIO
L01FF05 atezolizumab - TECENTRIQ
L01FF06 cemiplimab - LIBTAYO
L01FF07 dostarlimab - JEMPERLI
L01FG01 bevacizumab - AVASTIN a.o. (+ biosimilar)
L01FG02 ramucirumab - CYRAMZA
L01FX02 gemtuzumab ozogamicin - MYLOTARG
L01FX04 ipilimumab - YERVOY
L01FX05 brentuximab vedotin - ADCETRIS
L01FX06 dinutuximab beta - QARZIBA
L01FX07 blinatumomab - BLINCYTO
L01FX08 elotuzumab - EMPLICITI
L01FX09 mogamulizumab - POTELIGEO
L01FX12 tafasitamab - MINJUVI
L01FX13 enfortumab vedotin - PADCEV
L01FX14 polatuzumab vedotin - POLIVY
L01FX15 belantamab mafodotin - BLENREP
L01FX17 sacituzumab govitecan - TRODELVY
L01FX20 tremelimumab - IMJUDO
L01FX24 teclistamab - TECVAYLI
L01FX27 epcoritamab - TEPKINLY
L01FX28 glofitamab - COLUMVI
L01FY02 nivolumab and relatlimab - OPDUALAG

Table 28: List of reimbursed molecules in pharmacological class L01F.

Class L01F continued its sustained growth in 2024, although the pace of gross expenditure slowed slightly compared with previous years. As shown in Figure 45, hospital volumes[12] (expressed in DDD) increased by a factor of almost six between 2015 and 2024, while gross NIHDI expenditure rose by a similar factor, from around €204 million to €1.3 billion. Following a phase of rapid expansion up to 2019 (+25-70%/year), growth has stabilised at around +10 to +20% per year, reflecting a phase of partial maturity for this class.

Volumes rose by a further +15.6% in 2024, while gross expenditure rose by just +8.6%, indicating a favourable price effect due to price cuts and more availability of biosimilars (in particular for bevacizumab and rituximab).

[12] No specialties are reimbursed in public pharmacies or nursing homes.

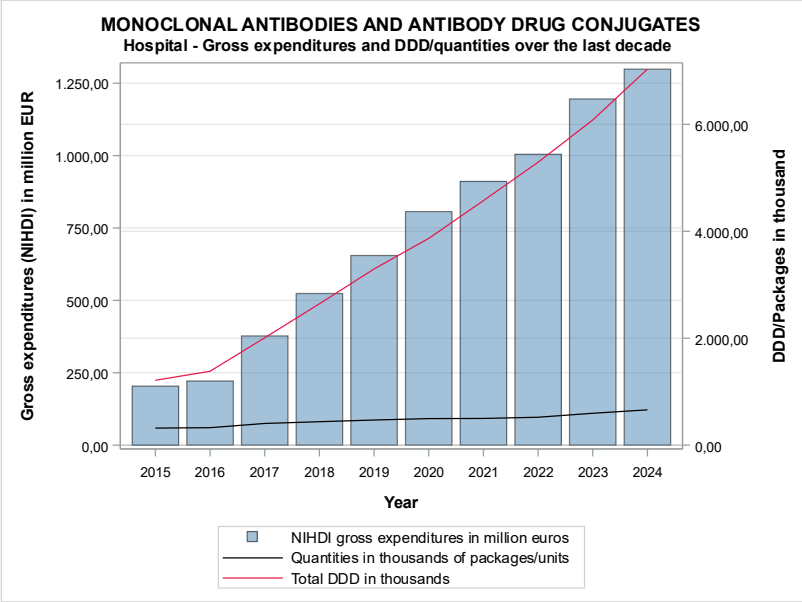

Figure 45: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class L01F.

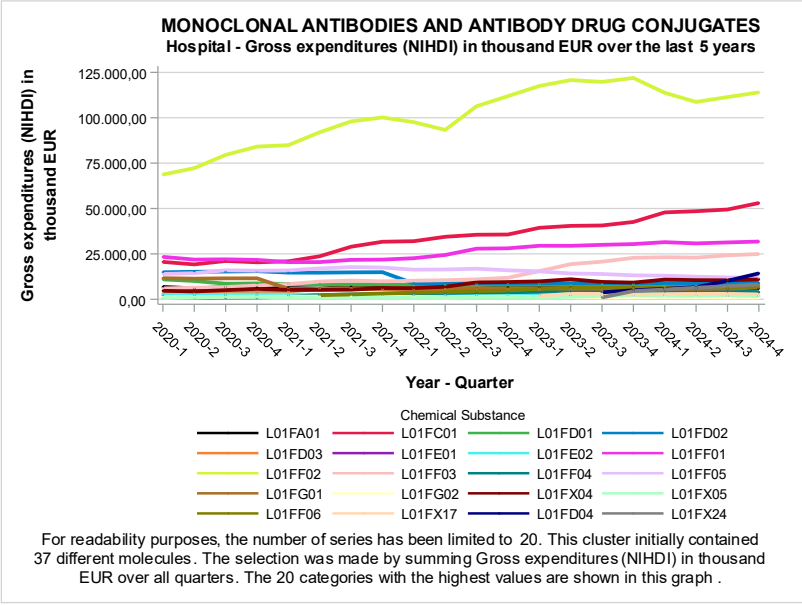

Figure 46: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class L01F.

We see that the highest expenditure is still on Keytruda® (pembrolizumab), and that both expenditure and DDDs continue to grow.

- Keytruda® is used in new indications and is being used earlier, as a (neo)adjuvant treatment.
- Darzalex® (daratumumab), indicated for multiple myeloma, is being used at increasingly earlier stages. As such, the specialty now ranks number 2 in terms of expenditure and DDD.
- Opdivo® (ipilimumab) completes these specialties in third place.

Over the recent period, momentum has been driven by the arrival of new generation antibodies and conjugates:

- Trastuzumab deruxtecan (Enhertu) L01FD04 saw volumes more than double from reimbursement between 2023 and 2024, helped by indications for the drug being expanded (HER2-low breast, gastric and lung cancers).

- Teclistamab (Tecvayli) L01FX24, a bispecific antibody targeting BCMA, has seen major growth (+146%) and is gradually establishing itself in relapsed or refractory multiple myeloma.
- Similarly, tafasitamab (Minjuvi) L01FX12 continues to grow in DLBCL R/R.

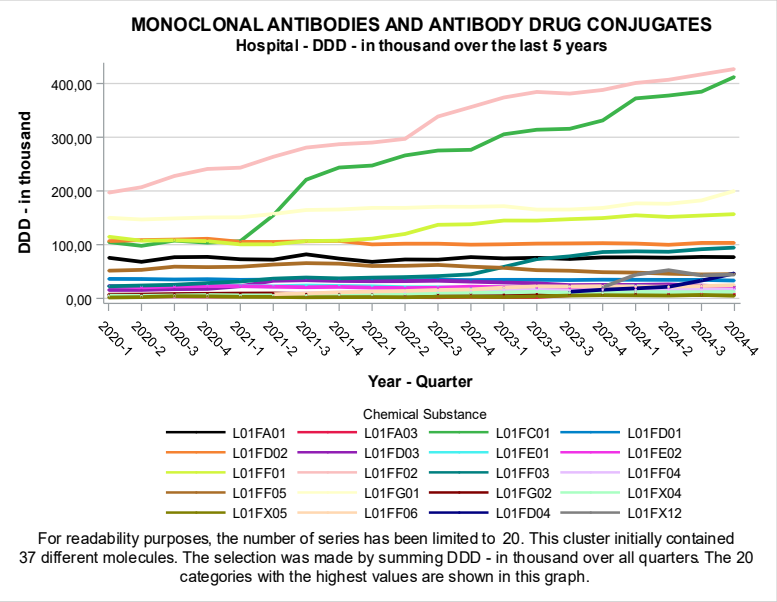

Figure 47: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class L01F.

Conversely, certain older molecules are experiencing significantly lower volumes. Belantamab mafodotin (Blenrep) has fallen sharply following its withdrawal from the European market, while elotuzumab (Empliciti) is gradually being replaced by new anti-BCMA combinations.

Overall, the L01F class is still the main contributor to hospital expenditure in oncology, but its structure is changing rapidly: first-generation antibodies (pembrolizumab, nivolumab, daratumumab, rituximab, bevacizumab) retain significant shares in absolute terms, while growth is now driven by innovative therapies - conjugates, bispecifics and new-generation antibodies - marking a profound reshaping of the therapeutic landscape.

These specialties are temporarily reimbursed under an agreement between the company concerned and the NIHDI. It is important to emphasise that the costs mentioned here are based on the face value price of these medicines. The actual costs for the NIHDI are confidential and must be calculated on the basis of compensation recorded in an agreement between the pharmaceutical company concerned and the NIHDI.

X. Class L01X - Other antineoplastic agents

Chemical Substance
L01XA01 cisplatin - CISPLATIN (+ generic)
L01XA02 carboplatin - CARBOSIN
L01XA02 carboplatin - CARBOSIN a.o. (+ generic)
L01XA03 oxaliplatin - ELOXATIN (+ generic)
L01XB01 procarbazine - PROCARBAZINE
L01XD03 methyl aminolevulinate - METVIX
L01XD04 aminolevulinic acid - GLIOLAN a.o.
L01XD05 temoporfin - FOSCAN
L01XF01 tretinoin - VESANOID
L01XF03 bexarotene - TARGRETIN
L01XG01 bortezomib - VELCADE (+ generic)
L01XG02 carfilzomib - KYPROLIS
L01XG03 ixazomib - NINLARO
L01XH03 panobinostat - FARYDAK
L01XJ01 vismodegib - ERIVEDGE
L01XJ02 sonidegib - ODOMZO
L01XK01 olaparib - LYNPARZA
L01XK02 niraparib - ZEJULA
L01XK04 talazoparib - TALZENNA
L01XK52 niraparib and abiraterone - AKEEGA
L01XL03 axicabtagene ciloleucel - YESCARTA
L01XL04 tisagenlecleucel - KYMRIAH
L01XL06 brexucabtagene autoleucel - TECARTUS
L01XL09 Tableecleucel - EBVALLO
L01XX01 amsacrine - AMSIDINE
L01XX02 asparaginase - ASPARAGINASE a.o.
L01XX05 hydroxycarbamide - HYDREA a.o.
L01XX11 estramustine - ESTRACYT
L01XX23 mitotane - LYSODREN
L01XX24 pegaspargase - ONCASPAR
L01XX27 arsenic trioxide - TRISENOX (+ generic)
L01XX35 anagrelide - XAGRID (+ generic)
L01XX41 eribulin - HALAVEN
L01XX44 aflibercept - ZALTRAP
L01XX52 venetoclax - VENCLYXTO
L01XX62 ivosidenib - TIBSOVO
L01XX75 tebentafusp - KIMMTRAK
L01XY01 cytarabine and daunorubicin - VYXEOS

Table 29: List of reimbursed molecules in pharmacological class L01X.

Hospital expenditure for class L01X continues to grow steadily, albeit unevenly from one period to the next. Between 2015 and 2024, volumes (DDD) rose from around 1.8 million to 2.16 million (+19%), while gross NIHDI expenditure increased almost fourfold (€47m → €182m). The following three figures show these evolutions in hospitals.

Following a phase of stagnation in 2018-2019 due to the loss of exclusivity for certain molecules (in particular bortezomib - Velcade®) and the reclassification of monoclonal antibodies (to L01F) and kinase inhibitors (to L01E), growth has returned to positive territory since 2020.

- 2020-2022: average growth of +15-20%/year, driven by the expansion of oral drug indications and targeted therapies (venetoclax, olaparib, etc.). As the new specialties have a higher price, expenditure has grown, while DDDs have remained relatively stable.
- 2024 saw a marked acceleration (+52% in gross expenditure), despite a moderate increase in volumes (+9%), reflecting the arrival of very expensive, individualised treatments (CAR-T, specialised immunotherapies).

53 - Detailed analysis of different pharmacological classes

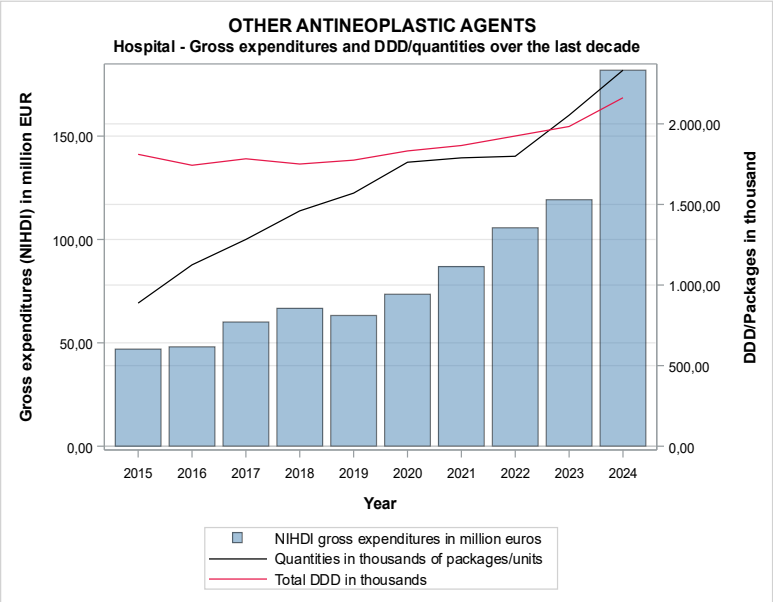

Figure 48: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class L01X.

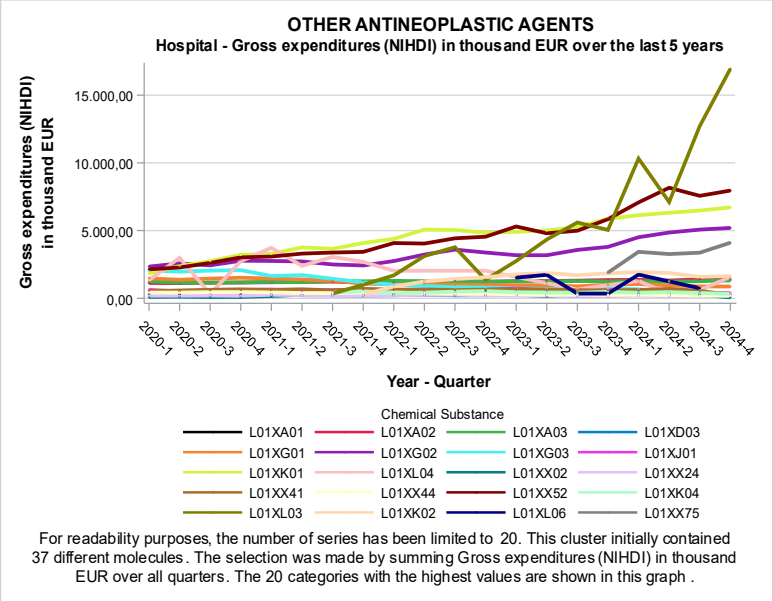

Figure 49: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class L01X.

In 2024, the structure of class L01X continued to evolve under the combined effect of targeted therapies, cell-based treatments and the gradual decline of certain conventional chemotherapies. Among the highest-contributing specialties (between 2023 and 2024):

- Yescarta® (axicabtagene ciloleucel) recorded spectacular growth, with a rise of around +165% in gross expenditure and a parallel rise in DDDs, reflecting the rapid uptake of CAR-T therapies following reimbursement in diffuse large-cell B lymphoma, and improved availability.
- Kimmtrak® (tebentafusp) almost doubled its volumes (+87% in expenditure, with a similar rise in DDDs) and is now the leading treatment for metastatic uveal melanoma, a rare disease but with very high unit cost, making it a significant contributor to growth in the class.
- Venclyxto® (venetoclax) continues to grow, with a rise of around +47% in expenditure and a concurrent growth in DDDs, reflecting wider use in haematological malignancies such as chronic lymphocytic leukaemia and acute myeloid leukaemia, often in combination with other agents (obinutuzumab, azacitidine).

- Kyprolis® (carfilzomib), already well established in multiple myeloma, continues to grow (+43% in expenditure, +40% in DDD), confirming its position in combination regimens despite growing competition from anti-BCMA bispecific antibodies.
- Expenditure on Lynparza® (olaparib) continues to rise. As such, Lynparza® is in the top 3 in terms of expenditure, since several indications are now reimbursed.

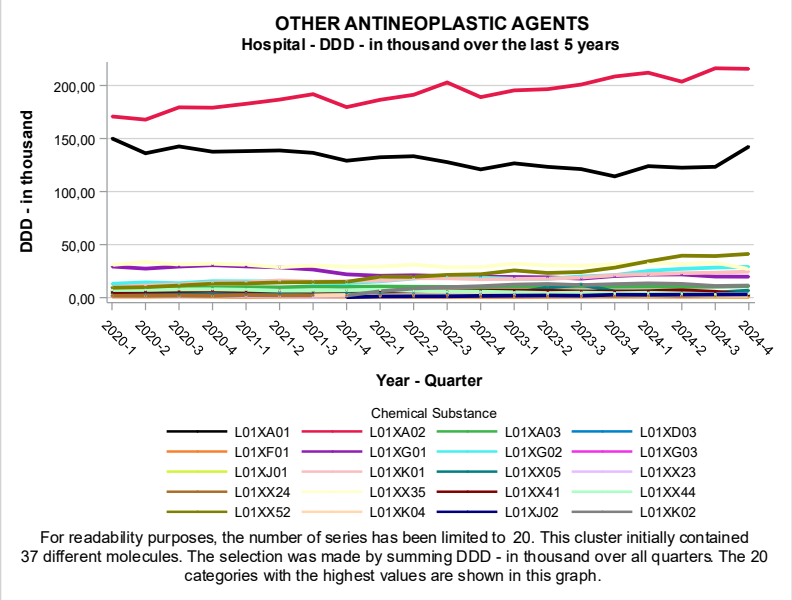

Figure 50: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class L01X.

Conversely, a number of specialties have declined significantly. Kymriah® (tisagenlecleucel) saw a 44% drop in expenditure and a proportionate reduction in volumes, likely due to the rise of Yescarta®.

Ninlaro® (ixazomib) fell sharply (-46% in expenditure and DDD), as a result of its more limited use in maintenance treatment or in specific cases of multiple myeloma, which have now been replaced by other therapeutic options.

Finally, Vyxeos® (cytarabine/daunorubicin) also saw its volumes and expenditure fall by around -58%, as consumption remains limited to specific sub-populations of high-risk acute myeloid leukaemias.

A large proportion of these specialties are temporarily reimbursed under an agreement between the company concerned and the NIHDI. It is important to emphasise that the costs mentioned here are based on the face value price of these medicines. The actual costs for the NIHDI are confidential and must be calculated on the basis of compensation recorded in a convention between the pharmaceutical company concerned and the NIHDI.

Platinum-based chemotherapies (cisplatin and carboplatin) still have the highest DDD numbers, since they are administered in a wide range of indications, either as monotherapy or, more frequently, in combi-therapy with new molecules.

XI. Class M05B - Drugs affecting bone structure and mineralization

Chemical Substance
M05BA03 pamidronic acid (+ generic)
M05BA04 alendronic acid - FOSAMAX (+ generic)
M05BA06 ibandronic acid - BONVIVA (+ generic)
M05BA07 risedronic acid - ACTONEL (+ generic)
M05BA08 zoledronic acid - ACLASTA a.o. (+ generic)
M05BB03 alendronic acid and colecalciferol - FOSAVANCE (+ generic)
M05BB04 risedronic acid, calcium and colecalciferol, sequential - ACTONEL COMBI D
M05BB05 alendronic acid, calcium and colecalciferol, sequential - ALENCA a.o.
M05BC01 dibotermin alfa - INDUCTOS
M05BX04 denosumab - PROLIA a.o.
M05BX05 burosumab - CRYSVITA
M05BX06 romosozumab - EVENITY

Table 30: List of reimbursed molecules in pharmacological class M05B.

Following the stabilisation of expenditure on drugs affecting bone structure and mineralisation between 2017 and 2021, an increase in expenditure on these drugs can be observed from 2022 onwards, both in community pharmacies (Figure 51) and in hospitals (Figure 52).

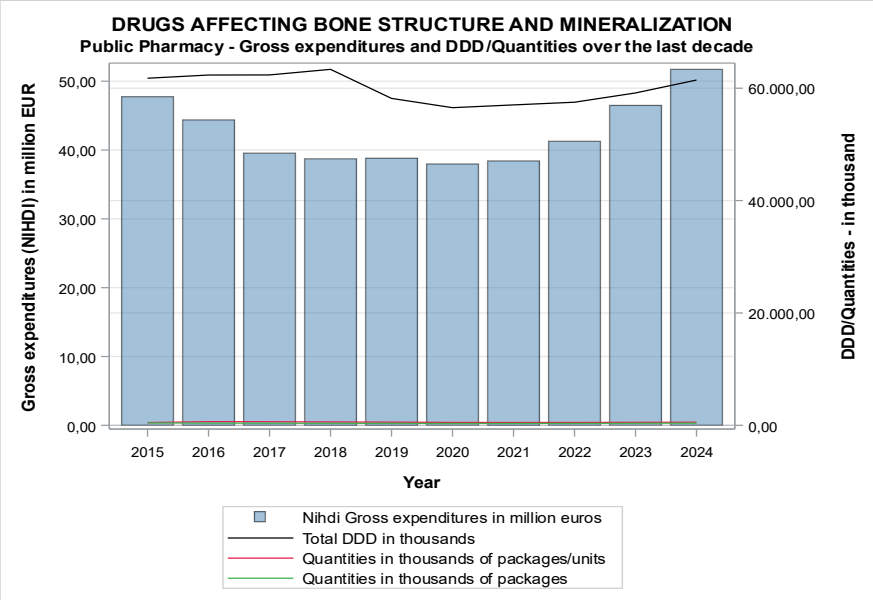

Figure 51: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class M05B.

Expenditure in public pharmacies in 2024 for this class of medicines (€51.72 million) is 3.5 times higher than in hospitals (€15.54 million).

The increase in expenditure can also be observed when looking at individual molecules, both in public pharmacies (Figure 53) and in hospitals (Figure 54), although the reasons for the increase in expenditure in public pharmacies and in hospitals for this class of medicines are not entirely the same.

In public pharmacies, the largest cost within this class is the molecule denosumab (M05BX04) (Prolia®/Xgeva®), for which a slow increase in expenditure can be seen from 2022 onwards (Figure 53).

In addition, there has been a notable increase in expenditure due to the arrival of a new molecule, romosozumab (M05BX06) (Evenity®), which has been reimbursable since 1 December 2021 for the treatment of post-menopausal osteoporosis.

Expenditure on other molecules in this class (mainly bisphosphonates) remained stable.

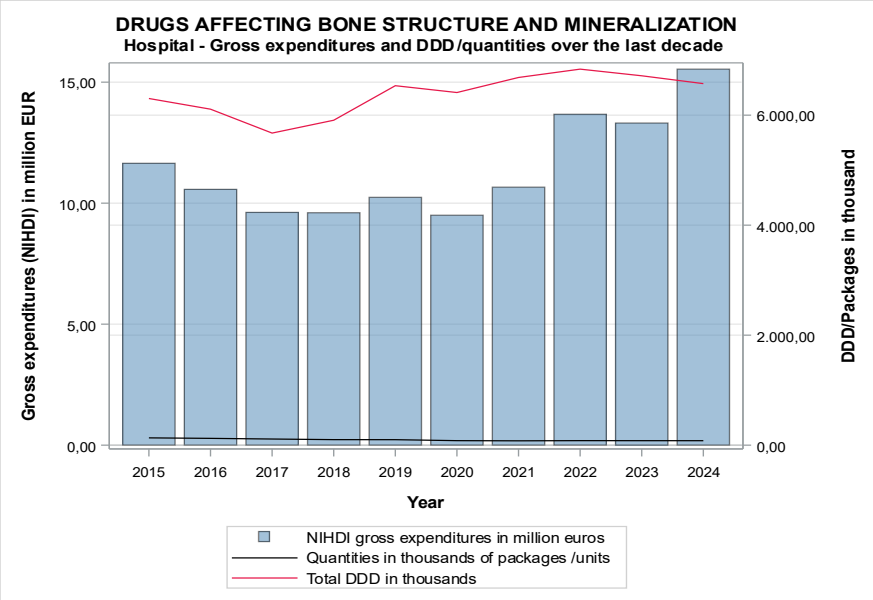

Figure 52: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class M05B.

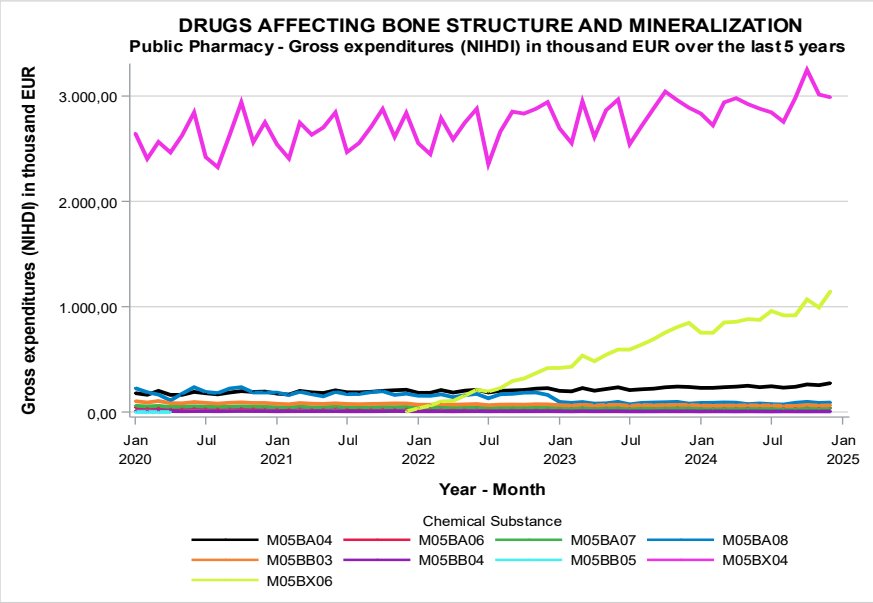

Figure 53: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class M05B.

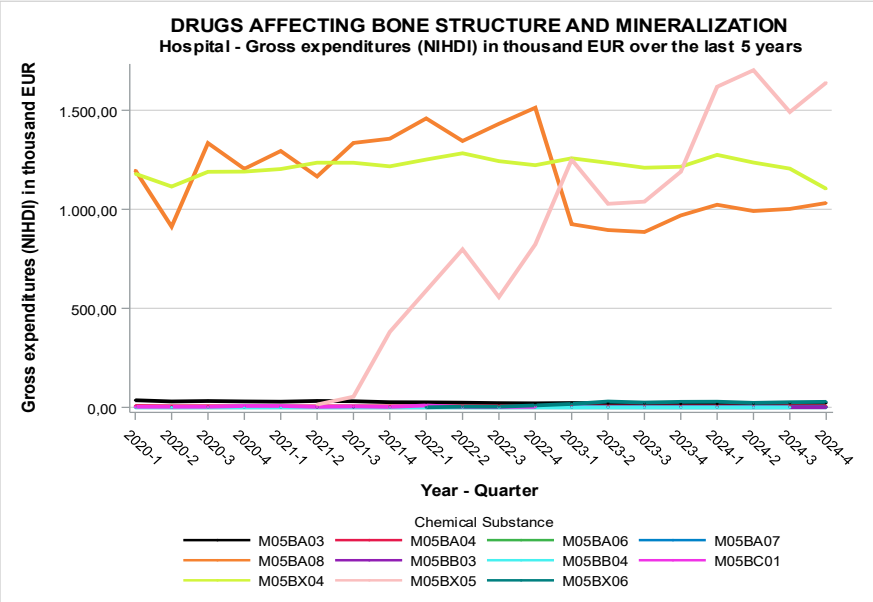

Figure 54: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class M05B.

In hospitals, the largest expenditure within this class until 2021 was on the molecules denosumab (M05BX04) (Prolia®/Xgeva®) and zoledronic acid (M05BA08) (Aclasta®) (Figure 54).

For denosumab (M05BX04), expenditure remained more or less stable after 2021; for zoledronic acid (M05BA08), expenditure fell after January 2023 due to a price reduction following the inclusion of zoledronic acid (M05BA08) in the reference reimbursement system.

However, from 2021 onwards, there has been a sharp increase in costs due to a new molecule, burosumab (M05BX05) (Crysvita®), an orphan drug for the treatment of X-linked hypophosphataemia in children.

When looking at consumption in DDD and the number of patients, we can see that, from 2021 onwards, there was an increase in the total number of patients treated with medicines in this class in public pharmacies: 142,500 patients in 2022 versus 155,600 patients in 2024 (Figure 55).

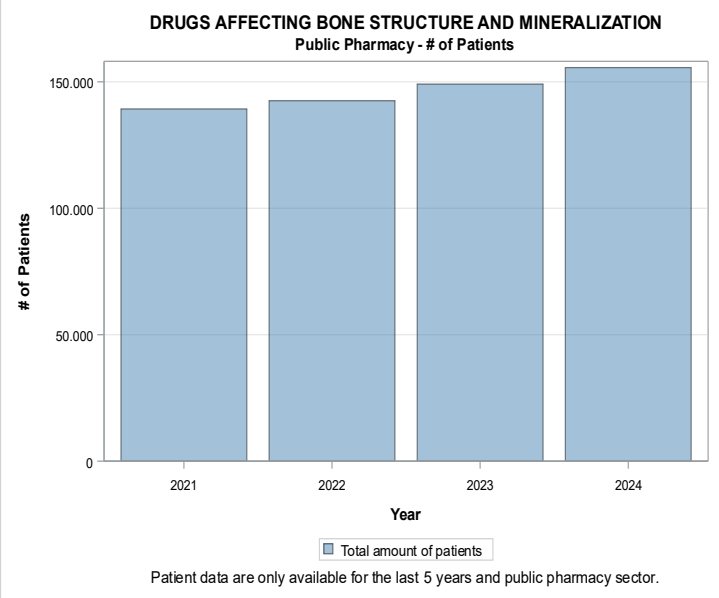

Figure 55: Annual evolution in the number of patients using specialties from pharmacological class M05B reimbursed in public pharmacies and nursing homes.

This can likely be explained by the ageing of the population on the one hand and the availability of new treatments on the other.

Denosumab-based specialties (M05BX04) are the most commonly used, followed by alendronate-based specialties, either as monotherapy (M05BA04) or in fixed combination with vitamin D (M05BB03) (Figure 56).

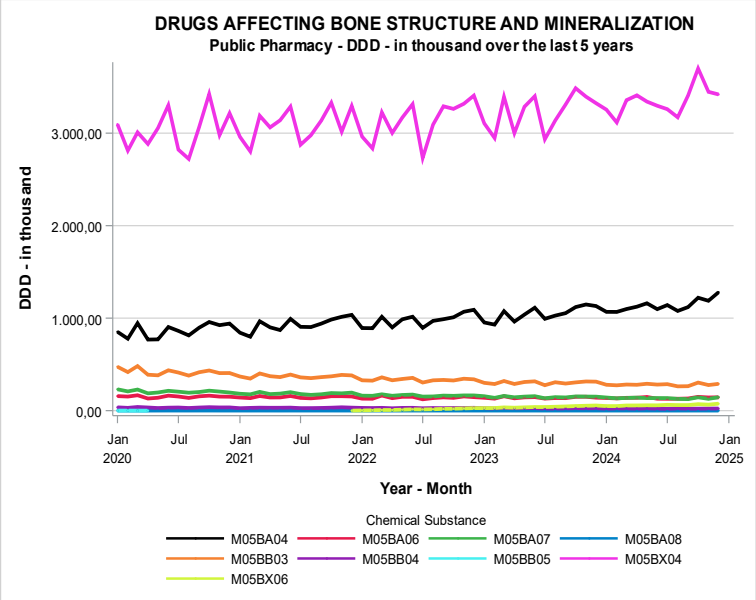

Figure 56: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class M05B.

Although expenditure on romosozumab in public pharmacies accounts for more than 20% of total expenditure on drugs affecting bone structure and mineralisation, this is not reflected in the limited number of DDDs.

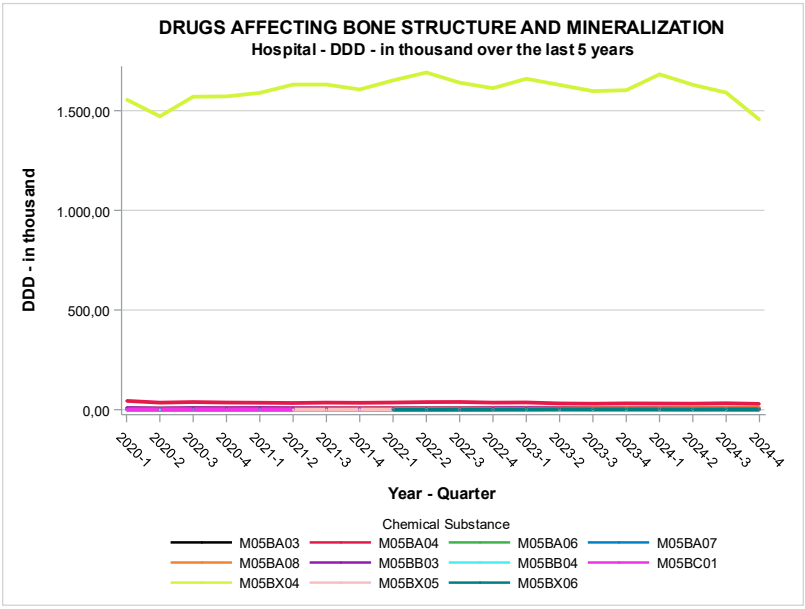

Figure 57: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class M05B.

In hospitals, the total number of DDDs declined after 2022 (see Figure 52). Denosumab-based specialties (M05BX04) are the most commonly used (see Figure 57). Although hospital expenditure on burosumab accounts for more than 40% of total expenditure on drugs affecting bone structure and mineralisation, this is not reflected in the number of DDDs, which is very limited.

In conclusion, we can state that NIHDI expenditure for this class of medicines has been on the rise in recent years, both in public pharmacies and in hospitals, on the one hand because more patients have been treated in total, and on the other hand due to the arrival of new, more expensive molecules. Although the number of patients treated with these new molecules is relatively limited, the higher cost of treatment per patient means that expenditure in this area is on the rise.

XII. Class N02C - Antimigraine preparations

Chemical Substance
N02CC01 sumatriptan - IMITREX (+ generic)
N02CC02 naratriptan (+ generic)
N02CC02 naratriptan - generic
N02CC03 zolmitriptan (+ generic)
N02CC03 zolmitriptan - generic
N02CC05 almotriptan (+ generic)
N02CC05 almotriptan - generic
N02CD01 erenumab - AIMOVIG
N02CD02 galcanezumab - EMGALITY
N02CD03 fremanezumab - AJOVY
N02CD05 eptinezumab - VYEPTI
N02CD07 atogepant - AQUIPTA

Table 31: List of reimbursed molecules in pharmacological class N02C.

Over the last decade, class N02C in public pharmacies has seen very pronounced growth (see Figure 58). Volumes (DDD) rose from around 0.67 million in 2015 to 7.52 million in 2024 (×11), while NIHDI gross expenditure rose from around €1.53 million to €57.5 million (×38). Following a steady rise until 2020, 2021 marked a major turning point (+92% DDD; +662% expenditure), confirmed in 2022-2024 (DDD +61% then +18% and +14%; expenditure +129% then +32% and +15%). This acceleration reflects the rise in the use of anti-CGRP as migraine prophylaxis, whose distribution in public pharmacies has profoundly reconfigured the class mix, to the detriment of crisis molecules individually.

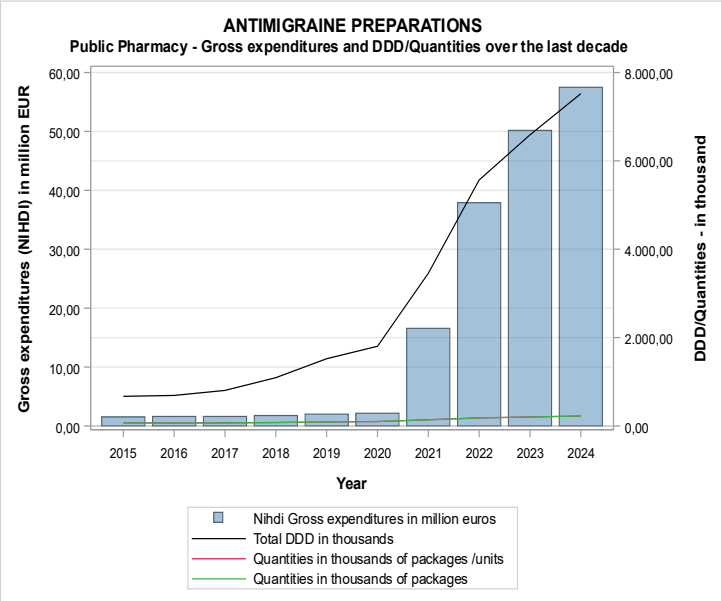

Figure 58: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class N02C.

Monthly analysis over the period 2020-2024 (see Figure 59) corroborates this shift: we observe a high and steady base of crisis treatments (triptans) and, on top of this, a growing component linked to preventive treatments (anti-CGRP) which has reduced expenditure much faster than DDDs (cost/day of treatment effect). In short, public pharmacies now account for the bulk of the growth in N02C, driven by targeted prophylaxis rather than merely treating crises.

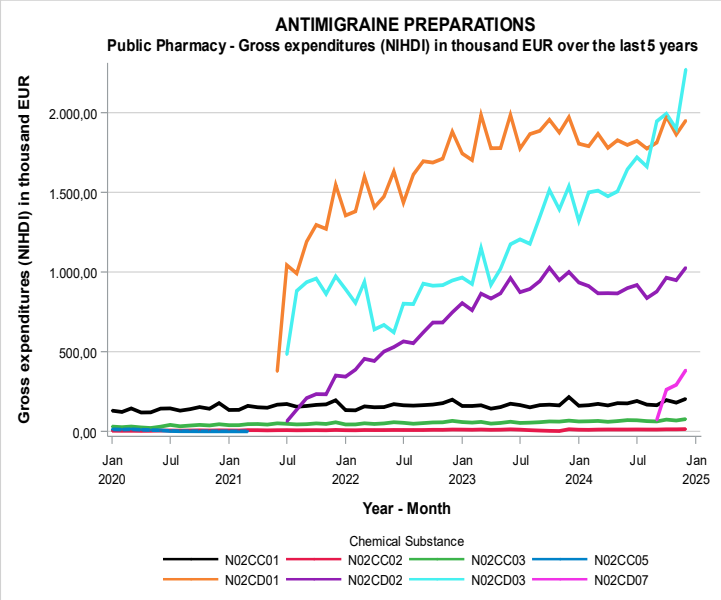

Figure 59: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class N02C.

In hospitals (see Figure 60), class N02C is still modest in quantitative terms, but has been expanding rapidly in recent years. From 2015 to 2024, DDD rose from around 6.4 k to 22.6 k (×3.5), and gross expenditure from €0.03 M to €0.32 M (×10). Following a relatively contained dynamic until 2021, 2022 marked the first leap (expenditure ~×2), and the trend accentuated in 2024 (+272% expenditure; +36% DDD vs 2023).

Quarterly data for 2023→2024 (see Figure 61) reveal increases for individual molecules, with very pronounced growth for eptinezumab, the only anti-CGRP drug administered intravenously in hospitals.

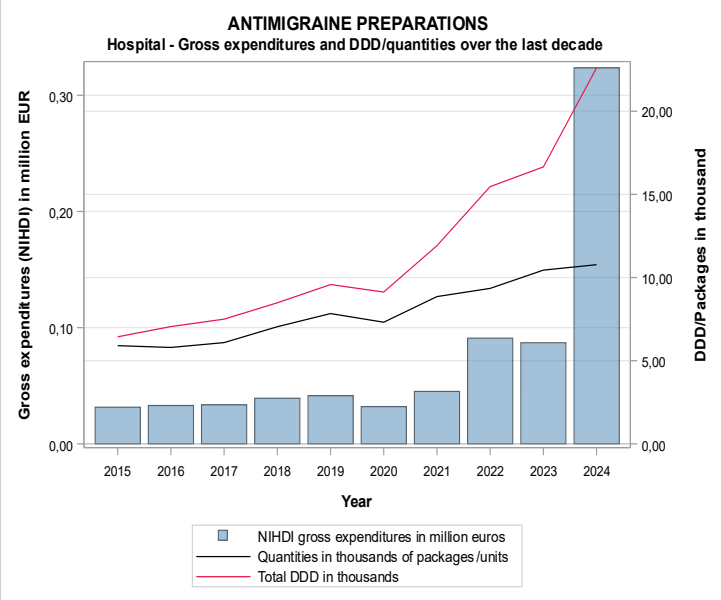

Figure 60: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class N02C.

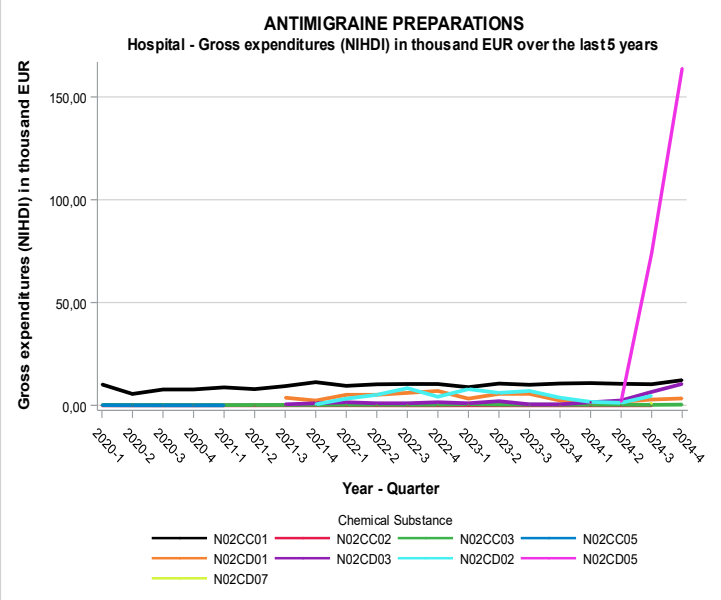

Figure 61: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class N02C.

XIII. Class N07X - Other nervous system drugs

Chemical Substance
N07XX02 riluzole - RILUTEK (+ generic)
N07XX04 sodium oxybate - XYREM (+ generic)
N07XX06 tetrabenazine - NITOMAN (+ generic)
N07XX07 fampridine - FAMPYRA
N07XX08 tafamidis - VYNDAQEL
N07XX11 pitolisant - WAKIX
N07XX12 patisiran - ONPATTRO
N07XX18 vutrisiran - AMVUTTRA

Table 32: List of reimbursed molecules in pharmacological class N07X.

Expenditure on this group of medicines in public pharmacies rose sharply from 2016 onwards, peaking around 2019–2021. Since then, they have remained stable at a high level of around €3 million. Consumption, expressed in DDD, followed the same upward trend and reached a plateau in 2021, which has since declined slightly. The number of packages is rising less sharply, suggesting that the growth in DDD is mainly due to higher dosages or longer treatments per patient.

The number of patients using medicines from this group has remained stable at around 2,500 to 2,700 over the last five years (see Figure 63). This confirms that the increase in consumption and expenditure is not so much due to more patients, but rather to more intensive consumption per patient and more expensive treatments.

Within this group, three subgroups account for the largest share of expenditure: fampridine, riluzole and tetrabenazine. Fampridine is the dominant cost driver, with expenditure structurally higher than the other subgroups (see Figure 64). Riluzole and tetrabenazine show a stable to slightly increasing profile, but at a lower level of expenditure. The relative proportions have remained fairly constant over the past five years.

The same subgroups are also dominant in terms of consumption volume (DDD) (see Figure 65). Fampridine remains the largest in terms of DDD, with a slight downward trend after 2021. Riluzole shows a stable trend, while tetrabenazine is slowly increasing. This pattern reflects a shift whereby certain therapies are being used more frequently, while others remain at a stable level.

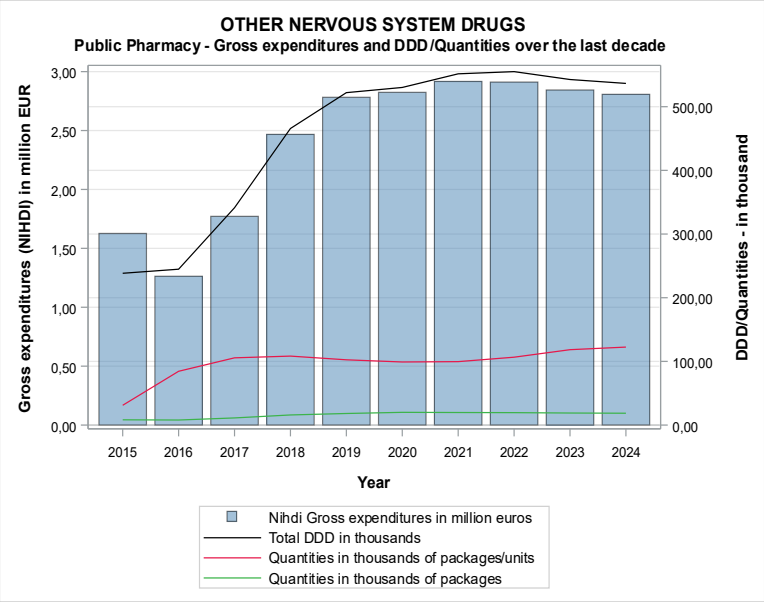

Figure 62: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class N07X.

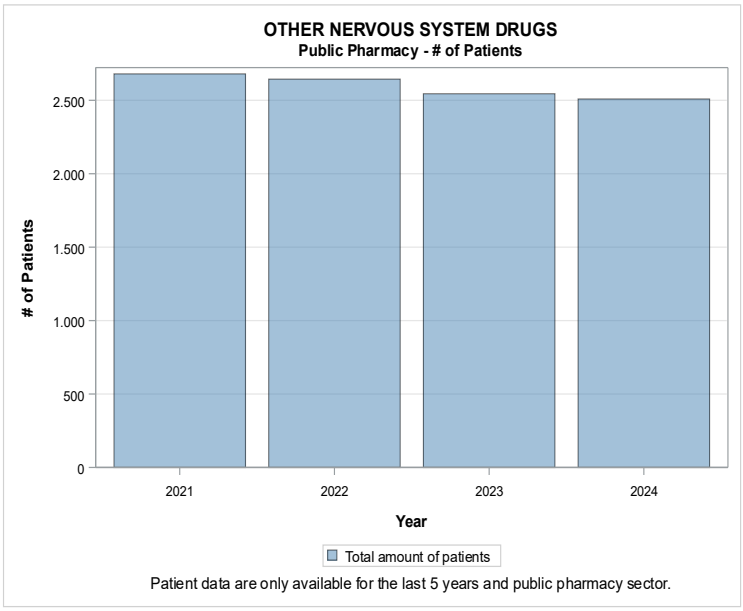

Figure 63: Annual evolution in the number of patients using specialties from pharmacological class N07X reimbursed in public pharmacies and nursing homes.

63 - Detailed analysis of different pharmacological classes

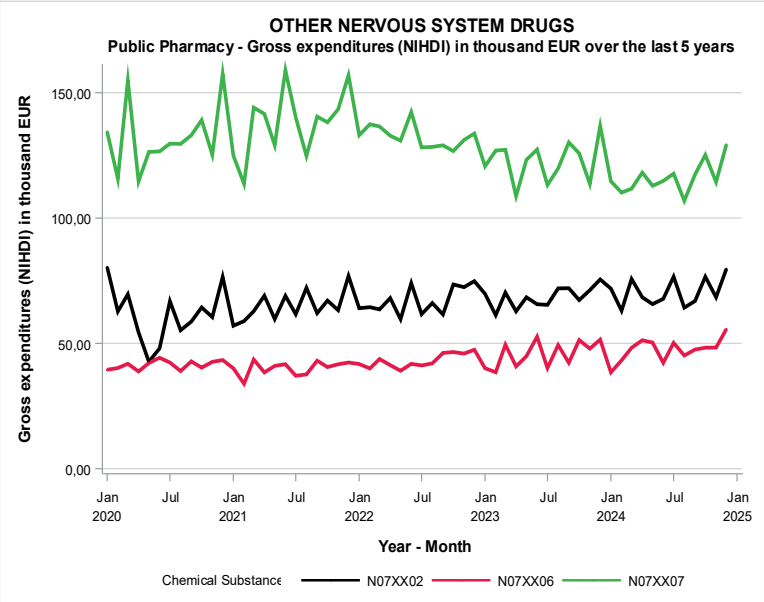

Figure 64: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class N07X.

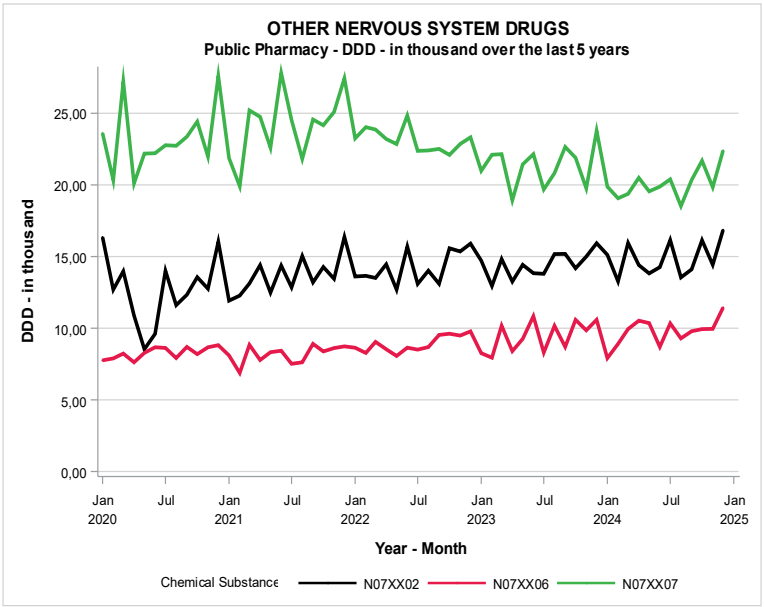

Figure 65: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class N07X.

Expenditure on medicines of the type 'Other nervous system drugs' in hospital pharmacies has risen spectacularly in recent years, as shown in Figure 66. While the costs were negligible until 2020, we see a sharp increase from 2021 onwards, rising to over €300 million in 2024. This is accompanied by a sharp increase in consumption, expressed in DDD and number of packages. The evolution clearly points to the introduction and rapid rise of a new, expensive therapy for amyloidosis in this segment.

Within hospital pharmacies, the sharp increase is almost entirely driven by tafamidis, which has shown exponential growth in expenditure since 2021 and had by far the largest budget impact in 2024 (see Figure 67). The other subgroups (such as riluzole, tetrabenazine and fampridine) remain marginal in comparison, with only limited and stable costs. This confirms that the recent growth in expenditure is concentrated around a new innovative treatment.

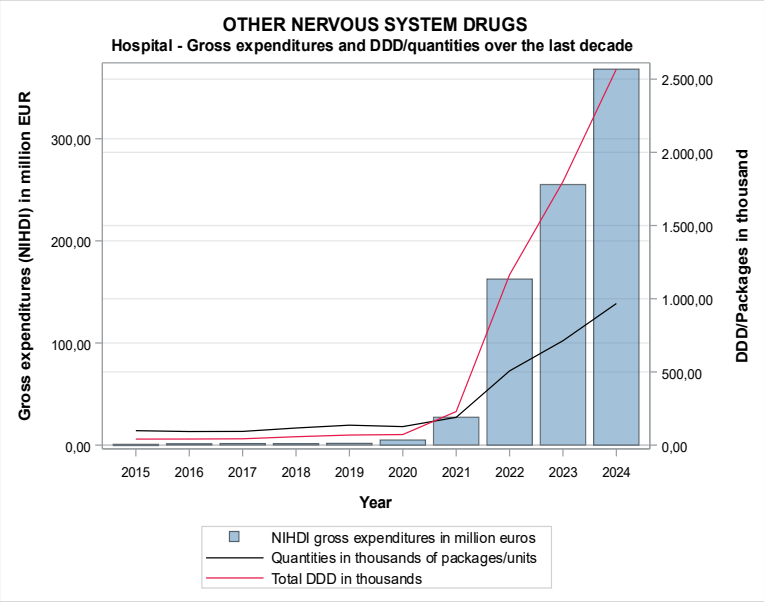

Figure 66: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class N07X.

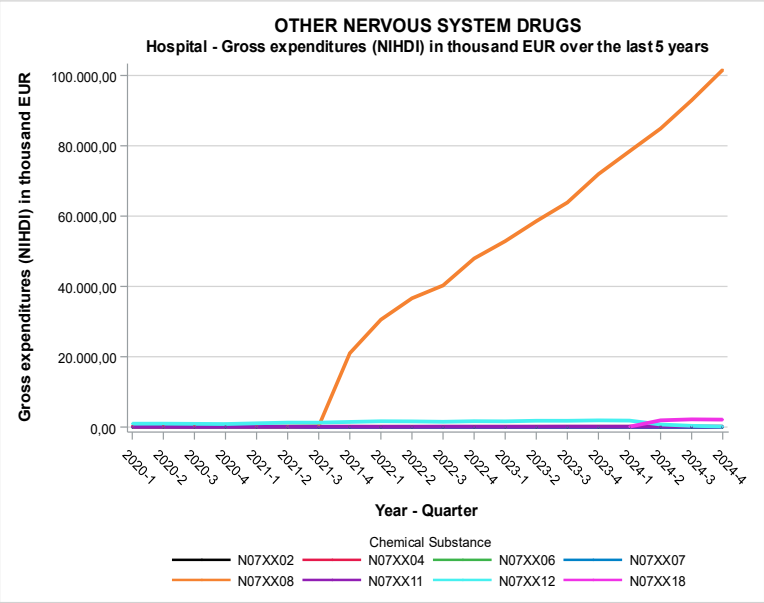

Figure 67: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class N07X.

In terms of consumption (DDD), we also see that tafamidis has experienced explosive growth since 2021, rising to more than 600,000 DDD in 2024 (see Figure 68). The other subgroups remain stable and at much lower levels. The strong parallel between expenditure and consumption makes it clear that the budgetary impact is directly related to the widespread and rapid implementation of this specific therapy.

65 - Detailed analysis of different pharmacological classes

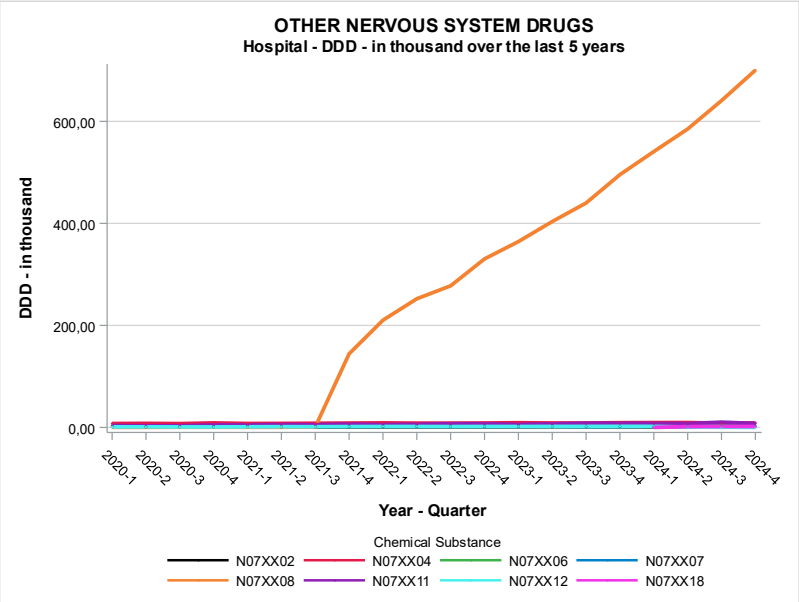

Figure 68: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class N07X. Analysis of files handled by the CRM

3. Analysis of the evolution of the number of files handled by the CRM between 2020 and 2024

I. The Commission for Reimbursement of Medicines

The NIHDI organises, manages and oversees compulsory insurance in Belgium. The NIHDI is under the supervision of the Minister of Social Affairs, and also organises consultation between the various actors involved in medical care insurance and benefits.

Within the NIHDI, the Commission for Reimbursement of Medicines (CRM) advises the Minister regarding the reimbursement of medicines. Requests for reimbursement are made by pharmaceutical companies. These proposals are submitted to the Minister of Social Affairs, who makes the decision to include them on the list of reimbursable medicines.

There are various types of procedures within the CRM for the reimbursement of pharmaceutical specialties which are described (with the wording of the following tables) as follows:

- Class 1: request for reimbursement of a pharmaceutical product for which the applicant claims therapeutic added value compared with existing therapeutic alternatives;
- Class 2: request for reimbursement of a pharmaceutical product for which the applicant does not claim therapeutic added value compared with existing therapeutic alternatives and which is not in class 3;
- Class 2 - biosimilar: request for reimbursement of a biosimilar drug;
- Class 3: request for reimbursement of a generic drug;
- Price: request for an increase in the reimbursement base for a reimbursable speciality;
- Modification: requests for changes in the reimbursement terms for a reimbursable specialty;
- Orphan: request for reimbursement of an orphan drug;
- Deletion: request to cancel the short-term reimbursement of a reimbursable product;
- Exception: request for exception to reference reimbursement;
- Ind. revision: individual revision of the reimbursement of a reimbursable product (procedure implemented between 12 months and three years after the initial decision subject to revision);
- Import: request for reimbursement of a speciality that is imported or the subject of parallel distribution.

II. Clarifications regarding the interpretation of results

The tables and graphs presented in this section primarily relate to changes in the number of unique files examined by the Commission for Reimbursement of Medicines (CRM), broken down by type of procedure (Class 1, Class 2, etc.). The analysis focuses on two variables that determine access to reimbursement for new medicines, whether innovative or not, in Belgium: on the one hand, the proposals made by the Committee, and on the other, the decisions taken by the Minister concerning medicines that have been the subject of a request.

When evaluating and interpreting the data, a number of important factors need to be taken into account:

- The reimbursement of medicines in Belgium is supply-driven, which means it depends on the requests for reimbursement submitted by pharmaceutical companies. This is the decisive factor for all reimbursable medicines, and an important one for the speed of reimbursement of new drugs, whether innovative or not. This puts into perspective the time lag between obtaining authorisation for placing on the market and the start of the CRM procedure, as described by EFPIA in the WAIT indicator 2023 survey (Newton et al., 2024). For orphan drugs and Class 1 requests, the request can already be submitted once the applicant has received a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA). This possibility has not really

been used up until now. Between 2020 and 2024, 9% of Class 1 requests and requests for reimbursement for orphan drugs were submitted on the basis of a positive opinion from the Committee for Medicinal Products for Human Use of the EMA, before authorisation for placing on the market was granted: 4 requests in 2020, 4 requests in 2021, 18 requests in 2022, 11 requests in 2023 and 3 requests in 2024.

- Pursuant to Article 1 of Royal Decree no. 20 of 13 May 2020 on temporary measures in the fight against the COVID-19 pandemic and aimed at ensuring continuity of care in compulsory health care insurance (published in the Belgian Official Gazette on 19 May 2020), the timetables that determine time frames for carrying out modification procedures on the list of reimbursable pharmaceutical specialties have been discontinued since 13 March 2020. This measure was repealed by Article 1 §3 of the Royal Decree of 28 December 2020 repealing certain temporary measures of Royal Decree no. 20 of 13 May 2020 on temporary measures in the fight against the COVID-19 pandemic and aimed at ensuring continuity of care in compulsory healthcare insurance, and Royal Decree no. 21 of 14 May 2020 making temporary modifications to the reimbursement conditions and administrative rules for compulsory healthcare insurance following the COVID-19 pandemic, and the timetables resumed on 1 April 2021.

III. Data processing methodology

Compared with previous reports, the data processing methodology has been substantially updated. As such, it is possible that differences will appear with the results presented in the past.

The data processed comes from the administrative database (CTG-CTI) used by the secretariat of the CRM for ongoing monitoring of procedures and implementation time frames. For the analysis of the number of files, we have taken into account all data for files submitted between 1 January 2020 and 31 December 2024, and which had been declared admissible at the time of writing.

For this analysis, only unique files are taken into account. This means that in the case of simultaneous requests for different dosages/packages of specialties, a unique file is kept for data processing purposes. An identification key was created by concatenating the first 5 characters of the product name, file type and sub-type, status of the closing of the file, date of submission of the file (day "0"), date of start of processing of the file, and date of end of file. Based on this identification key, all duplicates are removed from the analysed dataset.

As such, for a given specialty, there may be several files in the processing of data, depending on the type of procedure, the company making the request, or the dates marking the management of the file.

Files subject to purely administrative processing (i.e. without intervention by the CRM, for which the procedure is limited to 60 days) are not included in the analysis: files submitted in subclasses 2A, 3A and files requesting authorisation for specialties imported or subject to parallel distribution whose reference specialty is not the subject of an "Article 111/112/113" convention and whose requested reimbursement terms are identical to those of the reference specialty), procedures conducted in accordance with Article 130 of the Royal Decree of 1 February 2018 and files processed in accordance with Article 129 of the Royal Decree of 1 February 2018. This concerns 1,340 files (i.e. around 37% of requests) for the past period, broken down as follows:

Type	Subtype	Effective	Percentage
Class 2	Admin	37	2.76
Class 3	Admin	390	29.10
Import	Admin	325	24.25
Art. 129	Admin	1	0.07
Art. 130	Admin	587	43.81
Total	Admin	1340	100.00

Table 33: Files excluded from the analysis by type of purely administrative procedure.

IV. Evolution of the number of files by type of procedure

The total number of unique files handled by the CRM was relatively stable between 2020 and 2023 (around 420 to 460 files per year), before rising significantly in 2024 (532 files, or +23% compared with 2023). The trends are shown in Figure 69 and Table 34.

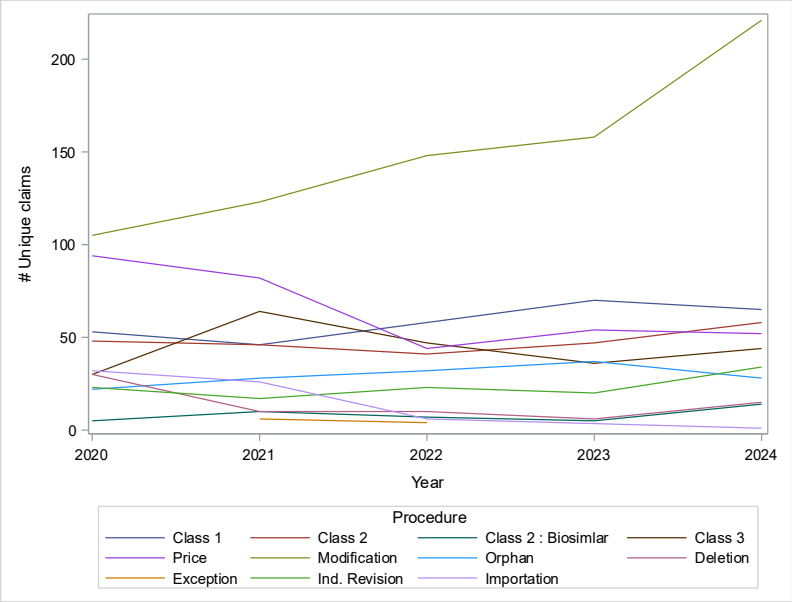

Figure 69: number of requests per year (unique files - including completed procedures, withdrawn or discontinued requests and ongoing procedures) from 2020 to 2024.

	2020		2021		2022		2023		2024		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
Class 1	53	12%	46	10%	58	14%	70	16%	65	12%	292	13%
Class 2	48	11%	46	10%	41	10%	47	11%	58	11%	240	11%
Class 2: Biosimilar	5	1%	10	2%	7	2%	5	1%	14	3%	41	2%
Class 3	30	7%	64	14%	47	11%	36	8%	44	8%	221	10%
Price	94	21%	82	18%	44	10%	54	12%	52	10%	326	14%
Modification	105	24%	123	27%	148	35%	158	36%	221	42%	755	33%
Orphan	22	5%	28	6%	32	8%	37	9%	28	5%	147	6%
Deletion	30	7%	10	2%	10	2%	6	1%	15	3%	71	3%
Exception	.	.	6	1%	4	1%	.	.	.	.	10	0%
Ind. Revision	23	5%	17	4%	23	5%	20	5%	34	6%	117	5%
Import	32	7%	26	6%	6	1%	.	.	1	0%	65	3%
Total	442	100%	458	100%	420	100%	433	100%	532	100%	2285	100%

Table 34: number of requests per year (unique files - including completed procedures, withdrawn or discontinued requests and ongoing procedures) from 2020 to 2024.

In terms of breakdown by type of procedure, a number of trends emerge, which among other things explain this substantial increase:

- Procedures to modify reimbursement terms account for the largest share, and their relative weight increases sharply over the years: from 24% in 2020 to 42% in 2024. This reflects a rise in requests to modify the reimbursement terms for medicines already on the market, whether at the request of the companies responsible for marketing the drugs or at the initiative of the CRM. It should be noted that these requests relate to both extensions of indications and more technical corrections. In 2022, a large number of files involved changes to reimbursement terms at the initiative of the CRM for contrast media, and in 2023 for growth hormones. In 2024, a large number of files involved changes to reimbursement procedures initiated by the CRM for new anticoagulants (NOACs), narcolepsy treatments and bortezomib-based specialties (transfer to Chapter I).
- Requests for admission to Class 1 show a moderate but steady rise, from 10-12% at the start of the period to a peak of 16% in 2023, before dropping back to 12% in 2024. However, they remained stable at around 13% over the period.
- Requests for admission to Class 2 remain broadly constant (10-11% per year), while the 'biosimilars' sub-category shows a slight increase, peaking at 3% in 2024.
- Requests for admission to Class 3 vary widely: 7% in 2020, peaking at 14% in 2021, then stabilising at around 8% at the end of the period.
- Requests to increase the reimbursement base, which were highly represented in 2020 (21%), have declined sharply over the years, stabilising at around 10-12% after 2022.

- Orphan drugs showed an upward trend until 2023 (from 5% to 9%), before declining to 5% in 2024.
- Requests for deletions from reimbursement with continued commercialisation (deletions) and requests for drugs imported or distributed in parallel declined sharply: from 7% each in 2020, they fell to 3% and 0% respectively in 2024.
- Individual revision procedures remained stable (4-6%), with no clear trend.
- Exceptions to the request for the reference reimbursement appeared occasionally in 2021-2022, but these were marginal (less than 1%).

V. Proposals of the CRM and decisions of the Minister

The Royal Decree of 1 February 2018, establishing the procedures, deadlines and conditions under which the compulsory health care and benefits insurance contributes to the cost of the pharmaceutical specialties, stipulates that the Minister's decisions on requests for reimbursement of new pharmaceutical specialties must be served on applicants within 180 calendar days, from the date of the request (day "0"), taking into account any suspensions of procedures.

The Minister's decision is based on the proposal of the Commission for Reimbursement of Medicines, which is required to make this proposal within 150 days of the request.

The Minister cannot derogate from the CRM's proposal, except for budgetary or social reasons, and can take this decision alone if the CRM fails to make a proposal within the 150-day time limit (the company can request a suspension of the procedure during the evaluation phase and during the proposal phase).

The CRM can make three types of proposal:

- A positive proposal;
- A negative proposal;
- In certain cases, a proposal to start a procedure in accordance with Article 112 of the Royal Decree of 1 February 2018, whereby the CRM proposes that the applicant enter into negotiations with a view to concluding an agreement with the NIHDI for the temporary inclusion of a speciality in the list of reimbursable pharmaceutical specialties (or where applicable, the temporary inclusion of a new therapeutic indication for a speciality already included in the list of reimbursable pharmaceutical specialties). To date, the CRM can make this type of proposal for requests submitted for class 1, requests submitted for class 2B or class 2C if the reference speciality is covered by an agreement, orphan drugs, requests for admission for specialties whose reference speciality is covered by an agreement, requests for admission for specialties imported or distributed in parallel whose reference speciality is covered by an agreement, biosimilar products whose reference product is covered by an agreement, requests for changes to reimbursement terms concerning the reimbursement of a new indication for which there is a therapeutic or social need, and requests for changes to reimbursement terms concerning the extension of reimbursement of an indication already reimbursable in adults to children for a product already covered by an agreement.

The proposals of the CRM are accepted by a two-thirds majority - not including abstentions. In other words, if a two-thirds majority is not reached, either for a proposal to list a (new) medicine, or for NOT listing it, among members entitled to vote who DO NOT abstain from voting, the CRM is deemed NOT to have made a proposal. A voting member who has declared a conflict of interest regarding a file will not take part in the vote on that file, even though he or she is a voting member of the CRM.

Table 35 shows, for the period 2020-2024, the frequency with which the CRM did not make a proposal, issued a negative opinion, issued a positive opinion or made a proposal to enter into negotiations with a view to concluding a convention in accordance with "article 112" of the Royal Decree of 1 February 2018 (grouped together under the heading "MEA" (Managed Entry Agreement). Detailed data, broken down by year, can be found in Appendix 2 of this report.

Between 2020 and 2024, the Commission for Reimbursement of Medicines (CRM) made 1,716 proposals. Most of these were positive (65%), followed by proposals to enter into negotiations with a view to concluding an "Art112" convention (18%) and negative opinions (15%), while files where the CRM did not make any proposal were marginal (3%). Two main dynamics stand out:

- Procedures to modify reimbursement terms made up the largest volume (one third of the total) of CRM procedures, with a large proportion of positive opinions, but also a significant percentage of proposals to enter into negotiations with a view to concluding an MEA.
- Class 1 and orphan drugs stand out for the high percentage of proposals to enter into negotiations with a view to concluding an MEA (40% and 58% respectively), reflecting the specific challenges involved in innovation and clinical and/or budgetary uncertainties.

Conversely, certain procedures, such as individual revisions and imports, had high negative proposal rates, reflecting a more restrictive approach.

2020 - 2024	CRM								Total	
	No Proposal		Positive		Negative		MEA			
	N	%	N	%	N	%	N	%	N	%
Class 1	12	25%	56	5%	35	14%	123	40%	226	13%
Class 2	3	6%	125	11%	13	5%	36	12%	177	10%
Class 2: Biosimilar	.	.	36	3%	1	0%	.	.	37	2%
Class 3	.	.	153	14%	14	6%	.	.	167	10%
Price	8	17%	214	19%	30	12%	.	.	252	15%
Modification	11	23%	423	38%	46	18%	78	25%	558	33%
Orphan	9	19%	16	1%	18	7%	59	19%	102	6%
Deletion	.	.	24	2%	12	5%	.	.	36	2%
Exception	.	.	4	0%	1	0%	.	.	5	0%
Ind. Revision	.	.	56	5%	49	20%	.	.	105	6%
Import	5	10%	2	0%	30	12%	14	5%	51	3%
Total	48	100%	1109	100%	249	100%	310	100%	1716	100%

Table 35: Number of unique requests for changes to the list of reimbursable pharmaceutical specialties versus proposal by the Commission for Reimbursement of Medicines (2020-2024)

Table 36 shows, for the period 2020-2024, the extent to which a positive proposal, a proposal to start a procedure in accordance with Article 112 of the Royal Decree of 1 February 2018, or a negative proposal made by the CRM, for the various types of requests, is followed by the Minister. In files where the CRM did not make a proposal, we examine the extent to which the Minister took a positive or negative decision. Appendix 1 of this report also contains detailed data for the various years.

Over the period 2020-2024, the decisions by the minister were positive overall, with 73% of decisions positive, 16% negative and 11% positive decisions subject to an MEA being concluded, while files where the regulatory deadline by which the Minister had to render a decision was exceeded were exceptional. A cross-check of the CRM's opinions and the Minister's decisions reveals that, in the vast majority of cases, the Minister follows the CRM's proposal. Although the Minister may depart from the CRM's proposal for social and/or budgetary reasons, this is only in a very limited number of cases.

When the CRM issues a positive opinion, the Minister almost systematically follows it, since 99% of these positive proposals result in a favourable decision.

Similarly, negative opinions are upheld in 86% of files by the Minister of Social Affairs, but around 12% of the files concerned still benefit from a positive decision by the Minister of Social Affairs, illustrating the scope for political arbitration.

The majority of proposals by the CRM to enter into negotiations with a view to concluding an MEA are followed: more than half result in a positive decision to conclude an MEA after negotiations, but almost a third are followed by a positive decision by the Minister of Social Affairs without an MEA being concluded, showing a certain flexibility in applying this mechanism.

Lastly, although the number of files where the CRM did not make a proposal was limited (48 files, i.e. 3.7% of the total), decisions were much more varied: 56% positive, 27% negative and 17% positive subject to an MEA being concluded, reflecting the Minister's enhanced decision-making autonomy in these particular cases.

71 - Analysis of the evolution of the number of files handled by the CRM between 2020 and 2024

2020 - 2024		Minister								
		Positive		Negative		MEA		Time Out: Admin Decision		total
		N	%	N	%	N	%	N	%	N
Class 1	No Proposal	8	67%	1	8%	3	25%	.	.	12
	Positive	54	96%	2	4%	.	.	.	.	56
	Negative	1	3%	31	89%	3	9%	.	.	35
	MEA	50	41%	10	8%	63	51%	.	.	123
	Total	113	50%	44	19%	69	31%	.	.	226
Class 2	No Proposal	3	100%	.	.	.	.	.	.	3
	Positive	125	100%	.	.	.	.	.	.	125
	Negative	2	15%	11	85%	.	.	.	.	13
	MEA	11	31%	.	.	25	69%	.	.	36
	Total	141	80%	11	6%	25	14%	.	.	177
Class 2: Biosimilar	Positive	36	100%	.	.	.	.	.	.	36
	Negative	1	100%	.	.	.	.	.	.	1
	Total	37	100%	.	.	.	.	.	.	37
Class 3	Positive	153	100%	.	.	.	.	.	.	153
	Negative	10	71%	4	29%	.	.	.	.	14
	Total	163	98%	4	2%	.	.	.	.	167
Price	No Proposal	8	100%	.	.	.	.	.	.	8
	Positive	214	100%	.	.	.	.	.	.	214
	Negative	6	20%	24	80%	.	.	.	.	30
	Total	228	90%	24	10%	.	.	.	.	252
Modification	No Proposal	6	55%	3	27%	2	18%	.	.	11
	Positive	418	99%	5	1%	.	.	.	.	423
	Negative	5	11%	41	89%	.	.	.	.	46
	MEA	25	32%	9	12%	44	56%	.	.	78
	Total	454	81%	58	10%	46	8%	.	.	558
Orphan	No Proposal	2	22%	4	44%	3	33%	.	.	9
	Positive	16	100%	.	.	.	.	.	.	16
	Negative	3	17%	11	61%	4	22%	.	.	18
	MEA	11	19%	9	15%	39	66%	.	.	59
	Total	32	31%	24	24%	46	45%	.	.	102
Deletion	Positive	24	100%	.	.	.	.	.	.	24
	Negative	1	8%	11	92%	.	.	.	.	12
	Total	25	69%	11	31%	.	.	.	.	36
Exception	Positive	4	100%	.	.	.	.	.	.	4
	Negative	.	.	1	100%	.	.	.	.	1
	Total	4	80%	1	20%	.	.	.	.	5
Ind. Revision	Positive	54	96%	1	2%	.	.	1	2%	56
	Negative	.	.	49	100%	.	.	.	.	49
	Total	54	51%	50	48%	.	.	1	1%	105
Import	No Proposal	.	.	5	100%	.	.	.	.	5
	Positive	2	100%	.	.	.	.	.	.	2
	Negative	.	.	30	100%	.	.	.	.	30
	MEA	.	.	14	100%	.	.	.	.	14
	Total	2	4%	49	96%	.	.	.	.	51
Total	No Proposal	27	56%	13	27%	8	17%	.	.	48
	Positive	1100	99%	8	1%	.	.	1	0%	1109
	Negative	29	12%	213	86%	7	3%	.	.	249
	MEA	97	31%	42	14%	171	55%	.	.	310
	Total	1253	73%	276	16%	186	11%	1	0%	1716

Table 36: Decisions of the Minister based on the CRM's proposal (2020-2024)

4. Analysis of ART. 111/112/113 conventions

I. General principles

1. Legal basis

- Law on compulsory healthcare and benefits insurance, consolidated on 14 July 1994 - art. 35bis, § 7
- Royal Decree of 1.2.2018 establishing the procedures, deadlines and conditions under which the compulsory health care and benefits insurance contributes to the cost of the pharmaceutical specialties - art. 111 to 117 inclusive
- Law containing provisions on the reimbursement of pharmaceutical products and on the administrative costs, efficiency and transparency of insurance organisations, coordinated 1 April 2019 - chapter 5.

2. Procedure regarding conventions

For certain new treatment options, there may be scientific and/or budgetary uncertainties regarding the reimbursement. These uncertainties may relate to the (relative) therapeutic value, the costs per treatment or the total budgetary impact of the medicine at the level of the population. Most of the time, it is a combination of several factors, and the uncertainty therefore relates to the relationship between the value and cost of the new therapy.

In order not to deprive patients of access to these sometimes promising new treatments, and to give the pharmaceutical company the opportunity to (continue to) demonstrate the value of the medicine in real-life situations, these treatments can be reimbursed on a temporary basis under certain conditions. The precise conditions that the pharmaceutical company must meet to make this temporary reimbursement possible are set out in a convention. Conventions are one of the instruments used in medicines policy to ensure better control over budgets.

There are generally two conditions to be met. On the one hand, the company is requested to collect additional information and evidence on specific uncertainties during the period of temporary reimbursement; on the other hand, the company jointly assumes responsibility for the uncertainties and/or problems related to the reimbursement during the period of temporary reimbursement. For example, a face value price charged by the company that is far too high, even for an individual who responds to the treatment, cost-effectiveness problems, prices proposed by the CRM that are not acceptable to the company, due to international pricing, etc. In practice, this means that a budget compensation scheme is included in the agreement. In this way, the risks are shared by both the health insurance system and the company.

In order to reach an agreement between the NIHDI and the company for the temporary reimbursement of a pharmaceutical speciality, a working group negotiates at one or more meetings organised by the NIHDI. This working group brings together representatives of the insurance companies (for the Insurance Committee), the CRM, the pharmaceutical company, the professional organisation of the drug industry if designated by the applicant, the Minister of Social Affairs, the Minister of the Budget and the Minister of the Economy. The Inspector of Finance is informed of the agendas and minutes of meetings of the working group, and may attend these meetings. The negotiation procedure may not exceed 120 days. The 120-day period also includes all the administrative steps required to formally close the negotiation procedure and, where applicable, put in place a temporary reimbursement system. If consensus can be reached within this timeframe, it is recorded in an agreement signed by the NIHDI and the pharmaceutical company. The list of reimbursable specialties then indicates with the letter "T" that temporary reimbursement via agreement is in force.

The possibility of concluding an agreement was introduced in 2010. Since then, the regulations have been amended on several occasions[13], but the fundamental principles have remained unchanged. The current procedure for concluding an agreement is described in Articles 111 et seq. of the Royal Decree of 1.2.2018 establishing the procedures, deadlines and conditions under which the compulsory health care and benefits insurance contributes to the cost

[13] Following extensive consultation with all stakeholders, the NIHDI drew up a "roadmap" in 2023 proposing 52 actions to modernise the reimbursement of medicines (NIHDI, 2023a).

of the pharmaceutical specialties. Before this RD entered into force, the relevant procedure was set out in articles 81 et seq. of the RD of 21.12.2001 establishing the procedures, deadlines and conditions under which the compulsory health care and benefits insurance contributes to the cost of the pharmaceutical specialties. The names "article 81/111 conventions" and "article 81/111 procedure" therefore come from the legal basis of these conventions.

The negotiation procedure to obtain an agreement can be initiated by the pharmaceutical company in three different ways, as shown in Figure 70:

- When the CRM is unable to make a definitive proposal by a two-thirds majority (art. 81/111).
- On the proposal of the CRM (art. 81bis/112)
- Until 1 July 2014, it was possible for a company to introduce a request for negotiation (Article 81) after a negative opinion from the CRM and a formal request from the Minister. This has been possible again since 1 February 2018, subject to certain conditions (art. 113).

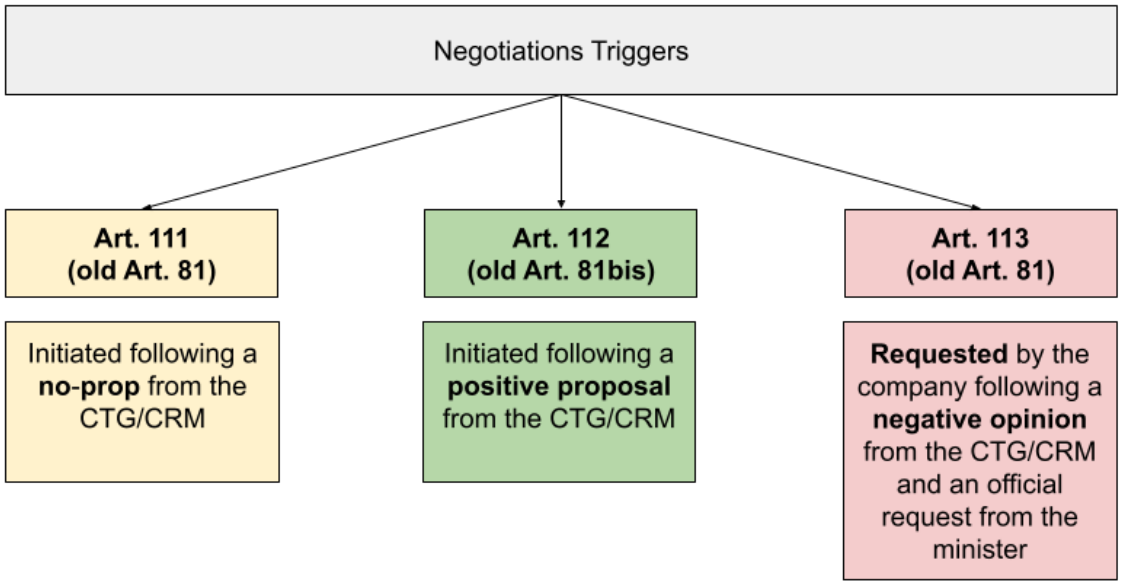

Figure 70: Schematic summary of situations that can potentially lead to negotiation procedures

Since 1 July 2014, it has been possible for companies to submit, under certain conditions, a request for an Article 81/111 procedure for files for Class 2 (no therapeutic added value) in cases where the reference specialty is on the positive list with the letter "T".

Since 2018, the CRM has been able to make a proposal to start negotiations for each pharmaceutical speciality for which reimbursement is requested, in cases where the reference speciality is on the positive list with the letter "T"; therefore also for generics, biosimilars, imported or parallel-distributed specialties (art. 112) among others.

3. Budget compensation mechanisms

As highlighted above, risks and uncertainties linked to the reimbursement of a new treatment can be managed through article 81/111 conventions. In practice, this often means setting up a budget compensation mechanism: the health insurance system covers the cost of the medicine in question (i.e. the NIHDI reimburses the speciality at the published reimbursement rate), and the pharmaceutical company then pays the NIHDI a specific amount on clearly defined dates and according to clearly defined calculation methods.

In the majority of conventions, this amount is calculated on the basis of total turnover generated on the Belgian market by the pharmaceutical speciality concerned, which is included in the list of reimbursable pharmaceutical specialties. To ensure that this process runs smoothly, the conventions clearly state when a company must declare its turnover figures to the NIHDI, and when the deadline for payment of the budget compensation is.

The amount of this budget compensation depends on what is stipulated in the convention. Various compensation mechanisms are applied in accordance with Article 115, 2° of the Royal Decree of 01.02.2018. A combination of these mechanisms is also possible:

- a percentage of the turnover generated for the specialty concerned is paid, with or without a ceiling on expenditure at individual level or at group level (e.g. by therapeutic class, by indication), where exceeding the expenditure ceiling must be fully or partly refunded;
- a fixed amount per unit sold is paid, corresponding to the difference between the proposed reimbursement base and the value corresponding to the assessment of the criteria referred to in article 4 of the Royal Decree of 1.2.2018;
- an amount corresponding to all or part of the difference between forecast and actual expenditure for the specialty concerned is paid;
- a reduction in the reimbursement base is applied for one or more other pharmaceutical specialties commercialised by the applicant, so that the health insurance system spends less on a medicine other than the specialty concerned;
- any other arrangement at the applicant's expense that helps limit expenditure.

These different methods of compensation could give the impression that the conventions pertain to purely financial aspects, whereas almost every mechanism involves an element of rationality, often scientific. For example, the mechanism where a percentage of turnover is paid may be based on a system where the health insurance system only bears the costs for patients who are deemed to benefit from treatment with the specialty concerned (outcomes-based agreement), or only reimburses costs when the specialty concerned is administered for a treatment for which there is sufficient scientific evidence that it is efficacious and safe, for example.

Information regarding the amount of a company's financial contribution, and a diagram explaining the precise way to calculate the budget compensation is appended to an article 81/111 convention. In accordance with article 35 §7 of the coordinated law of 14 July 1994, the content of the appendices to conventions is confidential. That means that budget compensation per medicine or, for certain conventions, per group of medicines, cannot be presented in this MORSE report if these data violate the confidentiality of individual conventions. In other words, the expenditure on pharmaceutical specialties stated elsewhere than in table 3 of the report and this chapter does not take into account the compensation received by the NIHDI in the context of article 81/111 conventions.

4. Repayments of budget compensation in practice

At specified times, in accordance with the provisions of articles 7 et seq. of the agreement, the applicant must notify the NIHDI of the turnover generated on the Belgian market by the pharmaceutical speciality concerned, which is included in the list of reimbursable pharmaceutical specialties. If possible, the applicant calculates the budget compensation to be paid out. The NIHDI always verifies the budget compensation due.

The compensation to be paid to the NIHDI comprises an 'advance' (explained in article 7 bis of the conventions; also known as "phase 1") and a final refund (explained in article 7 ter of the conventions; also known as "phase 2" or "balance").

The total duration of conventions is normally divided into one or more periods, with budget compensation for each period. These periods run from specific date x to date y and, in practice, do not usually correspond to a calendar year. As a result, periods often straddle two calendar years, and the timing of the final refund does not necessarily fall in the same calendar year as the period to which the refund pertains. In the context of these conventions, expenditure (gross, i.e. before the budget compensation is deducted) is therefore incurred in a given year T, but the final refund is not made in full or in part until year T+1, or even later in certain specific cases.

To ensure that there is not a significant discrepancy between the amount to be received by the NIHDI at the end of the period and the budget year to which it relates, the compensation is broken down into an advance and a balance. The advance is an amount to be paid at the end of the calendar year, corresponding to the proportion of turnover for the period covered in the year in question over the total duration of the period. At the end of the period, the balance is calculated based on the definition of final turnover. In certain situations, the NIHDI may therefore have to pay back sums to companies. For more information on how the compensation is calculated, please refer to Appendix 3.

Since October 2016, it has therefore been standard practice, when new conventions are concluded or amendments are drawn up, to estimate as accurately and reliably as possible the amount of compensation that the company has to pay to the NIHDI during the year in which the expenditure was actually made, to ensure that the companies pay this amount, i.e. the advance, calculated according to the mechanism set out in the convention, to the health insurance

system at the end of that calendar year. The difference between the total amount of the compensation and the advance already paid will represent the balance paid by the NIHDI or the company to the company or the NIHDI, respectively.

To summarise, we can state that under the "advance system", expenditure (gross, i.e. before budget compensation is deducted) incurred by the health insurance system for medicines under contract in a given year T, is offset by "art 81/111 refunds" in the same year T. Among other things, this system should provide a more reliable picture of actual net expenditure per calendar year, and bring health insurance expenditure more into line with reality.

Over the past few years, the general principle of this advance system has not changed much, but its implementation has been gradually refined in order to approximate the forecast net expenditure per calendar year as much as possible.

5. Management of scientific and budgetary uncertainties

The aim of the conventions is to compile additional information and evidence to resolve clearly identified uncertainties. These uncertainties may be scientific and/or budgetary, and are primarily identified by the CRM. They are explicitly mentioned in the convention, and the pharmaceutical companies must have clarified them by the end of the agreement.

These uncertainties are also behind the increase in the number of conventions in recent years. The CRM often identifies significant therapeutic uncertainty (files often include immature data as they were submitted too early to the EMA, e.g. with results from phase II study(s)), and/or significant budgetary uncertainties (high treatment cost per patient not proportional to the CRM's assessment of the criteria - based on the available evidence, significant budget impact often due to a large (estimated) target population). Furthermore, the pharmaceutical companies are increasingly keen to conclude an agreement (even after the patent expires) to maintain a virtually high face value price in the context of international reference pricing, under the guise of budget uncertainty, while seeking to preserve this image to the outside world. International Reference Pricing (IRP), also known as external reference pricing, is a price control mechanism whereby a government considers the price of a medicine in other countries to inform or establish the price in its own country. Nevertheless, we observe that, despite the wish to maintain a high face value price, a substantial amount is paid back, taking into account the overall compensation received from the NIHDI via articles 81/111.

Although the intention of the CRM is to ensure definitive inclusion in the list of reimbursable pharmaceutical specialties, and to increase transparency regarding the costs paid by the health insurance system, initiating a negotiation process is often the only way to make medicines accessible to patients in a way that is somewhat controllable in budget terms.

In cases of therapeutic uncertainty, the emphasis is on providing evidence of efficacy, safety, impact on quality of life, etc. of a given therapy. As a result, the pharmaceutical companies are asked to collect data during the term of the agreement that will clarify the existing uncertainties. It is up to the pharmaceutical companies to decide how best to clarify any uncertainties. For example, a company may present new study results (e.g. a post-marketing study), or interim analyses (e.g. an ongoing Phase III study), or the results of a new non-randomised clinical study that highlights new data relating to the original uncertainties.

For real life data, a company can also use registers or request data from a third party, such as the Inter-Mutual Insurance Agency (AIM). Via the AIM, it is possible to obtain guidance from the data billed to insurance companies on - for example - the number of patients or packages per indication for the same molecule, the duration of treatment, possible co-medication, etc.

For a limited number of specialties, data are collected via Sciensano, often in collaboration with the NIHDI. In the first instance, these are clinical data that are not included in billing databases, and for which specific registers must be set up or adapted. Further information is available on their website (Sciensano, 2025).

A company collects all relevant data and integrates it into an evaluation report, which is forwarded a few months before the end of the agreement to the working group responsible for negotiating the agreement. This report is then comprehensively assessed. Given the data provided and its probative value, the working group will consider whether an extension (with or without modifications) of the agreement is advisable, or whether the CRM should instead carry out a new assessment. If the latter option is chosen, the working group advises the company to start a new CRM procedure with the data obtained during the term of the agreement, so that the CRM can carry out a new assessment. In such cases, the agreement is renewed for a maximum of one year, in accordance with the terms of the last year of the agreement.

In conclusion, an article 81/111 convention can be a temporary solution for making promising therapies available to patients. However, there is always a risk-benefit assessment. In deciding whether to grant temporary reimbursement, it will be taken into account whether the investment of public funds is sufficient to ensure that there is no loss of social welfare if the medicine ultimately proves to be cost-effective; but also whether public funds are being used responsibly if the product subsequently proves to be of little or no use to patients. There therefore also needs to be a clear exit strategy, involving difficult decisions. In the absence of further evidence, the medicine may no longer be reimbursed, or it will be reimbursed at a price known to the public that reflects its value. It must effectively be ensured that the budget is allocated to a therapy with a better cost-benefit profile, and not to one for which there is less evidence.

6. Methodological note on the data used

The data are encoded manually by the management team in charge of files requesting temporary reimbursement under convention. These data are handled on a daily basis and may be modified over time. As a result of these updates (and the deleting of old data - obsolete data are not saved), as well as methodological practices that evolve over time, differences may be observed in the results presented between different editions of the MORSE report.

The methodological practices mainly relate to the dates used to record conventions or amounts in a given year. Depending on the date used, the figures compiled will change from year to year. Figure 71 shows a schematic diagram of all the dates involved in the conventions. To the extent possible, the dates used to define the year in question will be indicated throughout this report. In general:

- the year in which the request for reimbursement is submitted will be used to group the conventions;
- the year of the date of actual payment of the balance will be used to calculate payments of turnovers;
- the year of the actual date of payment of the various amounts (advances or balances) for calculating MEA compensation.

Finally, only a ten-year interval will be taken into account for the presentation of the annual report. As such, the information presented in this report relates to reimbursement files for which a request to start a procedure in order to conclude an agreement has been submitted by the company to the Minister of Social Affairs, during the period 2015-2024 and as of 6 October 2025. Several package sizes or different indications for the same molecule for which reimbursement is requested may be grouped together in a single request. It is therefore up to the pharmaceutical company to decide whether or not to group requests for reimbursement. The tables below also include requests made in the context of a CRM procedure for a speciality distributed in parallel. In many of these procedures, the CRM proposed entering into negotiations in accordance with article 112 of the Royal Decree, but to date this has never resulted in an agreement being concluded.

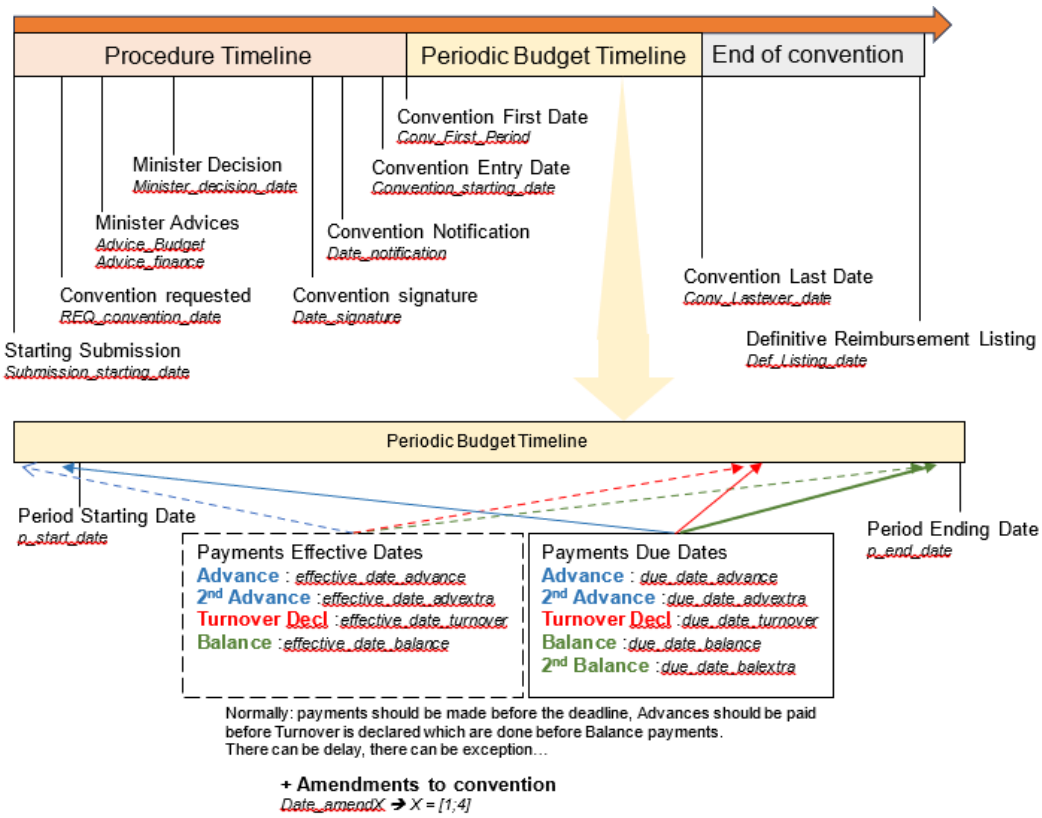

Figure 71: Schematic diagram of the key dates in an Article 81/111 procedure

II. Evolution of conventions processed between 2015 and 2024

1. Volume and outcome of requests for negotiation procedures

Over the period 2015-2024, the Minister of Social Affairs received 607 requests to start a procedure in order to conclude an article 81/111 convention. Figure 72 and Table 37 show the status of requests received between 2015 and 2024. Since 2022, there has been an increase in the number and percentage of files resulting in a convention (n2022=54 (78%); n2023=58 (73%); n2024= 56 (77%)), in contrast to 2021 (n=51 (52%)). By way of comparison, the averages for successful and unsuccessful conventions for all years combined over the period are 72% and 28% respectively. As such, the number of files resulting in an agreement has reverted to the mean.

The large number of requests in 2021 was undoubtedly the result of a dual phenomenon: a) the resumption of activities suspended or limited during the COVID-19 pandemic; and b) the steady rise in the number of molecules going through an article 81/111 procedure, visible since the introduction of the convention system. Nevertheless, these figures should be treated with caution, as some of the requests for an agreement lead directly to definitive registration on the list (see "Reasons why the procedure does not result in a convention" p.88). The list of pharmaceutical specialties currently under convention is presented in Appendix 3.

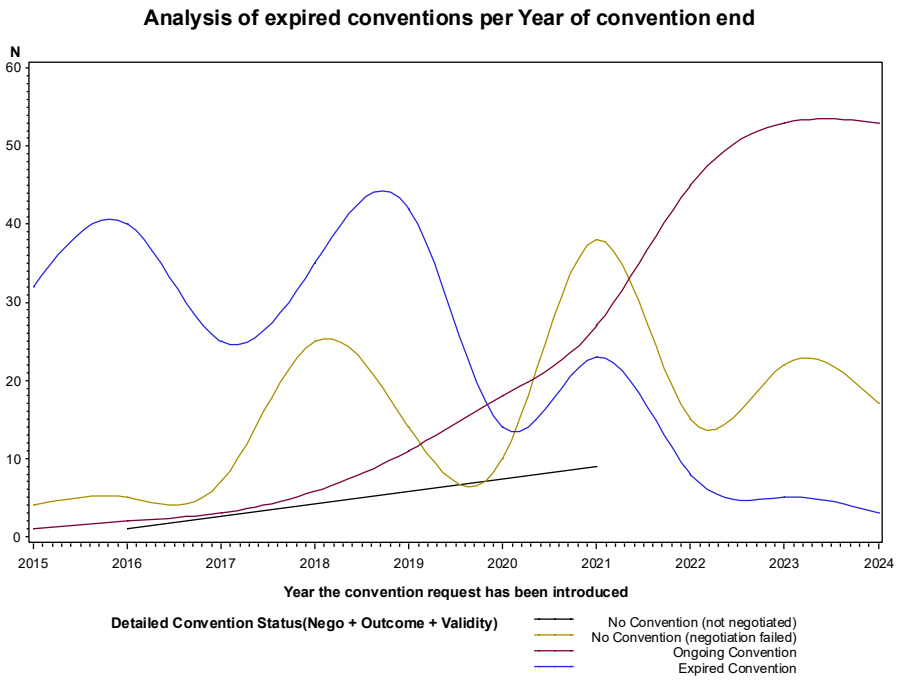

Figure 72: evolution in the number of requests to conclude an article 81/111 convention, by year in which the request was made

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Total
No Convention (not negotiated)	.	1	.	.	.	.	9	.	.	.	10
No Convention (negotiation failed)	4	5	7	25	14	10	38	15	22	17	157
Ongoing Convention	1	2	3	.	11	18	28	45	54	53	215
Expired Convention14	32	40	25	35	42	14	22	8	4	3	225
Subtotal No convention	4	6	7	25	14	10	47	15	22	17	167
Subtotal Convention	33	42	28	35	53	32	50	53	58	56	440
Total	37	48	35	60	67	42	97	68	80	73	607
% Convention (f)	89%	88%	80%	58%	79%	76%	52%	78%	73%	77%	72%

Table 37: evolution in the number of requests to conclude an article 81/111 convention, by year in which the request was made

The 10-year statistics presented in Figure 73 and Table 38 show that around half (two-thirds if only concluded conventions are counted) of all conventions are for new molecules ("new conventions"). Over the period 2018-2022, there was a stabilisation in that around one-third of conventions and amendments signed relate to a molecule that was not previously reimbursed under a convention. Moreover, since 2019 (with the exception of 2020), amendments have accounted for an increasingly large share of conventions. Since 2022, there has been a rebound in conventions for new molecules.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Total
No Convention	4	6	7	25	14	10	47	15	22	17	167
Amendment - additional package size	2	3	4	4	4	1	2	6	1	4	31
amendment - change reimbursement criteria	.	.	.	.	.	.	.	1	1	.	2
amendment - indication after New procedure	.	.	.	.	.	.	.	.	1	5	6
Amendment - new indication	2	9	7	5	12	3	15	13	20	8	94
Subtotal Amendments	4	12	11	9	16	4	17	20	23	17	133
New Convention	21	25	13	10	15	14	17	16	30	32	193
New convention - after new CRM procedure	4	3	4	12	17	13	14	12	2	6	87
New convention - new indication	4	2	.	4	5	1	2	5	3	.	26
Subtotal New Conventions	29	30	17	26	37	28	33	33	35	38	306
Total	37	48	35	60	67	42	97	68	80	72	606

Table 38: Number of requests to conclude an article 81/111 convention, by year in which the request was made - details depending on the outcome of the conventions signed.

If a new MCR assessment has been carried out after a convention, and this new assessment results in a new convention, it will be included in the statistics as a "new convention after new CRM procedure". In a number of cases, it is possible during this new CRM assessment that new, additional indications are evaluated and included in the new convention. It is also possible that changes in reimbursement conditions will be made to indications already temporarily

[14] Number of conventions per year of request for reimbursement submitted that are no longer in force at the time of writing. Table breakdown: of the 48 requests for conventions submitted for reimbursement in 2016, 42 resulted in a convention, of which 38 are no longer active at the time of writing and 4 are still active.

reimbursed, as a result of the new CRM procedure. All these specific cases can be found under the label "new convention after new CRM procedure". Since 2023, new forms of amendments have appeared.

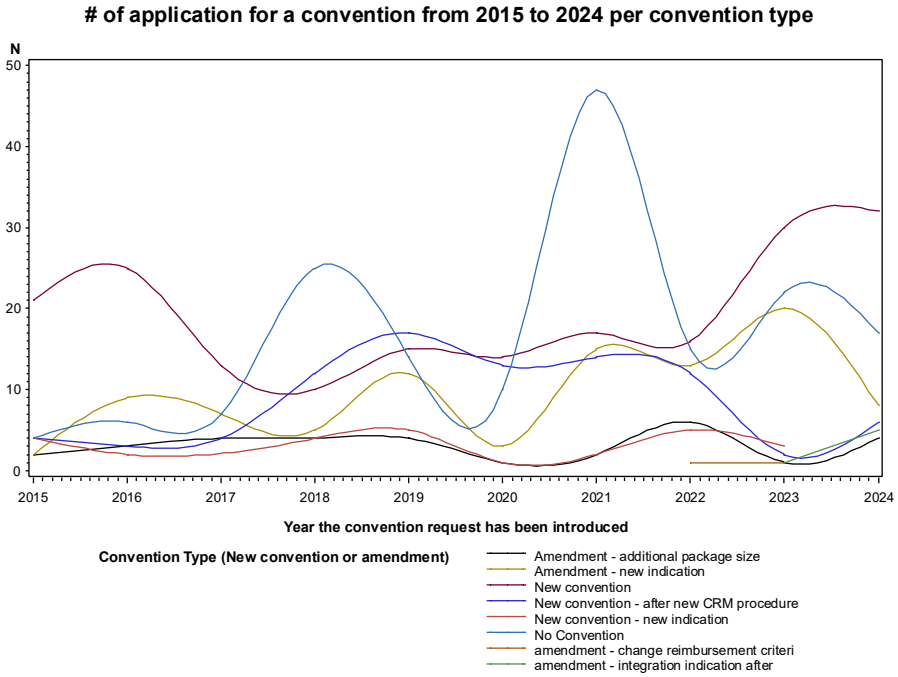

Figure 73: Number of requests to conclude an article 81/111 convention, by year in which the request was made - details depending on the outcome of the conventions signed

2. Time frames for reimbursement procedures and duration of conventions

The duration of a reimbursement procedure is specified in the Royal Decree of 01.02.2018. It is a maximum of 180 days. However, the reimbursement procedure (and therefore the 180-day deadline) may be suspended in the event of missing information when the request is submitted, or if there is no pricing. Furthermore, during the reimbursement procedure, the applicant can request a suspension of up to 90 days twice, and a suspension of up to 120 days once, which can be devoted to the negotiation procedure to conclude a convention. In the following analysis, any periods of suspension are included in the number of days in question.

It should be noted that during the COVID-19 crisis in 2020-2021, the planning for CRM procedures was temporarily halted (deadlines suspended from 13 March 2020 to 31 March 2021 inclusive). As a result, for this period the total duration of the suspension(s) in practice is often longer than the maximum suspension periods provided for in the Royal Decree of 01.02.2018. This is also evident from the figures for 2019 and 2020 (the year in which the request file was submitted to the CRM).

a. Total duration of the procedure

The various results relating to the average time in days to conclude a convention after the date of submitting the request for reimbursement are presented in Table 39. The average number of days between submitting a request for reimbursement and the actual start of the reimbursement for the period 2015-2024 is 345 days.

Procedure Starting Year	Average Time in Days	Minimum Time in Days	Max Time in Days
2015	330.28	220.00	467.00
2016	314.56	177.00	581.00
2017	312.68	186.00	443.00
2018	325.74	135.00	468.00
2019	387.15	187.00	688.00
2020	436.72	259.00	649.00
2021	335.52	196.00	465.00
2022	366.81	190.00	559.00
2023	314.59	83.00	484.00
2024	317.16	123.00	491.00
2015-2024	345.69	83.00	688.00

Table 39: Evolution of time between submitting the reimbursement file and actual reimbursement, by year in which the CRM procedure was initiated.

For 73% of the conventions signed, it took less than a year to obtain reimbursement via a convention. The shortest interval between submitting a request for reimbursement and the actual date of reimbursement was 83 days. The longest interval between submitting a request for reimbursement and the actual date of reimbursement was 688 days; this is due to the suspensions during the procedure and the pausing of the timetable during the COVID-19 crisis.

The average time needed to conclude a convention rose sharply after 2019. This is clearly a consequence of the COVID-19 crisis and the temporary timetable pauses in effect during this period. Although the figures for 2021 and 2022 tend to show a rise in processing times for cases, the average time over the period fell slightly. After 2023, average processing times seem to have recovered to pre-Covid durations.

b. Suspension periods during negotiations

As described above, according to the regulations, the discussions can take a maximum of 120 days to conclude a possible 81/111 convention. Due to the fact that during the COVID-19 crisis in 2020-2021, the timetable for CRM procedures was temporarily suspended, it was provisionally possible that the suspension in the context of an article 81/111 discussion lasted more than 120 days. This can also be seen in the figures for 2019-2020. According to the regulations, at least 10 of these days are devoted to evaluation by the Minister for the Budget.

Procedure Starting Year	Average Time in Days	Min Time in Days	Max Time in Days
2015	108.91	77.00	124.00
2016	103.38	36.00	119.00
2017	94.32	30.00	119.00
2018	92.86	11.00	119.00
2019	108.62	48.00	119.00
2020	156.16	41.00	378.00
2021	106.12	19.00	194.00
2022	108.55	50.00	121.00
2023	101.12	17.00	119.00
2024	97.87	20.00	119.00
2015-2024	107.82	11.00	378.00

Table 40: evolution in the time between submitting the request for an Article 81/111 convention and the signing of the convention by year in which the request was submitted.

With regard to Table 40, discussions lasted an average of 108 days (taking into account the COVID-19 situation) over the period 2015-2024. The smallest and longest negotiation windows observed range from 11 to 378 days.

3. Outcome when convention is ended

Figure 74 and Table 41show the distribution of the outcome of conventions when they end.

- For 12 of the 223 conventions that were due to end in the period 2015-2024, a new CRM procedure was not initiated (5.38%).
- For 74 of the conventions that ended (33.18%), a new CRM procedure was launched, and the speciality/indication was definitively included in the list of reimbursable pharmaceutical specialties.
- For 129 of the conventions that ended (57.85%), a new CRM procedure was launched and the speciality/indication was temporarily re-added to the list of reimbursable pharmaceutical specialties via a new convention.

- In 8 of the expired conventions (3.59%), a new CRM procedure was started, but the reimbursability (definitively or temporarily) was lost. As a result, the specialty/indication was no longer reimbursable.

Outcome when convention is ended	Frequency	Percent	Cumulative Frequency	Cumulative Percent
definitive listing after new CRM procedure	74	33.18	74	33.18
new convention after new CRM procedure	129	57.85	203	91.03
no reimbursement - no new CRM procedure	12	5.38	215	96.41
no reimbursement after new CRM procedure	8	3.59	223	100.00

Table 41: Overview of conventions that ended.

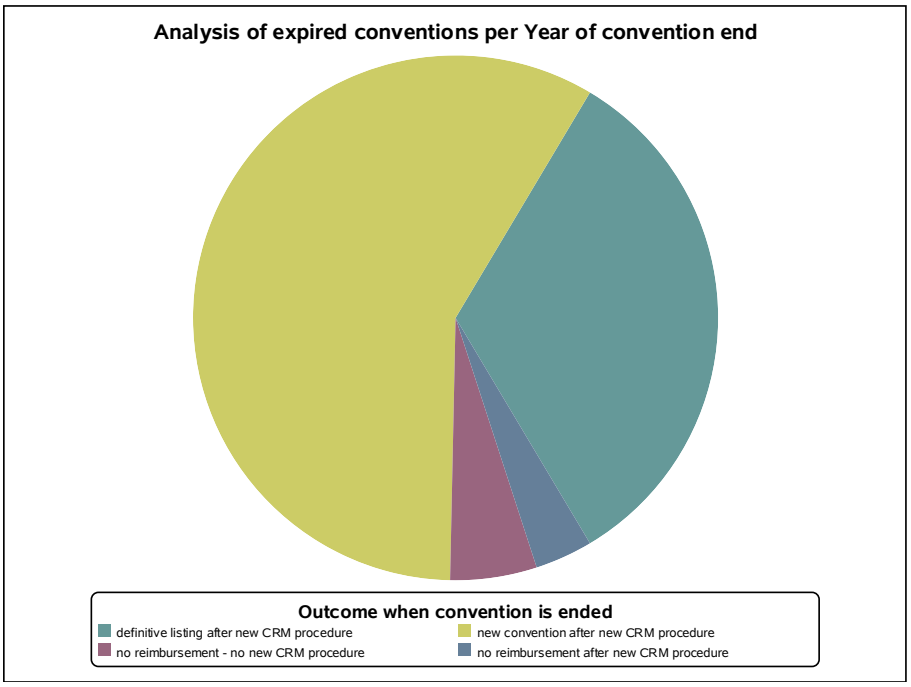

Figure 74: Overview of conventions that ended.

Figure 75 and Table 42 show the same statistics but by year over the period 2015-2024. From these data, it is possible to observe a certain stability in the proportions of the different outcomes over time. The closer the years get to 2024, the fewer the number of conventions coming to an end.

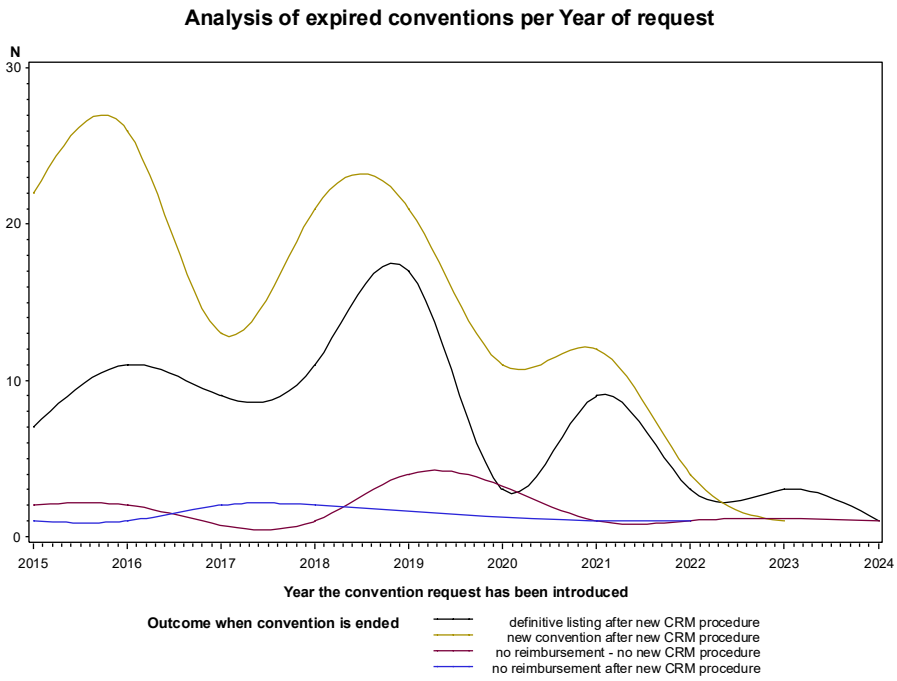

Figure 75: Evolution of the outcome of conventions by year of the request being submitted.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Total
definitive listing after new CRM procedure	7	11	9	11	17	3	9	3	3	1	74
new convention after new CRM procedure	22	26	13	21	21	11	11	4	.	.	129
no reimbursement - no new CRM procedure	2	2	.	1	4	.	1	1	.	1	12
no reimbursement after new CRM procedure	1	1	2	2	.	.	1	1	.	.	8
Total	32	40	24	35	42	14	22	9	3	2	223

Table 42: Evolution of the outcome of conventions by year of the request being submitted.

4. Volume of conventions by main anatomical class

Figure 76 and Table 43 show the number of annual requests made to the CRM to establish an ART. 81/111 convention, by ATC class. The 'antineoplastics and immunomodulating agents' anatomical group accounts for the majority of requests, with around 60% of total requests over the period 2015-2024. After these are pharmaceutical specialties for alimentary tract, metabolism and blood products, with 9% and 7% of total requests respectively.

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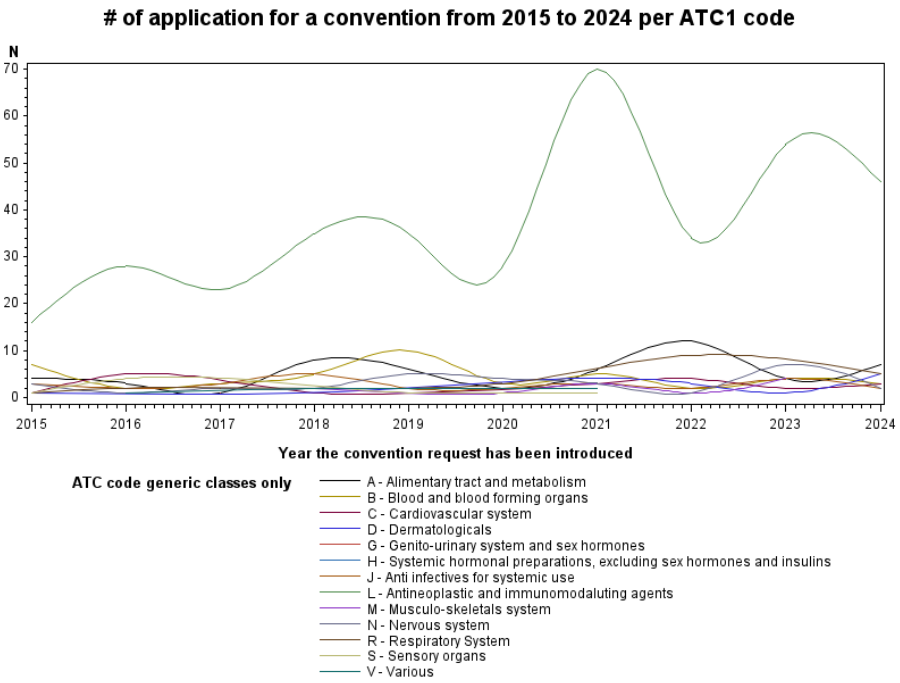

Figure 76: Number of requests for a convention by main anatomical class.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Total
A - Alimentary tract and metabolism	4	3	1	8	6	2	6	12	4	7	53
B - Blood and blood forming organs	7	2	3	5	10	3	5	2	4	3	44
C - Cardiovascular system	1	5	.	1	1	.	3	4	2	3	20
D - Dermatologicals	1	.	.	.	2	.	.	3	1	5	12
G - Genito-urinary system and sex hormones	.	.	1	.	.	.	.	.	.	.	1
H - Systemic hormonal preparations, excluding sex hormones and insulins	.	.	.	.	.	.	1	.	.	.	1
J - Anti infectives for systemic use	3	2	3	5	2	.	3	2	4	2	26
L - Antineoplastic and immunomodaluting agents	16	28	23	35	35	28	70	34	54	46	369
M - Musculo-skeletal system	.	.	.	2	1	1	3	1	4	.	12
N - Nervous system	3	1	2	2	5	4	3	1	7	2	30
R - Respiratory System	1	2	2	.	2	3	.	9	.	5	24
S - Sensory organs	1	4	.	.	1	1	1	.	.	.	8
V - Various	.	1	.	2	2	.	2	.	.	.	7
Total	37	48	35	60	67	42	97	68	80	73	607

Table 43: Number of requests for a convention by main anatomical class.

Figure 77 and Table 44 break down all requests made by major anatomical group according to the status of the convention (refused or unsuccessful negotiations, current convention, expired convention) over the period 2013-2023. The same L class of antineoplastics and immunomodulating agents accounts for around 60% of successful conventions. After these are Class A and B pharmaceutical specialties, with around 9% and 7% of requests concluded during the same period. It should be noted that several conventions have been signed for certain pharmaceutical specialties.

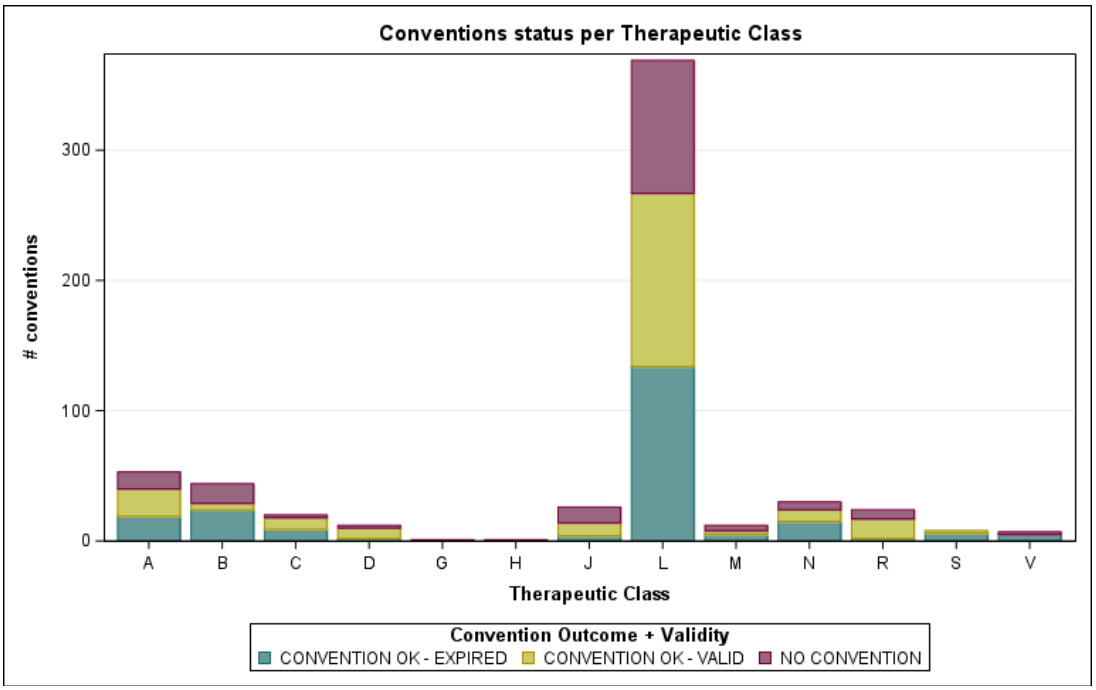

Figure 77: Outcomes of Art. 81/111 discussions by main anatomical class

	A	B	C	D	G	H	J	L	M	N	R	S	V	Total
Convention OK - Expired	19	24	9	2	0	0	4	133	3	15	2	6	5	222
%	3.13	3.95	1.48	0.33	0.00	0.00	0.66	21.91	0.49	2.47	0.33	0.99	0.82	36.57
Convention OK - Valid	21	5	9	8	0	0	10	134	5	9	15	2	0	218
%	3.46	0.82	1.48	1.32	0.00	0.00	1.65	22.08	0.82	1.48	2.47	0.33	0.00	35.91
No Convention	13	15	2	2	1	1	12	102	4	6	7	0	2	167
%	2.14	2.47	0.33	0.33	0.16	0.16	1.98	16.8	0.66	0.99	1.15	0.00	0.33	27.51
Total	53	44	20	12	1	1	26	369	12	30	24	8	7	607
%	8.73	7.25	3.29	1.98	0.16	0.16	4.28	60.79	1.98	4.94	3.95	1.32	1.15	100.00

Table 44: Outcomes of Art. 81/111 discussions by main anatomical class

5. Number of molecules under convention

Figure 78 shows the number of molecules under convention by ATC class over the period 2015-2024, for a total of 186 different molecules. In line with previous results, the vast majority of molecules under convention are in therapeutic class L (n=100, 53.76%), followed by ATC classes A, A (n=21, 11.29%) and N (n=15, 8.06%).

Figure 79 shows the number of different molecules under convention, by year of the request being submitted. A gradual increase in the number of specialties under convention has been observable for many years. Since 2019, with the notable exception of 2020 and all the consequences of the slowdown in activities caused by the COVID crisis, around 40 specialties were accepted for reimbursement per year. However, 2024 showed a slight increase compared to 2019-2023.

Not all molecules reimbursed under a convention are included in the list of reimbursable specialties for the first time. As already explained, several conventions may be signed for each molecule, and/or amendments may be made to include other indications or packaging in the initial convention for the speciality. In all, nearly 186 new molecules were accepted for reimbursement over the period 2015-2024. Of course, the number of new molecules was higher at the start of the contracts (see Figure 80). The number of new molecules therefore increased up until 2016, before suddenly decreasing in 2017. Since 2017, the number of new molecules appears to be stable, at around 15 per year.

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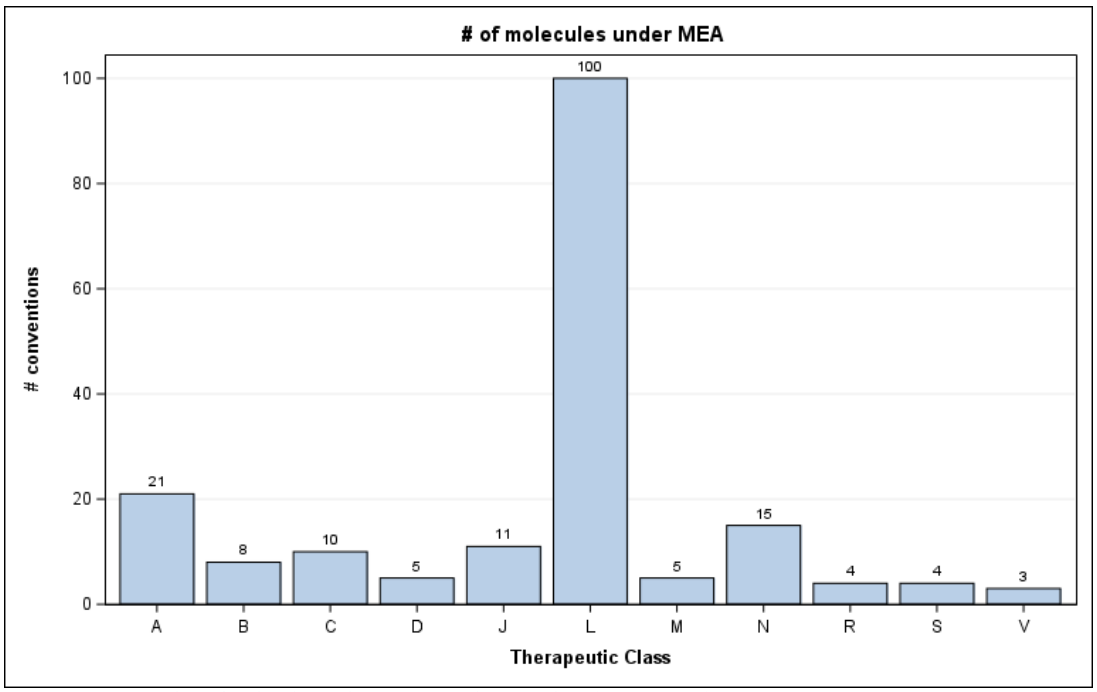

Figure 78: Number of molecules under convention by ATC class (2015 – 2024)

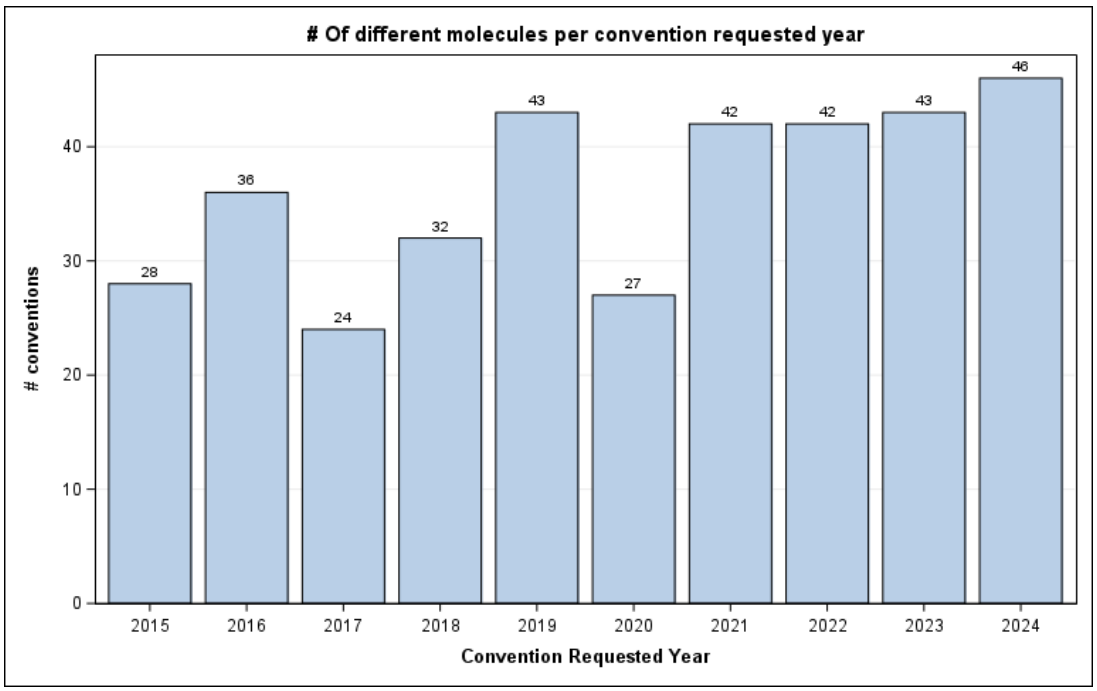

Figure 79: Number of different molecules under convention, by year in which the convention was submitted.

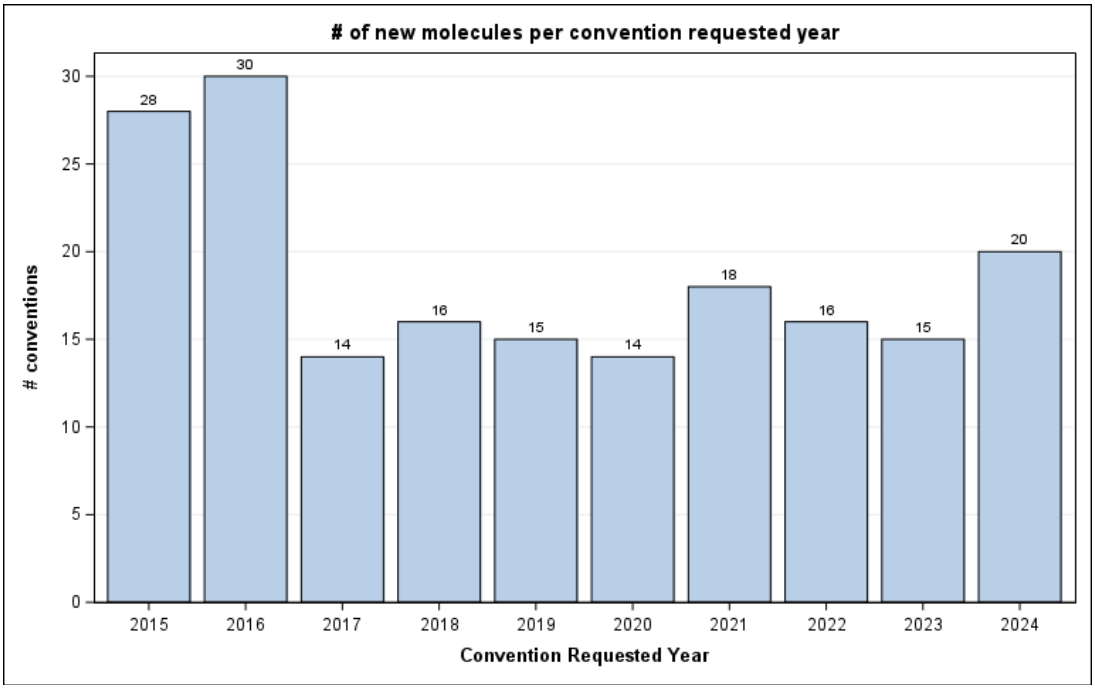

Figure 80: Number of new molecules accepted for reimbursement, by year in which the convention was submitted.

6. Status of conventions according to CRM opinion

Until 1 July 2014, it was possible for a company to introduce a request for negotiation after a negative opinion from the CRM. Since 1 February 2018, this has again been possible, but only at the explicit request of the Minister of Social Affairs, for the company to submit a request to start negotiations following a negative opinion from the CRM.

In 10 of the 22 files (45%) where the CRM issued a negative opinion, a convention was finally concluded. In 55% of cases, the negotiations had started but did not result in a convention.

A convention was concluded in 369 of the 471 cases (78%) following a negotiation proposal by the CRM, and in 57 of the 106 cases (54%) in the absence of an opinion from the CRM. Almost 21% of the conventions that received a positive opinion from the CRM were unable to reach an agreement after negotiations started.

	NO negotiation - NO convention	Negotiation - NO convention	Negotiation - convention	Total Col %
Positive opinion	5	97	369	471
Line %	1.06	20.59	78.34	78.63
Negative opinion	0	12	10	22
Line %	0	54.55	45.45	3.37
No proposal	5	44	57	106
Line %	4.72	41.51	53.77	17.70
Total	10	153	436	599
Line %	1.67	25.54	72.79	100.00

Table 45: Outcomes of article 81/111 discussions according to CRM opinion

In a limited number of cases (n=5), the CRM proposed a negotiation procedure, the company submitted a request to the Minister of Social Affairs, and the medicine was definitively listed - usually after consultation with the working group and in return for a price reduction. This situation is illustrated in Figure 81 and Table 45 under the modality "Negotiation - NO convention". On one occasion, before consultation with the working group, the Minister decided to list the medicine definitively with a reduction in the face value price (in previous MORSE reports, it was incorrectly stated that no request for an article 81/111 procedure had been submitted for this file).

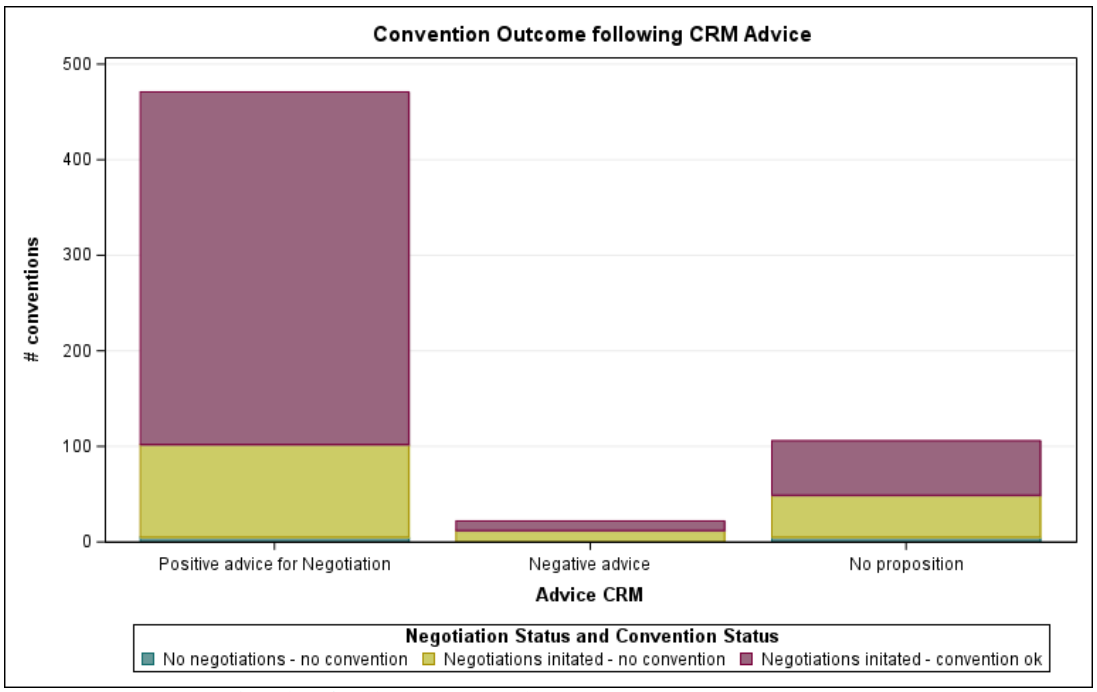

Figure 81: Outcomes of article 81/111 discussions according to CRM opinion

7. Status of conventions by type of request for reimbursement submitted

Table 46 and Figure 82 show the number of negotiations which did or did not lead to a convention, broken down by category of request for reimbursement.

	No convention	Signed Convention	Total
Class 1 Line %	45 20.27	177 79.73	222
Class 2 Line %	8 12.70	55 87.30	63
Class 3 Line %	2 100.00	0 0.00	2
Orphan Line %	29 22.31	101 77.69	130
Parallel Distribution Line %	51 100.00	0 0.00	51
Modification Line %	18 14.75	104 85.25	122
Total	153	437	590

Table 46: Outcomes of article 81/111 discussions according to the type of request for reimbursement submitted by the pharmaceutical company.

In 80% of cases (177/222), where the pharmaceutical company claimed added therapeutic value (Class 1), temporary reimbursement was put in place via a convention. A convention was concluded for 78% (101/130) of requests relating to orphan drugs. If the company does not claim any added value (classes 2 and 3), in 85% (55/65) of requests for article 81/111 procedures, the product is temporarily registered. In these cases, the reference specialty is also "under contract", which probably increases the chances of concluding a convention. If a change in the reimbursement terms is requested, it results in a temporary reimbursement in 85% (104/122) of requests for an article 81/111 procedure: either a new convention has been agreed, or this has led to an amendment to the existing convention. No convention was concluded in the context of parallel distributions.

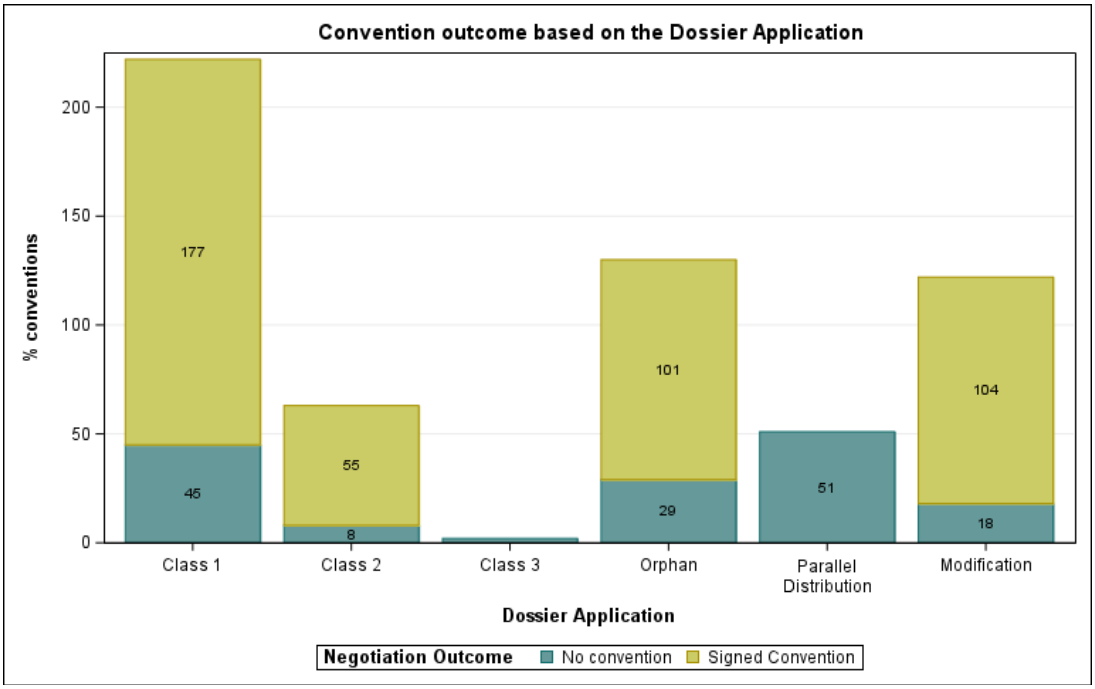

Figure 82: Outcomes of article 81/111 discussions according to the type of request for reimbursement submitted by the pharmaceutical company.

8. Reasons why the procedure does not result in a convention

Despite the fact that the pharmaceutical company has submitted a request for negotiation to the Minister of Social Affairs, the procedure does not always result in a convention. Figure 83 and Table 47 show the percentages of reasons that led to a convention not being signed at the end of the procedure.

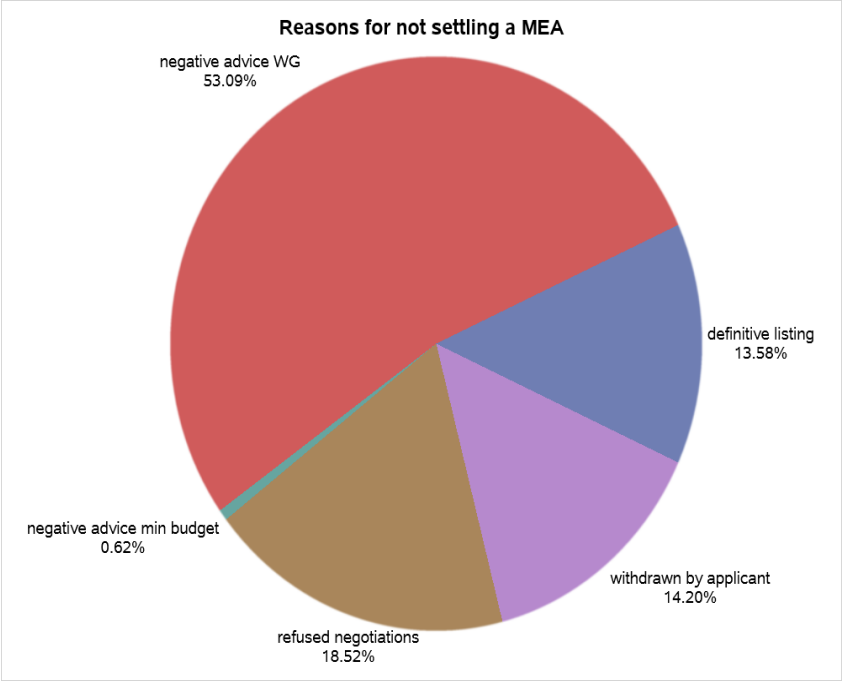

Figure 83: Overview of reasons why a convention was not concluded

In 13.5% of cases, the speciality is permanently registered on the list of reimbursable pharmaceutical specialties, without convention. This is often accompanied by a direct reduction in the face value price.

In 18.5% of cases, the Minister of Social Affairs does not consider it appropriate to enter into negotiations. This may be the case when the available clinical data are too immature to consider temporary reimbursement. It is also possible that the applicant has submitted a request to start negotiations that was invalid (the request was submitted outside the time limit stipulated by the Royal Decree of 01.02.2018; the request did not contain the information stipulated in articles 111, 112 or 113 of the Royal Decree of 01.02.2018; etc.).

In 53% of cases, the working group conducting the negotiations concludes that no agreement has been reached, and the Minister is informed accordingly.

In 23% of cases, the pharmaceutical company terminated the reimbursement procedure.

The Minister for the Budget made a negative decision regarding one case.

Reason no convention	Frequency	Percent
definitive listing	22	13.58
Negative opinion WG	86	53.09
negative opinion Minister for budget	1	0.62
refused negotiations	30	18.52
withdrawn by applicant	23	14.20
Total	162	100.00

Table 47: Overview of reasons why a convention was not concluded.

9. Mobilised budget compensation mechanisms

Figure 84 and Table 48 show the various budget mechanisms mobilised in the context of the conventions concluded. In 90% of cases, a single budget compensation mechanism was used.

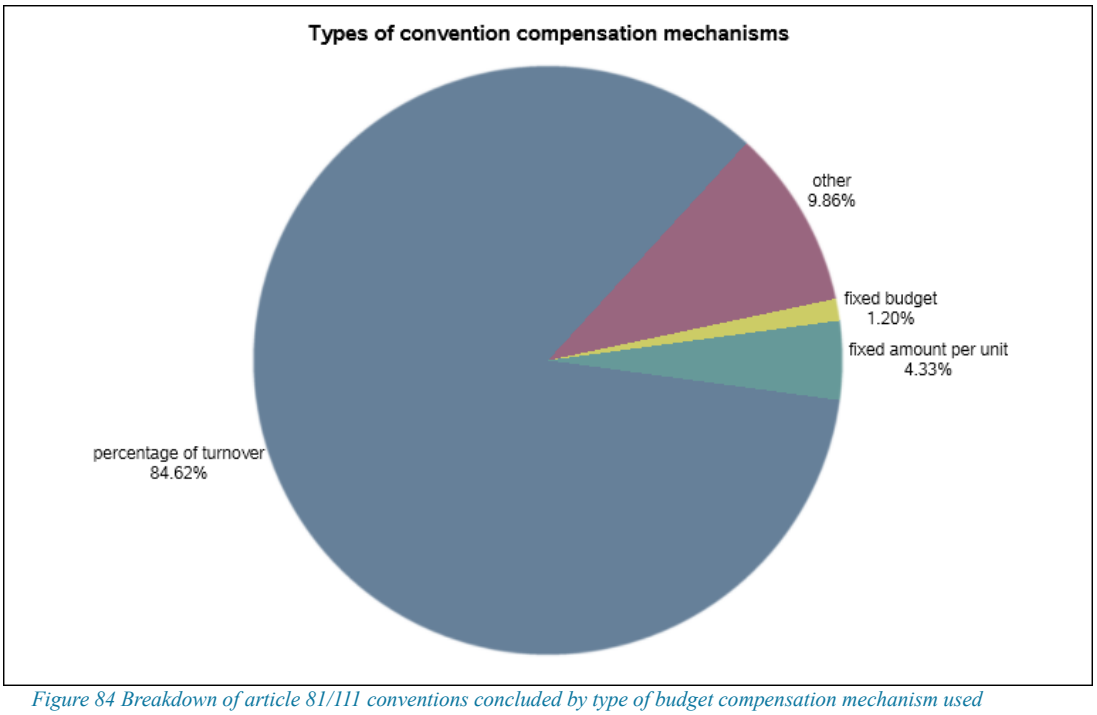

Figure 84 Breakdown of article 81/111 conventions concluded by type of budget compensation mechanism used

Most of them (84%) opted to pay back a portion of their generated turnovers. This compensation mechanism can be made up of a fixed percentage of turnover generated, or an increasing percentage based on pre-established turnover brackets. As mentioned above, when calculating this refund percentage, the percentage of therapy failure (non-responders) must be taken into account in particular, as observed in clinical studies, a situation where it may then be a question of an "outcomes-based" compensation mechanism at population level, insufficient evidence of efficacy or inadequate package sizes that may possibly lead to waste.

Type of compensation mechanism	Frequency	Percent
fixed amount per unit	18	4.33
fixed budget	5	1.20
other	41	9.86
percentage of turnover	352	84.62

Table 48 Breakdown of article 81/111 conventions concluded by type of budget compensation mechanism used

In 4% of the conventions signed, the applicant is required to pay a fixed amount per unit sold.

In around 1% of cases, an amount must be refunded, corresponding to all or a fraction of the difference between forecast and actual expenditure for the specialty in question is paid. This may involve, for example, reimbursement of a fixed amount established in advance, irrespective of turnover generated, or full reimbursement of the portion of turnovers achieved in excess of the presupposed turnover figure.

For the remaining 10% of conventions concluded, two or more compensation mechanisms were combined. Applying two or more compensation mechanisms in a single convention is complex and logistically more difficult to monitor than if only one mechanism is applied. One possible advantage of combining compensation mechanisms - and more specifically combining them with a reduction in the price of a product in the portfolio - seems to be that it is possible to achieve higher total compensation, given that the financial pressure for a company is not exerted on just one product in its portfolio. However, this system leads to even more uncertainty, since it is based on the principle of forecasting, not only with regard to the pharmaceutical speciality that is temporarily reimbursed, but also with regard to the product in the portfolio. Sometimes, more 'alternative' compensation mechanisms are also incorporated into conventions, such as financial compensation with a view to optimise data exchange via Sciensano, or compensation on medicines that are not part of the applicant's portfolio but have a (therapeutic) link with the medicine to which the convention applies. To ensure more budget security, it is possible - usually in combination with other compensation mechanisms - to introduce a cap above which a significant percentage of the amount must be refunded. This cap is based on a percentage of forecast turnover and varies from convention to convention, but is often set at less than 100% of forecast turnover.

III. Evolution in amounts of compensation for conventions over the period 2015-2024

1. Methodological note on how compensation is processed

The evolution of expenditure for medicines reimbursed under article 81 conventions (Royal Decree 21.12.2001) and article 111 conventions (new Royal Decree 1.2.2018) are described by calendar year in the tables and figures in this section. As these data are mainly relevant for accounting purposes, the situation is also presented cumulatively since the introduction of confidential conventions in Belgium, and by ATC class (as long as a minimum of 5 different molecules are involved) - see reform 31 of the roadmap (NIHDI, 2023b).

The following elements must be borne in mind when interpreting these figures:

- As already mentioned (see p. 73), there is no separate budget for pharmaceutical specialties reimbursed via a convention. Conventions are one of the instruments used in medicines policy to ensure better control over budgets.
- Amounts are summed up by actual "years of service". The conventions are broken down by year, with compensation provided by the pharmaceutical company on the basis of the provisions of the conventions. To this end, the pharmaceutical company must declare gross turnover (before deducting budget compensation) for a given period to which the convention relates. The conventions run from date to date, meaning that the period to which the convention relates may last one, two or three calendar years, and the time of settlement does not necessarily correspond to the same calendar year as the period to which the settlement relates. In the context of these conventions, (gross) expenditure is actually incurred in year T, but the repayments are only made in full or in part in year T+1, or even later in certain specific cases (e.g. when a P4P mechanism is involved), at the time of the declaration made by the company. In the tables below, a proportional recalculation has been made to bring these turnovers and compensation mechanisms back to the actual years in which the turnovers and compensation were generated.

- For compensation mechanisms, only direct financial compensation mechanisms are taken into account. Indirect compensation, such as price reductions for other specialties, is not taken into account (the amounts paid are therefore underestimates of the total compensation).
- For turnovers, in some cases the total turnovers for the specialty are taken into account, and therefore also the turnovers for this specialty for indications that are 'not under contract'. It is therefore not possible, on the basis of these data, to calculate a separate budget for drugs reimbursed under a convention.

Since October 2016, when new conventions are concluded or amendments drawn up, it has been standard practice to estimate as accurately and reliably as possible the amount of compensation to be paid by the company to the NIHDI in year T (in which the expenditure was actually made). According to the mechanism provided for in the convention, a system of advance payments has been set up to relieve the financial burden on the disability insurance system. At the end of the financial year, the difference between the total amount of compensation and the advance already paid is the balance to be paid by either the company or the NIHDI. Among other things, this system is intended to generate a more reliable picture of actual net expenditure per calendar year. A methodological note explaining how the compensation is calculated is available in Appendix 3.

- For both turnovers and repayments, the starting point is known data, namely turnovers declared by companies, advances paid, provisional and final settlements for conventions concluded. If the data are not available, estimates are used as a basis for negotiating the contract, in order to establish the compensation mechanism.
- For practical reasons, all amounts shown are ex-works prices. The figures therefore do not reflect total expenditure on health insurance, as they do not include expenditure on margins, fees or VAT. To obtain a complete picture of health insurance expenditure, we need to add margins, fees and VAT. Most molecules reimbursed under a convention are medicines that are only reimbursed when dispensed in hospital pharmacies, and for which margins are capped, given the often high face value prices. For medicines reimbursed in public pharmacies, margins can be high, particularly for high-volume medicines. When calculating the compensation needed to achieve an acceptable cost for the health insurance system, since 2024, the difference in margins, fees and VAT linked to the difference between the face value price and the acceptable cost reimbursed under the convention has been structurally taken into account.
- The data relate to the situation on 06.10.2025, source: Pharmaceutical Policy Department (database for monitoring the article 81/111 convention process).

NOTE ON THE BUDGET FOR MEDICINES

The budget for medicines for year t + 1 is set every year in October t and is based on technical estimates, with consultations in May t and September t of each year between the NIHDI and the pharmaceutical industry. The estimates from the NIHDI are compared with those of the pharmaceutical industry.

Given the fact that budgets and accounting are organised on a yearly basis, it is not possible to correctly adjust expenditure and income under Article 81 conventions, for which expenditure t or t-1 (gross) has been incurred, but for which reimbursements will only be made in full or in part in year t + 1 or later. Contracts run from date to date, and as a result the period to which the reimbursement relates may extend over two (or more) calendar years, and the actual time of the payment does not necessarily fall within the same calendar year as the period to which the payment relates.

To take this into account, provisions have been introduced into financial compensation mechanisms, where possible, in contracts which provide for full or partial payment of the compensation due in the same calendar year as the expenditure (in other words, a system of "advances"). These amounts are collected and entered in the current year, thereby making it possible to estimate "net" expenditure amounts: as a result, it is possible to correctly assess the actual budget cost of medicines for the health insurance system. In practice, these are standardised provisions for collecting financial compensation, in which a financial provision is made for the compensation mechanism.

This is based on virtual annual turnover, extrapolated on the basis of the available information, to ensure that the provision is as close as possible to expected reality.

2. Overall analysis of compensation

Table 49 shows the annual evolution in turnover generated by companies (in millions of euros) of their pharmaceutical specialties under convention, and the associated compensation paid to the NIHDI. Increases can be seen at all levels: declared turnover (T), advance amounts[15] (a), balances (b) - the settlement on the advance already paid - and consequently total compensation (R), as well as the percentage of the refund.

Figures for years marked with an asterisk * should be interpreted with caution, as not all turnover has been reported or is currently known; uncertain figures are also in brackets. This implies that the compensation share of companies is probably overestimated at present, until the turnover figures have been received. In this respect, although the compensation share can be calculated, it will not be included in the report because it is biased.

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Turnover (T)	466.08	652.61	1071.17	1314.40	1539.68	1887.75	2085.71	2488.19	2894.23	[2877.23]
Balance (b)	56.63	121.32	172.65	162.07	218.10	213.50	310.51	587.53	801.45	[499.02]
Advance (a)	.	.	100.49	195.50	387.04	540.46	707.65	675.39	754.12	[1340.58]
Refund (R: a+b)	56.63	121.32	273.14	357.57	605.14	753.96	1018.16	1262.92	1555.57	[1839.60]
Net (N: T - R)	409.45	531.29	798.02	956.82	934.55	1133.79	1067.56	1225.27	1338.66	[1037.63]
Compensation	12.2%	18.6%	25.5%	27.2%	39.3%	39.9%	48.8%	50.8%	53.7%	[63.9%]
# Conventions	59	86	98	118	123	127	142	156	163	189
# Molecules	57	72	86	96	100	98	118	127	135	149

Table 49: Overview of turnovers, compensation and net turnover by calendar year (ex-works price level, in millions of euros)

The increase in the various budget figures goes hand in hand with an increase in the number of molecules and, consequently, in the number of conventions. While 57 molecules in the same amount of conventions were in force in 2015, almost 149 molecules for 189 conventions were in force in 2024. In no successive year has the number of conventions been lower than in the previous year, highlighting the ever-increasing use of the convention system. However, it is possible to observe an increase in the cost of these conventions, irrespective of how many there are. As such, the NET cost borne by the NIHDI rose from €6.9M per convention in 2015 to €8.2M in 2023, as shown in Figure 85.

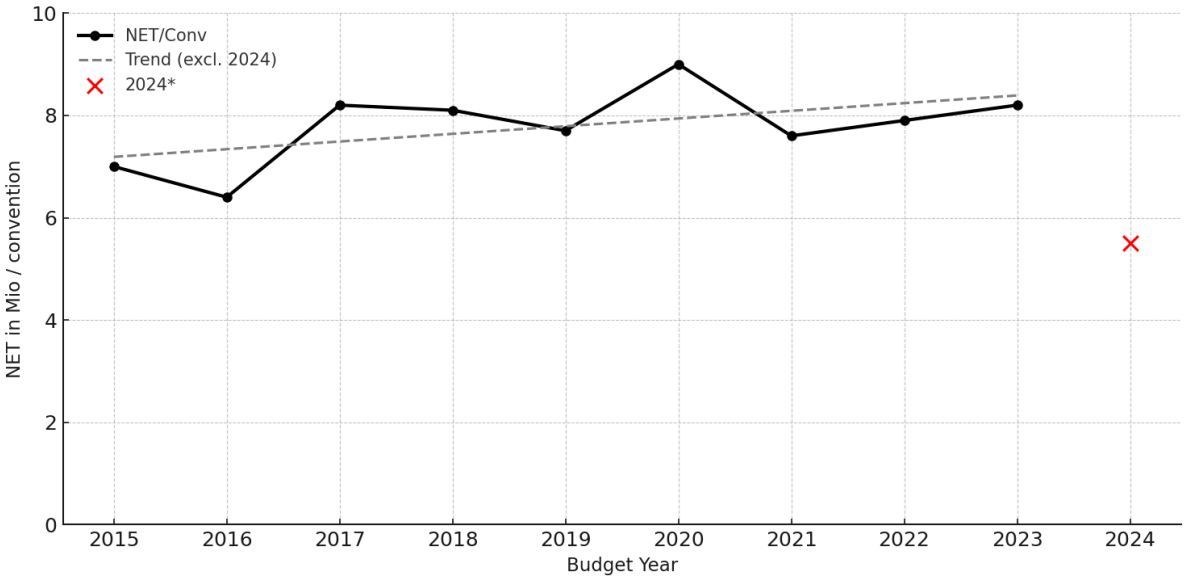

Figure 85: Net cost borne by the NIHDI per convention, by accounting year in millions of euros.

Figure 86 and Table 50 present the same information, but in millions of euros. Over the period 2015-2024, the companies generated turnover of €17.3 billion on pharmaceutical specialties under convention, and would have paid back around €7.8 billion to the CRM, i.e. 45.4%. As these figures have yet to be fully validated, it is likely that the actual cumulative reimbursement percentage will be between 41.7 and 45.4%, continuing the linear upward trend observable since 2018.

[15] system introduced in 2016

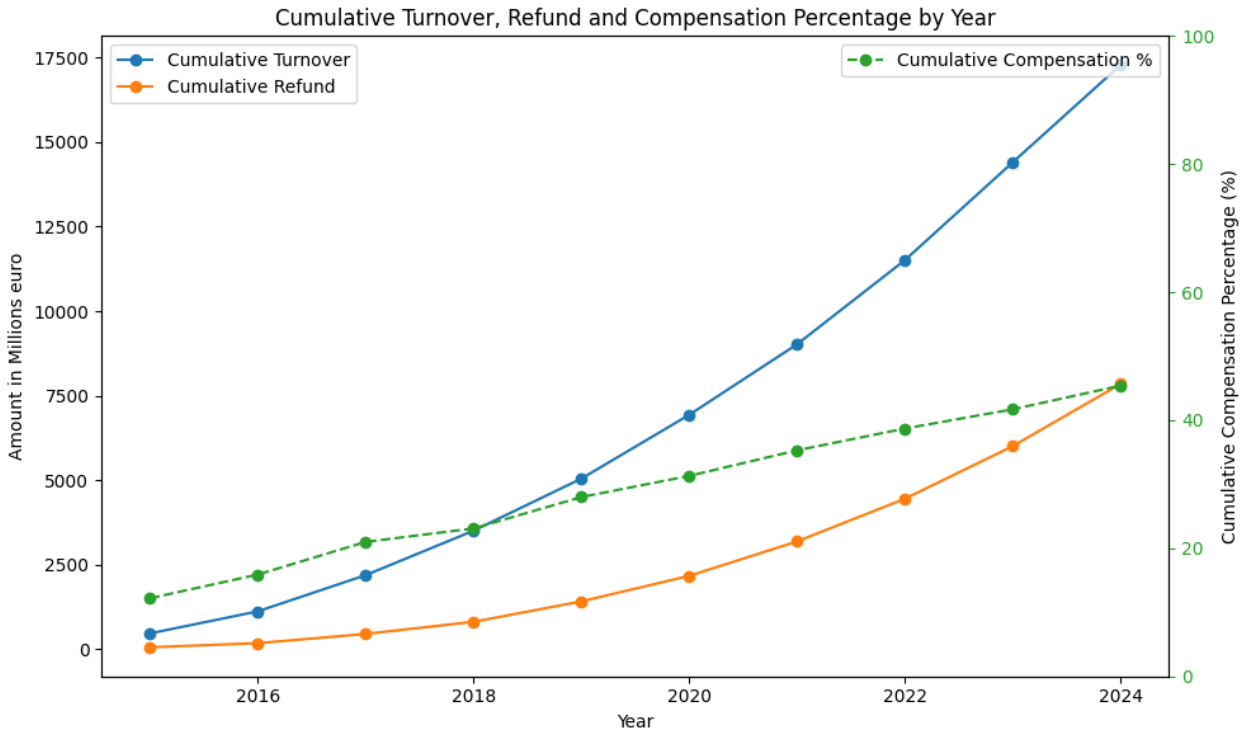

Figure 86: Cumulative overview of turnovers, compensation and net turnover (ex-works price level, in millions of euros)

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Cumulative Turnover	466.1	1118.7	2189.9	3504.3	5043.93	6931.7	9017.4	11505.6	14399.8	[17277.0]
Cumulative Advance			100.5	296.0	683.03	1223.5	1931.1	2606.5	3360.7	[4701.2]
Cumulative Refund	56.6	178.0	350.6	512.7	730.76	944.3	1254.8	1842.3	2643.8	[3142.8]
Cumulative Compensation	56.6	178.0	451.1	808.7	1413.79	2167.8	3185.9	4448.8	6004.4	[7844.0]
Cumulative Net	409.5	940.7	1738.8	2695.6	3630.14	4763.9	5831.5	7056.8	8395.4	[9433.0]
Cumulative Comp Percentage	12.2%	15.9%	21.0%	23.1%	28.0%	31.3%	35.3%	38.7%	41.7%	[45.4%]

Table 50: Cumulative overview of turnovers, compensation and net turnover (ex-works price level, in millions of euros)

3. Analysis by main anatomical group

This section presents an analysis similar to that shown in Table 49, but segmented by main anatomical group. For reasons of confidentiality, only budget years for which a minimum of five separate molecules contribute to the amounts are shown. Figures are not cumulative.

a. Class A: Alimentary tract and metabolism

	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Turnover	3,868.6	7,698.5	13,424.5	23,639.9	31,734.5	39,772.7	56,395.3	84,012.6	[79,119.1]
Balance	75.0	423.1	948.3	1,926.0	2,612.3	3,857.8	4,313.8	5,994.7	[12,329.2]
Advance	.	0.2	126.2	3,902.9	6,156.2	7,329.6	10,678.0	20,307.6	[29,854.6]
Refund	75.0	423.3	1,074.5	5,828.9	8,768.5	11,187.4	14,991.8	26,302.3	[42,183.8]
Net	3,793.6	7,275.1	12,350.0	17,811.0	22,966.0	28,585.3	41,403.5	57,710.3	[36,935.4]
Compensation	1.94%	5.50%	8.00%	24.7%	27.6%	28.1%	26.6%	31.3%	[53.3%]
# Conventions	6	6	13	10	12	14	15	15	18
# Molecules	6	6	8	7	10	13	13	14	15

Table 51: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class A (alimentary tract and metabolism) presenting at least 5 different molecules per budget year presented.

b. Class B: Blood and blood-forming organs

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Turnover	92,713.2	120,023.9	144,221.8	165,249.2	191,472.5	249,885.6	300,967.1	337,668.8	359,733.1	[342,804.5]
Balance	24,864.0	27,522.7	37,045.6	37,062.0	45,568.4	58,762.4	40,025.4	41,022.2	50,353.0	[72,443.2]
Advance	.	.	7,572.3	12,784.9	17,049.6	77,402.2	100,204.7	110,640.9	115,075.2	[88,299.1]
Refund	24,864.0	27,522.7	44,617.8	49,846.9	62,618.0	136,164.6	140,230.2	151,663.1	165,428.2	[160,742.3]
Net	67,849.1	92,501.2	99,604.0	115,402.2	128,854.5	113,720.9	160,736.9	186,005.7	194,304.9	[182,062.2]
Compensation	26.8%	22.9%	30.9%	30.2%	32.7%	54.5%	46.6%	44.9%	46.0%	[46.9%]
# Conventions	5	9	8	7	7	14	8	9	10	11
# Molecules	5	5	6	6	6	7	7	8	8	8

Table 52: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class B (Blood and blood forming organs) presenting at least 5 different molecules per budget year presented.

c. Class C: Cardiovascular system

	2016	2017	2018	2019	2020	2022	2023	2024*
Turnover	1,498.7	7,349.9	15,398.3	24,083.8	17,935.4	30,194.6	51,580.6	[74,669.4]
Balance	0.0	1,456.5	2,672.6	6,995.0	5,902.9	6,419.8	10,773.5	[7,616.8]
Advance	.	.	.	0.0	0.0	9,594.6	29,070.6	[53,769.5]
Refund	0.0	1,456.5	2,672.6	6,995.0	5,902.9	16,014.5	39,844.1	[61,386.3]
Net	1,498.7	5,893.5	12,725.7	17,088.9	12,032.5	14,180.1	11,736.5	[13,283.1]
Compensation	.000%	19.8%	17.4%	29.0%	32.9%	53.0%	77.2%	[82.2%]
# Conventions	5	6	6	5	5	6	7	9
# Molecules	5	6	6	5	5	5	5	6

Table 53: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class C (Cardiovascular system) presenting at least 5 different molecules per budget year presented.

d. Class J: Anti-infectives for systemic use

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Turnover	90,256.4	57,087.3	91,807.5	40,424.5	76,472.8	37,333.8	33,744.0	27,039.5	28,490.6	[31,852.9]
Balance	0.0	40,662.9	14,391.4	-2,168.2	-119.3	2,488.2	219.3	-150.2	307.4	[553.9]
Advance	.	.	22,544.0	5,483.7	35,728.5	15,730.1	14,591.8	9,487.0	11,150.5	[46,887.1]
Refund	0.0	40,662.9	36,935.5	3,315.5	35,609.2	18,218.4	14,811.1	9,336.7	11,457.8	[47,441.0]
Net	90,256.4	16,424.4	54,872.0	37,109.0	40,863.6	19,115.5	18,932.8	17,702.7	17,032.7	[-15,588.1]
Compensation	.000%	71.2%	40.2%	8.20%	46.6%	48.8%	43.9%	34.5%	40.2%	[149%]
# Conventions	7	7	8	10	11	7	7	9	9	[10]
# Molecules	7	7	8	10	11	7	7	8	8	[10]

Table 54: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class J (Anti-infectives for systemic use) presenting at least 5 different molecules per budget year presented.

e. Class L: Antineoplastics and immunomodulating agents

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Turnover	266,048.4	394,000.3	702,571.5	930,174.2	1,042,612.4	1,370,555.3	1,409,035.0	1,550,411.4	1,697,842.2	[1,583,276.4]
Balance	27,716.8	49,974.2	85,580.2	82,581.1	111,032.6	116,351.5	225,333.2	388,007.7	477,041.1	[285,505.6]
Advance	.	.	70,374.9	169,471.4	279,348.6	387,213.6	467,571.1	380,700.1	393,707.6	[693,622.3]
Refund	27,716.8	49,974.2	155,955.1	252,052.5	390,381.2	503,565.0	692,904.3	768,707.9	870,748.7	[979,127.9]
Net	238,331.6	344.026.1	546,616.4	678,121.8	652,231.2	866,990.2	716,130.7	781,703.6	827,093.5	[604,148.5]
Compensation	10.4%	12.7%	22.2%	27.1%	37.4%	36.7%	49.2%	49.6%	51.3%	[61.8%]
# Conventions	32	46	55	65	73	71	85	87	95	106
# Molecules	30	37	46	50	55	53	64	66	74	83

Table 55: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class L (Antineoplastics and immunomodulating agents) presenting at least 5 different molecules per budget year presented.

f. Class M: Musculo-skeletal system

	2022	2023	2024*
Turnover	61,139.2	81,023.6	[77,912.5]
Balance	13,209.7	11,195.7	[13,023.4]
Advance	27,687.2	35,241.0	[36,063.7]
Refund	40,896.9	46,436.6	[49,087.1]
Net	20,242.3	34,587.0	[28,825.4]
Compensation	66.9%	57.3%	[63.0%]
# Conventions	5	5	7
# Molecules	5	5	5

Table 56: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class M (Musculo-skeletal system) presenting at least 5 different molecules per budget year presented.

g. Class N: Nervous system

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024*
Turnover	5,643.6	18,610.1	24,721.0	27,147.1	20,326.4	9,099.2	61,746.4	204,613.0	309,745.6	[409,307.7]
Balance	131.1	2,807.2	4,699.8	5,781.8	6,679.6	1,105.1	1,079.4	93,244.0	161,069.0	[15,710.7]
Advance	.	.	.	290.9	507.0	2,289.2	31,984.5	48,090.4	78,952.4	[306,988.1]
Refund	131.1	2,807.2	4,699.8	6,072.7	7,186.7	3,394.3	33,063.9	141,334.5	240,021.4	[322,698.8]
Net	5,512.6	15,802.9	20,021.2	21,074.5	13,139.7	5,705.0	28,682.5	63,278.6	69,724.2	[86,608.9]
Compensation	2.32%	15.1%	19.0%	22.4%	35.4%	37.3%	53.5%	69.1%	77.5%	[78.8%]
# Conventions	5	5	6	7	7	7	11	12	10	16
# Molecules	5	5	6	7	7	6	10	10	10	12

Table 57: Overview by calendar year of turnover, compensation and net turnover (ex-works price level, in thousand EURO) for specialties in ATC class N (Nervous system) presenting at least 5 different molecules per budget year presented.

4. Difference between estimates and actual amounts

The amounts to be collected by the NIHDI are estimated in the first instance. These estimates are based on data from the report of the Medicines Reimbursement Committee (CRM), and on discussions between the working group and the company concerned. They are then included in the confidential appendices to the conventions. The NIHDI uses these estimates to plan budgets for future years.

As explained above, most conventions are based on a compensation mechanism based on a percentage of turnover, generally structured in tranches: the higher the tranche of turnovers, the higher the rate of refund applied[16]. As such, when actual expenditure exceeds the estimates, the budget comes under additional pressure - more packaging has to be reimbursed. This is because these conventions often relate to high-cost products, for which even a small proportion of reimbursement corresponds to large absolute amounts. Conversely, a significant overestimate of expenditure compared with the amounts actually observed results in a loss of revenue for the NIHDI. This imbalance reflects an inadequate definition of the tranches and, consequently, an inaccurate calculation of the refund rate.

This section analyses the differences between estimated amounts and amounts actually received for each accounting period. For the purposes of this analysis, only conventions for which both information - estimated amounts and amounts received - was available were included. The differences were calculated for items relating to turnover, advances, balances, balances based on IMA data and total compensation. A negative figure indicates an overestimate of the amounts to be collected, while a positive figure indicates an underestimate. If the files submitted to the CRM had all been correctly estimated, this table would not be filled with zeros. The bigger the discrepancies, the bigger the differences between estimates and actual budgets.

Table 58 shows the overall differences by year of payment. The same analysis was carried out and shown in Table 59, but grouping the different estimates by year of request for reimbursement of the specialty. There is always a tendency to over-estimate, but there is above all an extremely high concentration during the COVID years. Compensation for specialties under convention in 2021 (Table 58) was therefore underestimated by €34 million. Conversely, the compensation was overestimated by €153M for conventions introduced in 2023 (all periods combined).

[16] The final tranches of conventions can reach refund rates of over 85%. In some cases, there is a total refund.

Year of payment	Turnover	Advances	Balances	Prov/Def	Total Refund
2015	-3,322.027	.	18,642,293	-935,856	17,706,437
2016	3,444,739	.	37,327,750	-795,496	36,532,254
2017	-87,784,459		-28,930,478	-1,654,867	-30,585,345
2018	-94,445,755		-38,597,524	-4,690,756	-43,288,280
2019	14,241,854		31,220,590	-9,955,384	21,265,206
2020	8,218,119	30,678,996	2,213,404	-5,698,260	27,194,140
2021	-40,774,181	-16,992,944	51,256,213	-168,651	34,094,618
2022	-86,574,251	-174,312,021	32,793,688	-211,403	-141,729,735
2023	-297,039,898	-153,685,996	119,294,768.	-2,415,031	-36,806,258
2024*	[-563,872,111]	[-149,893,095]	[-17,957,425]		[-167,850,520]

Table 58: Difference between estimated and actual amounts by payment year.

Year requesting MEA	Turnover	Advances	Balances	Prov/Def	Total Refund
2015	-114,854,464	2,893,252	-45,550,881		-42,657,629
2016	-995,249	26,924,840	56,775,632	-15,701,284	67,999,189
2017	-39,523,893	31,150,314	-15.398.313	-4,530,408	11,221,593
2018	-48,368,282	-34,223,402	58,701,276	.	24,477,873
2019	-99,647,689	-14,425,037	-18,371,998	.	-32,797,036
2020	-134,848,579	-63,928,400	33,995,367	.	-29,933,033
2021	-444,363,414	-254,560,787	98,702,828		-155,857,959
2022	-46,322,784	15,796,456	4,644,238	.	20,440,694
2023	-185,997,750	-111,705,606	-39,822,802	-2,349,900	-153,878,309
2024*	[-110,855,966]	[-30,236,119]	[-4,754,042]		[-34,990,161]

Table 59: Difference between estimated and actual amounts by year the request for convention was submitted

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Appendix 1: Additional visualisations by pharmacological class

CLASS A10B: DRUGS USED IN DIABETES

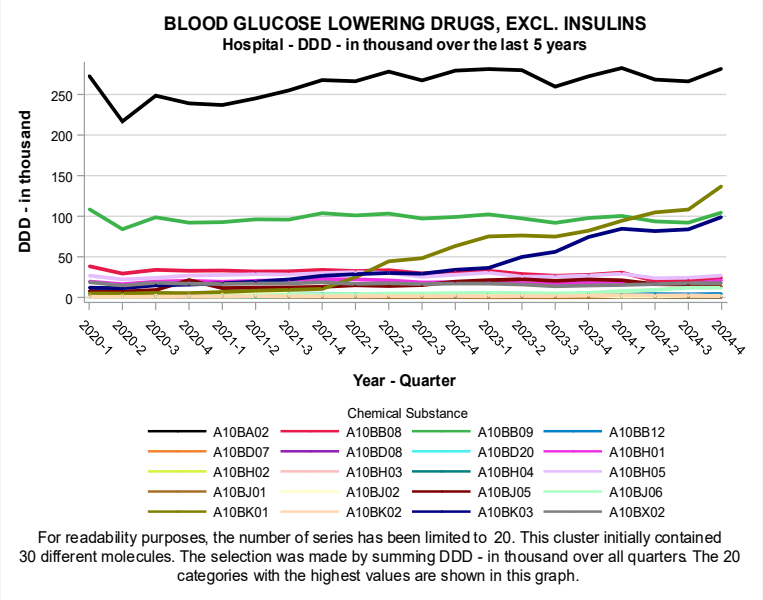

Figure 87: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class A10B.

CLASS C01E - SERUM LIPID-LOWERING AGENTS

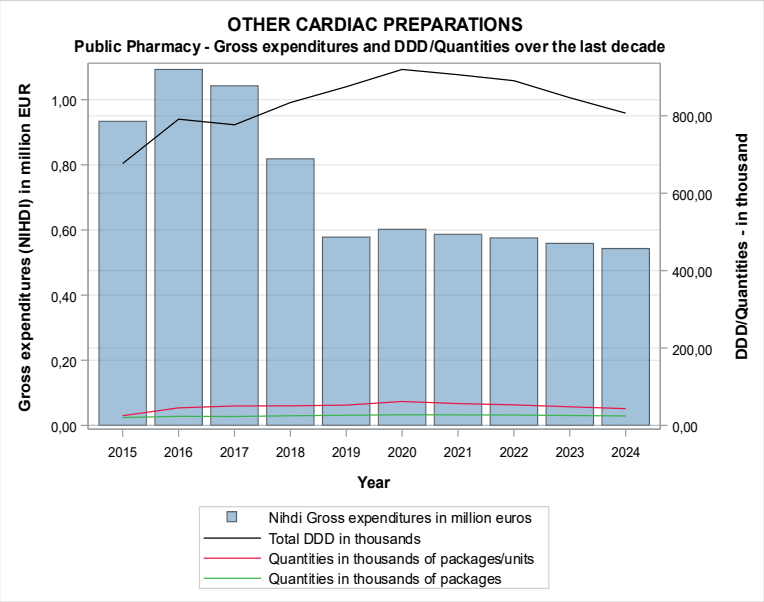

Figure 88: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class C01E.

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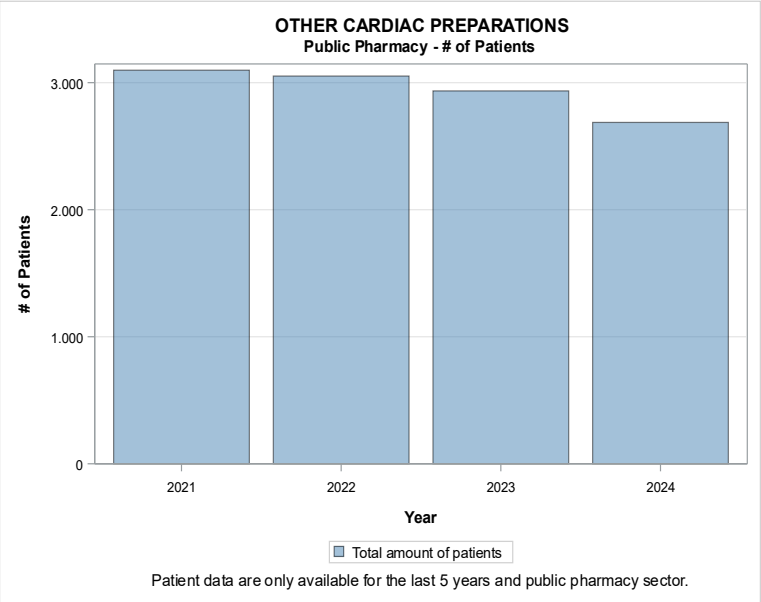

Figure 89: Annual evolution in the number of patients using specialties from pharmacological class C01E reimbursed in public pharmacies and nursing homes.

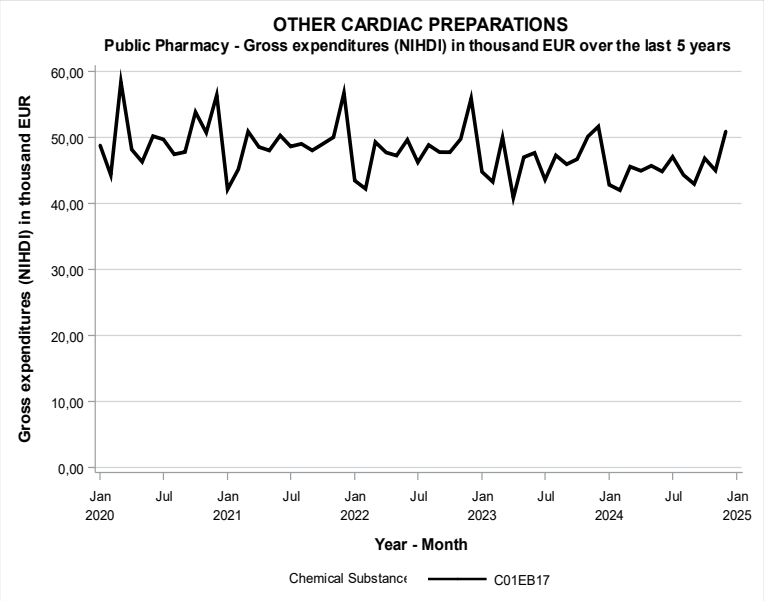

Figure 90: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class C01E.

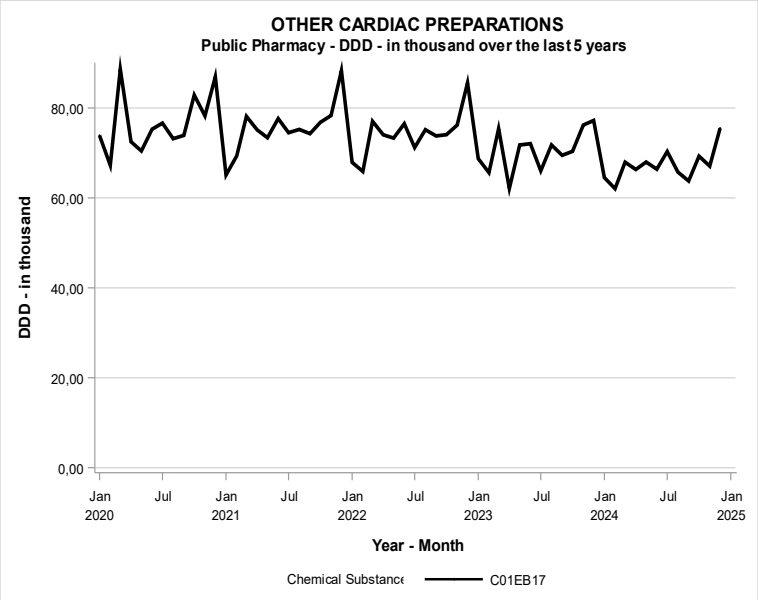

Figure 91: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class C01E.

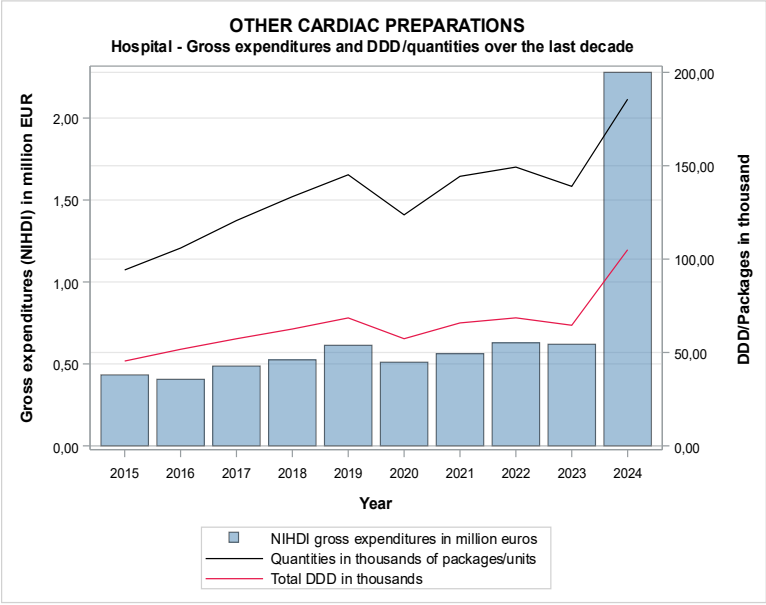

Figure 92: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class C01E.

109 - Appendix 1: Additional visualisations by pharmacological class

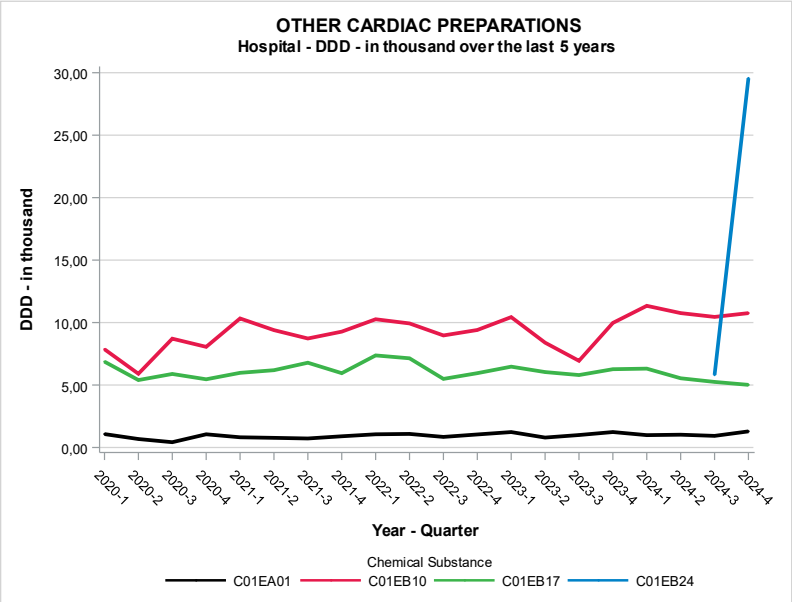

Figure 93: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class C01E.

CLASS C10A – SERUM-LIPID REDUCING AGENTS, NOT COMBINED

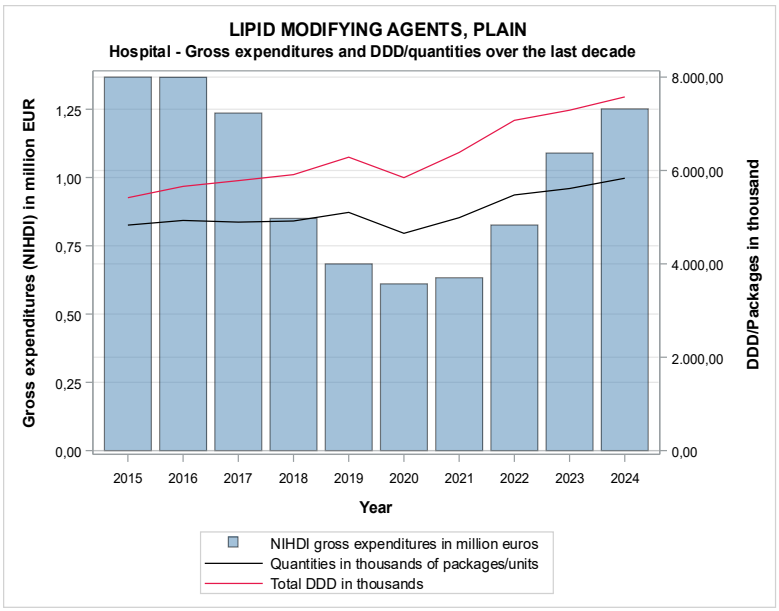

Figure 94: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class C10A.

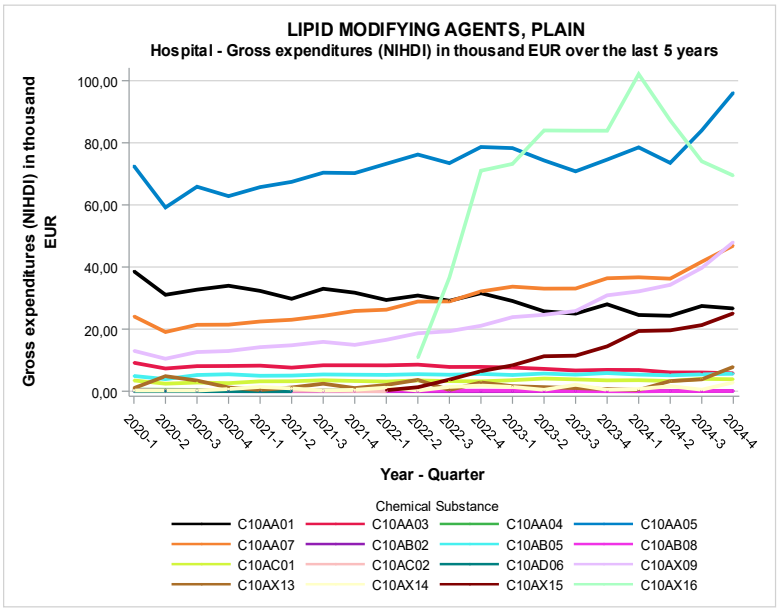

Figure 95: Quarterly evolution in NIHDI expenditure in hospitals (in thousands of euros) by molecule in pharmacological class C10A.

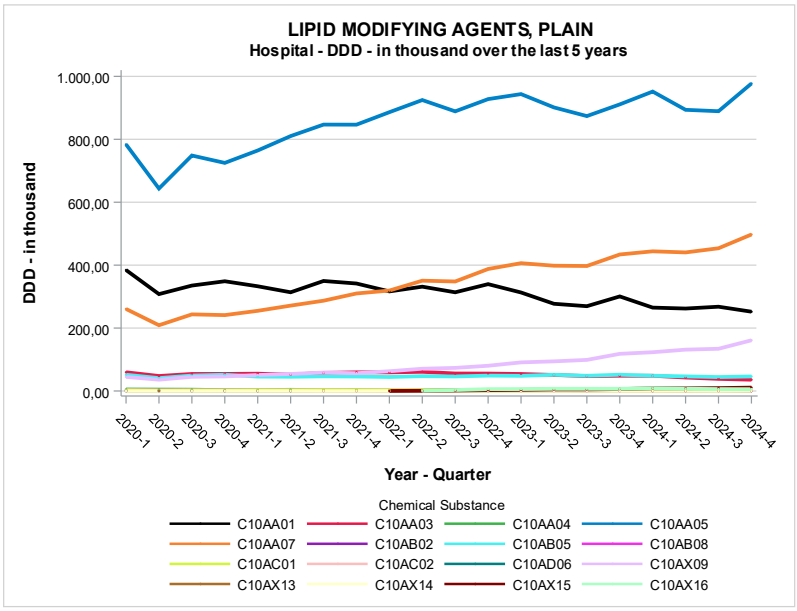

Figure 96: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class C10A.

111 - Appendix 1: Additional visualisations by pharmacological class

CLASS J06B - IMMUNE SERA AND IMMUNOGLOBULINS

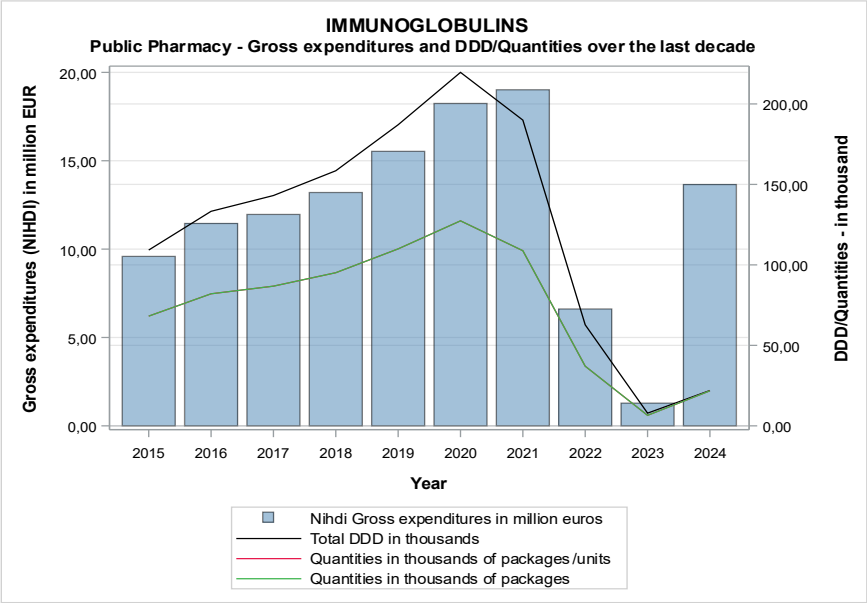

Figure 97: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class J06B.

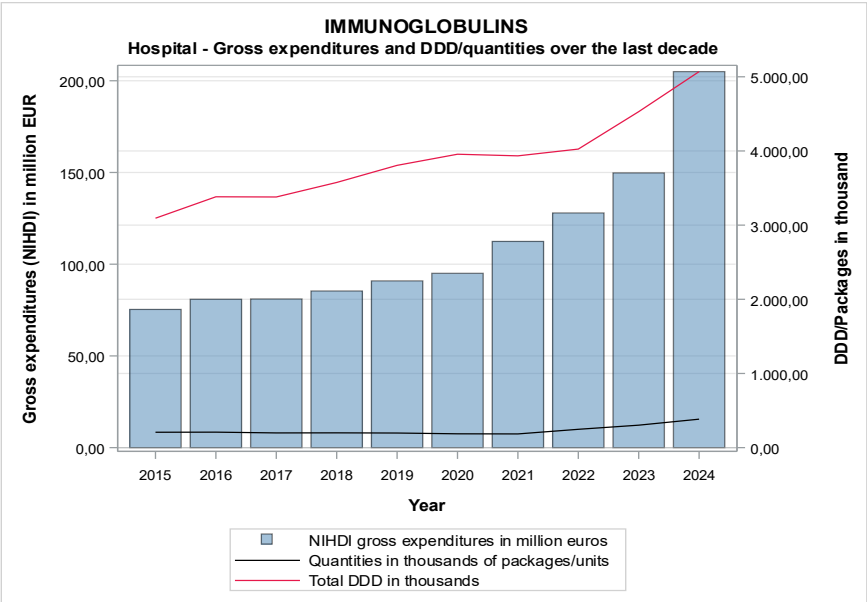

Figure 98: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of units reimbursed (in thousands) in hospitals for pharmacological class J06B.

CLASS L01E - PROTEIN KINASE INHIBITORS

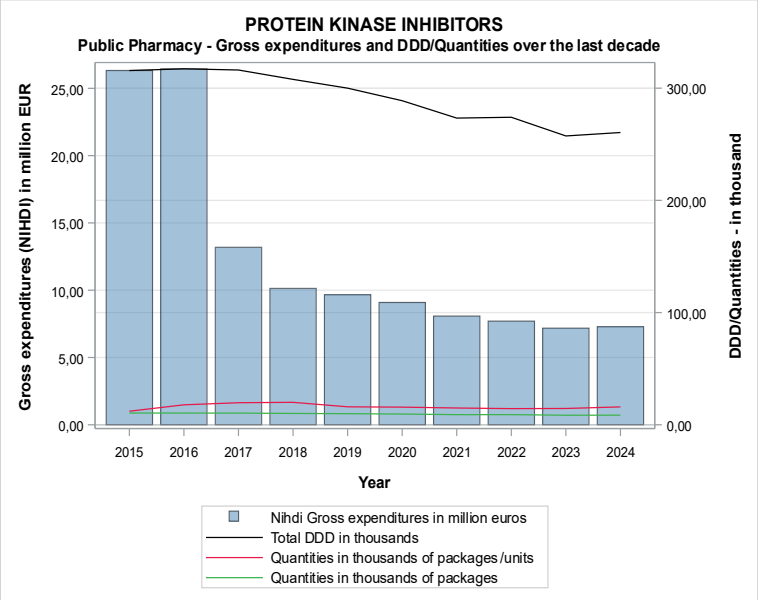

Figure 99: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class L01E.

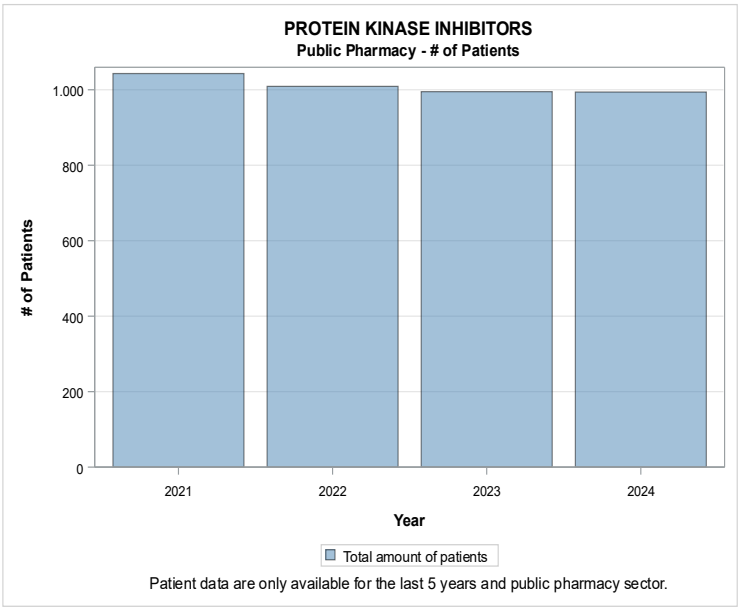

Figure 100: Annual evolution in the number of patients using specialties from pharmacological class L01E reimbursed in public pharmacies and nursing homes.

113 - Appendix 1: Additional visualisations by pharmacological class

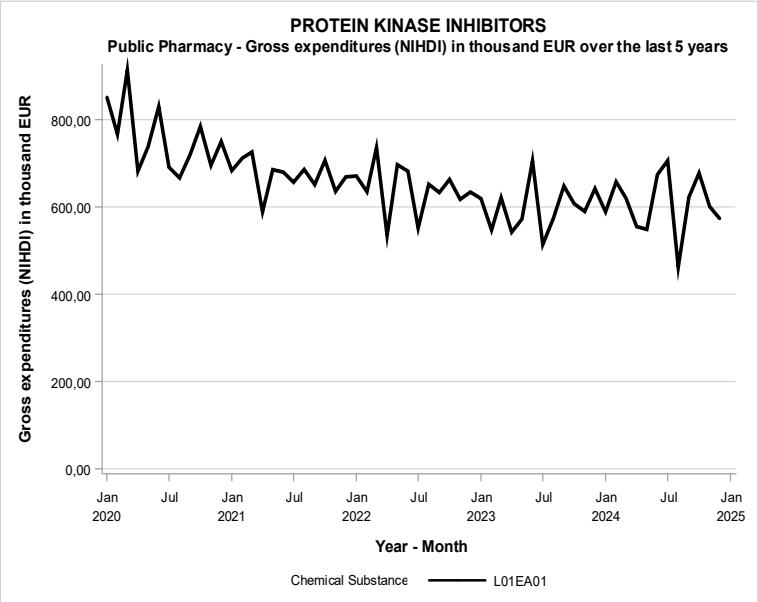

Figure 101: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class L01E.

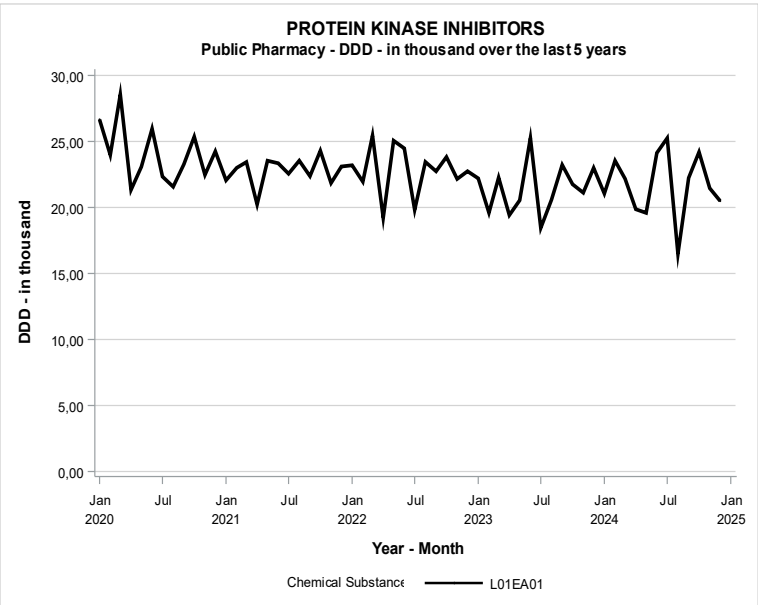

Figure 102: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class L01E.

CLASS L01X - OTHER ANTINEOPLASTIC AGENTS

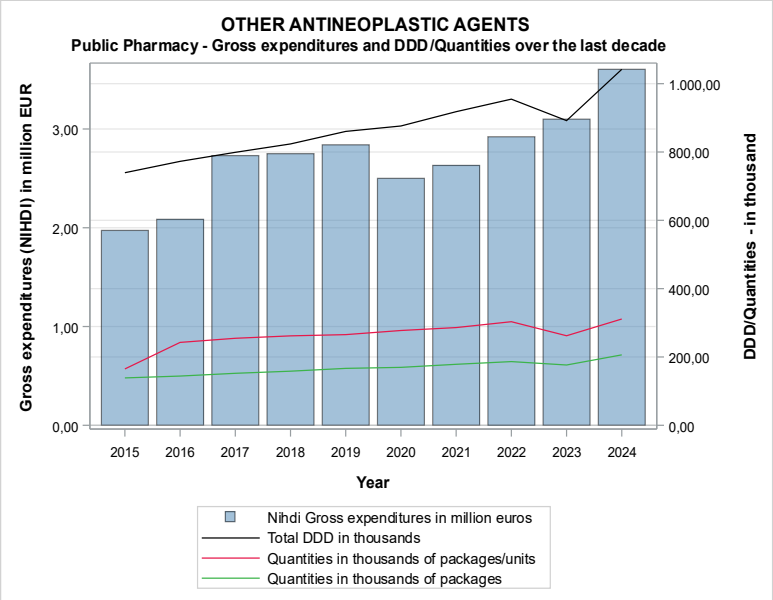

Figure 103: Annual evolution in gross NIHDI expenditure (in millions of euros), DDDs and quantities of packs and/or units reimbursed (in thousands) in public pharmacies and nursing homes for pharmacological class L01X.

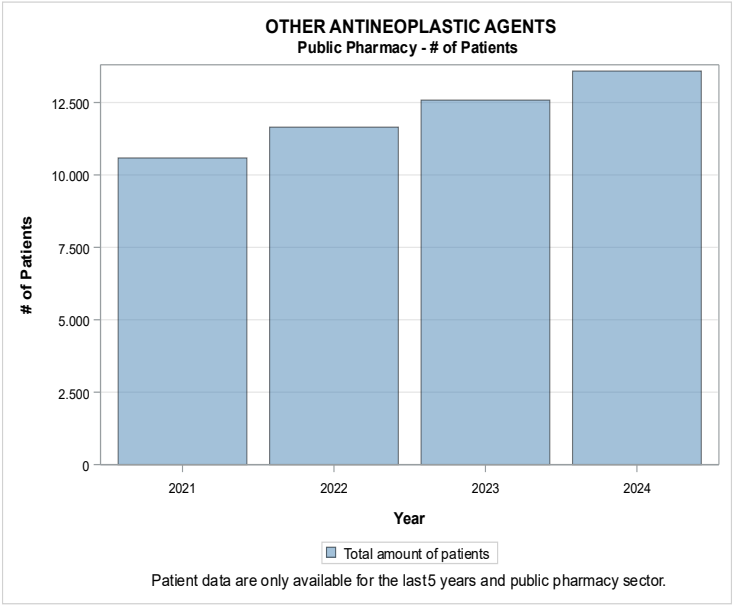

Figure 104: Annual evolution in the number of patients using specialties from pharmacological class L01X reimbursed in public pharmacies and nursing homes.

115 - Appendix 1: Additional visualisations by pharmacological class

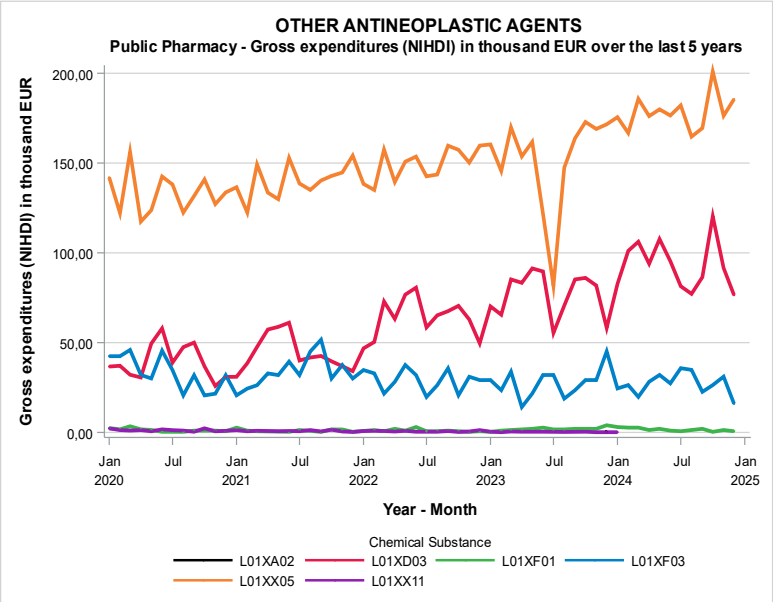

Figure 105: Monthly evolution of gross NIHDI expenditure (in thousands of euros) in public pharmacies and nursing homes per molecule in pharmacological class L01X.

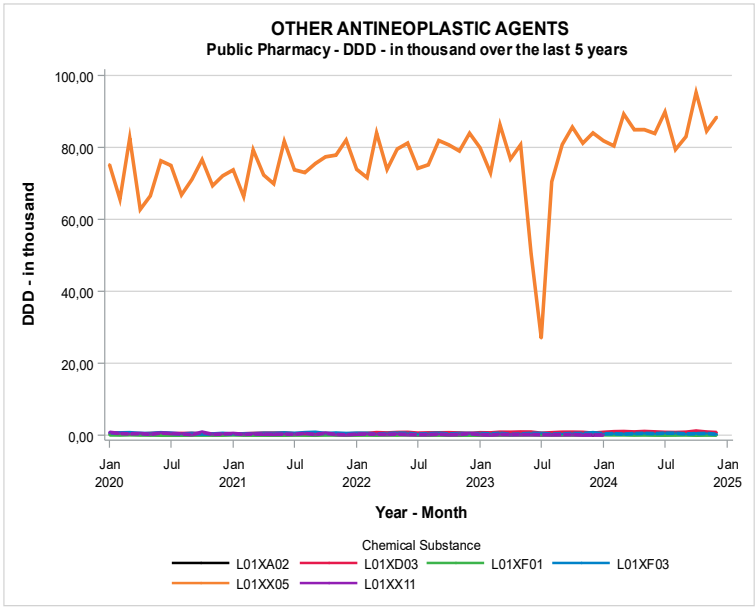

Figure 106: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class L01X.

CLASS N02C - ANTIMIGRAINE PREPARATIONS

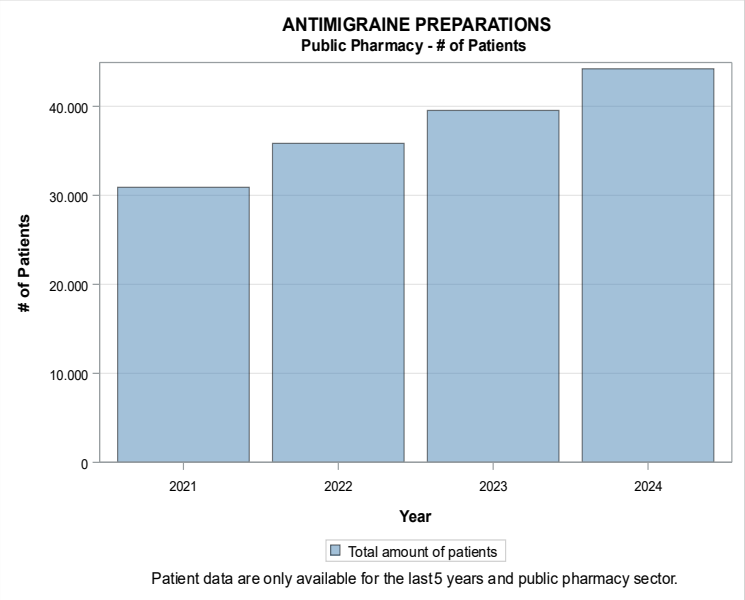

Figure 107: Annual evolution in the number of patients using specialties from pharmacological class N02C reimbursed in public pharmacies and nursing homes.

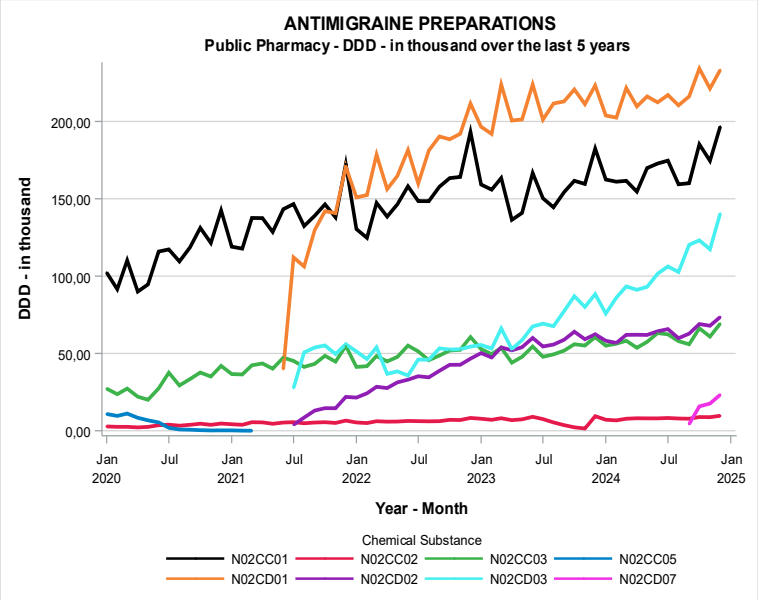

Figure 108: Monthly evolution in the number (in thousands) of DDDs dispensed in public pharmacies and nursing homes by molecule in pharmacological class N02C.

117 - Appendix 1: Additional visualisations by pharmacological class

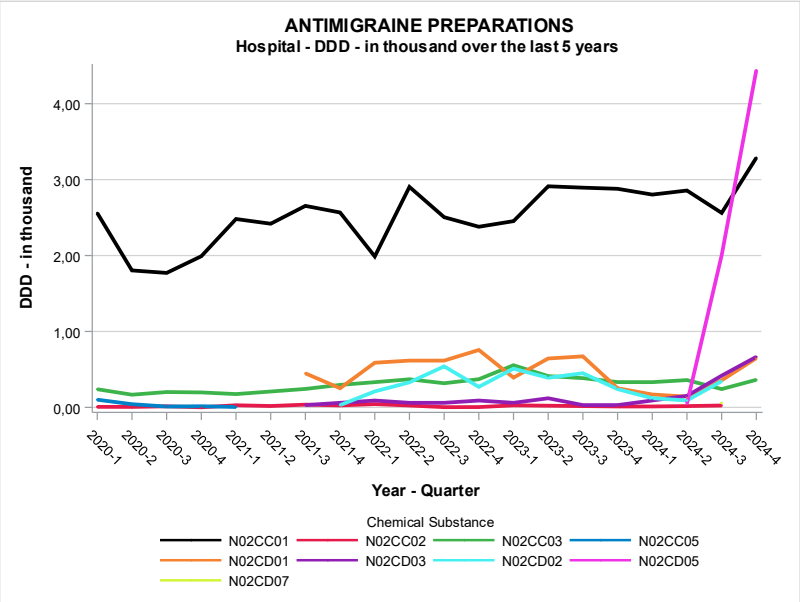

Figure 109: Quarterly evolution in the number of DDD (in thousands) dispensed in hospitals, by molecule, for pharmacological class N02C.

Appendix 2: Annual tables (2020-2024) of cases handled by the CRM

CRM PROPOSALS ACCORDING TO TYPE OF REQUEST

2020	CRM								Total	
	No Proposal		Positive		Negative		MEA			
	N	%	N	%	N	%	N	%	N	%
Class 1	5	45%	8	4%	2	4%	27	52%	42	13%
Class 2	.	.	22	11%	4	7%	7	13%	33	10%
Class 2: Biosimilar	.	.	4	2%	.	.	.	.	4	1%
Class 3	.	.	15	8%	2	4%	.	.	17	5%
Price	2	18%	68	35%	4	7%	.	.	74	23%
Modification	2	18%	55	28%	9	16%	9	17%	75	24%
Orphan	1	9%	1	1%	3	5%	9	17%	14	4%
Deletion	.	.	11	6%	5	9%	.	.	16	5%
Ind. Revision	.	.	12	6%	9	16%	.	.	21	7%
Import	1	9%	1	1%	19	33%	.	.	21	7%
Total	11	100%	197	100%	57	100%	52	100%	317	100%

Table 60: Number of unique requests for changes to the list of reimbursable pharmaceutical specialties versus proposal by the CRM (2020)

2021	CRM								Total	
	No Proposal		Positive		Negative		MEA			
	N	%	N	%	N	%	N	%	N	%
Class 1	2	13%	10	5%	6	11%	20	33%	38	11%
Class 2	1	6%	28	13%	2	4%	6	10%	37	10%
Class 2: Biosimilar	.	.	8	4%	.	.	.	.	8	2%
Class 3	.	.	43	19%	2	4%	.	.	45	13%
Price	5	31%	44	20%	15	26%	.	.	64	18%
Modification	3	19%	72	33%	7	12%	18	30%	100	28%
Orphan	1	6%	.	.	3	5%	10	16%	14	4%
Deletion	.	.	3	1%	3	5%	.	.	6	2%
Exception	.	.	2	1%	1	2%	.	.	3	1%
Ind. Revision	.	.	10	5%	7	12%	.	.	17	5%
Import	4	25%	1	0%	11	19%	7	11%	23	6%
Total	16	100%	221	100%	57	100%	61	100%	355	100%

Table 61: Number of unique requests for changes to the list of reimbursable pharmaceutical specialties versus proposal by the CRM (2021)

2022	CRM								Total	
	No Proposal		Positive		Negative		MEA			
	N	%	N	%	N	%	N	%	N	%
Class 1	1	11%	10	5%	9	18%	25	40%	45	13%
Class 2	1	11%	24	11%	.	.	5	8%	30	9%
Class 2: Biosimilar	.	.	6	3%	1	2%	.	.	7	2%
Class 3	.	.	33	15%	9	18%	.	.	42	12%
Price	1	11%	33	15%	5	10%	.	.	39	12%
Modification	2	22%	87	40%	10	20%	16	25%	115	34%
Orphan	4	44%	5	2%	6	12%	11	17%	26	8%
Deletion	.	.	5	2%	1	2%	.	.	6	2%
Exception	.	.	2	1%	.	.	.	.	2	1%
Ind. Revision	.	.	11	5%	10	20%	.	.	21	6%
Import	.	.	.	.	.	.	6	10%	6	2%
Total	9	100%	216	100%	51	100%	63	100%	339	100%

Table 62: Number of unique requests for changes to the list of reimbursable pharmaceutical specialties versus proposal by the CRM (2022)

119 - Appendix 2: Annual tables (2020-2024) of cases handled by the CRM

2023	CRM								Total	
	No Proposal		Positive		Negative		MEA			
	N	%	N	%	N	%	N	%	N	%
Class 1	4	67%	16	7%	9	25%	26	37%	55	16%
Class 2	1	17%	24	10%	3	8%	8	11%	36	10%
Class 2: Biosimilar	.	.	5	2%	.	.	.	.	5	1%
Class 3	.	.	32	13%	1	3%	.	.	33	9%
Price	.	.	37	15%	2	6%	.	.	39	11%
Modification	.	.	111	46%	10	28%	19	27%	140	40%
Orphan	1	17%	5	2%	2	6%	18	25%	26	7%
Deletion	.	.	.	.	2	6%	.	.	2	1%
Ind. Revision	.	.	10	4%	7	19%	.	.	17	5%
Total	6	100%	240	100%	36	100%	71	100%	353	100%

Table 63: Number of unique requests for changes to the list of reimbursable pharmaceutical specialties versus proposal by the CRM (2023)

2024	CRM								Total	
	No Proposal		Positive		Negative		MEA			
	N	%	N	%	N	%	N	%	N	%
Class 1	.	.	12	5%	9	19%	25	40%	46	13%
Class 2	.	.	27	11%	4	8%	10	16%	41	12%
Class 2: Biosimilar	.	.	13	6%	.	.	.	.	13	4%
Class 3	.	.	30	13%	.	.	.	.	30	9%
Price	.	.	32	14%	4	8%	.	.	36	10%
Modification	4	67%	98	42%	10	21%	16	25%	128	36%
Orphan	2	33%	5	2%	4	8%	11	17%	22	6%
Deletion	.	.	5	2%	1	2%	.	.	6	2%
Ind. Revision	.	.	13	6%	16	33%	.	.	29	8%
Import	.	.	.	.	.	.	1	2%	1	0%
Total	6	100%	235	100%	48	100%	63	100%	352	100%

Table 64: Number of unique requests for changes to the list of reimbursable pharmaceutical specialties versus proposal by the CRM (2024)

DECISIONS OF THE MINISTER ACCORDING TO CRM PROPOSALS

2020		Minister								total
		Positive		Negative		MEA		Time Out: Admin Decision		
		N	%	N	%	N	%	N	%	N
Class 1	No Proposal	3	60%	1	20%	1	20%	.	.	5
	Positive	7	88%	1	13%	.	.	.	.	8
	Negative	.	.	2	100%	.	.	.	.	2
	MEA	14	52%	1	4%	12	44%	.	.	27
	Total	24	57%	5	12%	13	31%	.	.	42
Class 2	Positive	22	100%	.	.	.	.	.	.	22
	Negative	1	25%	3	75%	.	.	.	.	4
	MEA	2	29%	.	.	5	71%	.	.	7
	Total	25	76%	3	9%	5	15%	.	.	33
Class 2: Biosimilar	Positive	4	100%	.	.	.	.	.	.	4
	Total	4	100%	.	.	.	.	.	.	4
Class 3	Positive	15	100%	.	.	.	.	.	.	15
	Negative	2	100%	.	.	.	.	.	.	2
	Total	17	100%	.	.	.	.	.	.	17
Price	No Proposal	2	100%	.	.	.	.	.	.	2
	Positive	68	100%	.	.	.	.	.	.	68
	Negative	1	25%	3	75%	.	.	.	.	4
	Total	71	96%	3	4%	.	.	.	.	74
Modification	No Proposal	2	100%	.	.	.	.	.	.	2
	Positive	55	100%	.	.	.	.	.	.	55
	Negative	.	.	9	100%	.	.	.	.	9
	MEA	2	22%	.	.	7	78%	.	.	9
	Total	59	79%	9	12%	7	9%	.	.	75
Orphan	No Proposal	1	100%	.	.	.	.	.	.	1
	Positive	1	100%	.	.	.	.	.	.	1
	Negative	.	.	3	100%	.	.	.	.	3
	MEA	3	33%	1	11%	5	56%	.	.	9
	Total	5	36%	4	29%	5	36%	.	.	14
Deletion	Positive	11	100%	.	.	.	.	.	.	11
	Negative	1	20%	4	80%	.	.	.	.	5
	Total	12	75%	4	25%	.	.	.	.	16
Ind. Revision	Positive	11	92%	.	.	.	.	1	8%	12
	Negative	.	.	9	100%	.	.	.	.	9
	Total	11	52%	9	43%	.	.	1	5%	21
Import	No Proposal	.	.	1	100%	.	.	.	.	1
	Positive	1	100%	.	.	.	.	.	.	1
	Negative	.	.	19	100%	.	.	.	.	19
	Total	1	5%	20	95%	.	.	.	.	21
Total	No Proposal	8	73%	2	18%	1	9%	.	.	11
	Positive	195	99%	1	1%	.	.	1	1%	197
	Negative	5	9%	52	91%	.	.	.	.	57
	MEA	21	40%	2	4%	29	56%	.	.	52
	Total	229	72%	57	18%	30	9%	1	0%	317

Table 65: Decisions of the Minister based on the CRM's proposal (unique files 2020)

121 - Appendix 2: Annual tables (2020-2024) of cases handled by the CRM

2021		Minister						total
		Positive		Negative		MEA		
		N	%	N	%	N	%	N
Class 1	No Proposal	2	100%	.	.	.	.	2
	Positive	10	100%	.	.	.	.	10
	Negative	1	17%	5	83%	.	.	6
	MEA	12	60%	.	.	8	40%	20
	Total	25	66%	5	13%	8	21%	38
Class 2	No Proposal	1	100%	.	.	.	.	1
	Positive	28	100%	.	.	.	.	28
	Negative	.	.	2	100%	.	.	2
	MEA	3	50%	.	.	3	50%	6
	Total	32	86%	2	5%	3	8%	37
Class 2: Biosimilar	Positive	8	100%	.	.	.	.	8
	Total	8	100%	.	.	.	.	8
Class 3	Positive	43	100%	.	.	.	.	43
	Negative	2	100%	.	.	.	.	2
	Total	45	100%	.	.	.	.	45
Price	No Proposal	5	100%	.	.	.	.	5
	Positive	44	100%	.	.	.	.	44
	Negative	5	33%	10	67%	.	.	15
	Total	54	84%	10	16%	.	.	64
Modification	No Proposal	.	.	1	33%	2	67%	3
	Positive	72	100%	.	.	.	.	72
	Negative	2	29%	5	71%	.	.	7
	MEA	9	50%	1	6%	8	44%	18
	Total	83	83%	7	7%	10	10%	100
Orphan	No Proposal	1	100%	.	.	.	.	1
	Negative	2	67%	1	33%	.	.	3
	MEA	2	20%	2	20%	6	60%	10
	Total	5	36%	3	21%	6	43%	14
Deletion	Positive	3	100%	.	.	.	.	3
	Negative	.	.	3	100%	.	.	3
	Total	3	50%	3	50%	.	.	6
Exception	Positive	2	100%	.	.	.	.	2
	Negative	.	.	1	100%	.	.	1
	Total	2	67%	1	33%	.	.	3
Ind. Revision	Positive	10	100%	.	.	.	.	10
	Negative	.	.	7	100%	.	.	7
	Total	10	59%	7	41%	.	.	17
Import	No Proposal	.	.	4	100%	.	.	4
	Positive	1	100%	.	.	.	.	1
	Negative	.	.	11	100%	.	.	11
	MEA	.	.	7	100%	.	.	7
	Total	1	4%	22	96%	.	.	23
Total	No Proposal	9	56%	5	31%	2	13%	16
	Positive	221	100%	.	.	.	.	221
	Negative	12	21%	45	79%	.	.	57
	MEA	26	43%	10	16%	25	41%	61
	Total	268	75%	60	17%	27	8%	355

Table 66: Decisions of the Minister based on the CRM's proposal (unique files 2021)

2022		Minister						total
		Positive		Negative		MEA		
		N	%	N	%	N	%	N
Class 1	No Proposal	1	100%	.	.	.	.	1
	Positive	9	90%	1	10%	.	.	10
	Negative	.	.	9	100%	.	.	9
	MEA	11	44%	2	8%	12	48%	25
	Total	21	47%	12	27%	12	27%	45
Class 2	No Proposal	1	100%	.	.	.	.	1
	Positive	24	100%	.	.	.	.	24
	MEA	1	20%	.	.	4	80%	5
	Total	26	87%	.	.	4	13%	30
Class 2: Biosimilar	Positive	6	100%	.	.	.	.	6
	Negative	1	100%	.	.	.	.	1
	Total	7	100%	.	.	.	.	7
Class 3	Positive	33	100%	.	.	.	.	33
	Negative	6	67%	3	33%	.	.	9
	Total	39	93%	3	7%	.	.	42
Price	No Proposal	1	100%	.	.	.	.	1
	Positive	33	100%	.	.	.	.	33
	Negative	.	.	5	100%	.	.	5
	Total	34	87%	5	13%	.	.	39
Modification	No Proposal	2	100%	.	.	.	.	2
	Positive	85	98%	2	2%	.	.	87
	Negative	3	30%	7	70%	.	.	10
	MEA	5	31%	3	19%	8	50%	16
	Total	95	83%	12	10%	8	7%	115
Orphan	No Proposal	.	.	1	25%	3	75%	4
	Positive	5	100%	.	.	.	.	5
	Negative	1	17%	3	50%	2	33%	6
	MEA	4	36%	1	9%	6	55%	11
	Total	10	38%	5	19%	11	42%	26
Deletion	Positive	5	100%	.	.	.	.	5
	Negative	.	.	1	100%	.	.	1
	Total	5	83%	1	17%	.	.	6
Exception	Positive	2	100%	.	.	.	.	2
	Total	2	100%	.	.	.	.	2
Ind. Revision	Positive	11	100%	.	.	.	.	11
	Negative	.	.	10	100%	.	.	10
	Total	11	52%	10	48%	.	.	21
Import	MEA	.	.	6	100%	.	.	6
	Total	.	.	6	100%	.	.	6
Total	No Proposal	5	56%	1	11%	3	33%	9
	Positive	213	99%	3	1%	.	.	216
	Negative	11	22%	38	75%	2	4%	51
	MEA	21	33%	12	19%	30	48%	63
	Total	250	74%	54	16%	35	10%	339

Table 67: Decisions of the Minister based on the CRM's proposal (unique files 2022)

123 - Appendix 2: Annual tables (2020-2024) of cases handled by the CRM

2023		Minister						total
		Positive		Negative		MEA		
		N	%	N	%	N	%	N
Class 1	No Proposal	2	50%	.	.	2	50%	4
	Positive	16	100%	.	.	.	.	16
	Negative	.	.	7	78%	2	22%	9
	MEA	10	38%	1	4%	15	58%	26
	Total	28	51%	8	15%	19	35%	55
Class 2	No Proposal	1	100%	.	.	.	.	1
	Positive	24	100%	.	.	.	.	24
	Negative	.	.	3	100%	.	.	3
	MEA	2	25%	.	.	6	75%	8
	Total	27	75%	3	8%	6	17%	36
Class 2: Biosimilar	Positive	5	100%	.	.	.	.	5
	Total	5	100%	.	.	.	.	5
Class 3	Positive	32	100%	.	.	.	.	32
	Negative	.	.	1	100%	.	.	1
	Total	32	97%	1	3%	.	.	33
Price	Positive	37	100%	.	.	.	.	37
	Negative	.	.	2	100%	.	.	2
	Total	37	95%	2	5%	.	.	39
Modification	Positive	111	100%	.	.	.	.	111
	Negative	.	.	10	100%	.	.	10
	MEA	5	26%	1	5%	13	68%	19
	Total	116	83%	11	8%	13	9%	140
Orphan	No Proposal	.	.	1	100%	.	.	1
	Positive	5	100%	.	.	.	.	5
	Negative	.	.	2	100%	.	.	2
	MEA	1	6%	1	6%	16	89%	18
	Total	6	23%	4	15%	16	62%	26
Deletion	Negative	.	.	2	100%	.	.	2
	Total	.	.	2	100%	.	.	2
Ind. Revision	Positive	9	90%	1	10%	.	.	10
	Negative	.	.	7	100%	.	.	7
	Total	9	53%	8	47%	.	.	17
Total	No Proposal	3	50%	1	17%	2	33%	6
	Positive	239	100%	1	0%	.	.	240
	Negative	.	.	34	94%	2	6%	36
	MEA	18	25%	3	4%	50	70%	71
	Total	260	74%	39	11%	54	15%	353

Table 68: Decisions of the Minister based on the CRM's proposal (unique files 2023)

2024		Minister						total
		Positive		Negative		MEA		
		N	%	N	%	N	%	N
Class 1	Positive	12	100%	.	.	.	.	12
	Negative	.	.	8	89%	1	11%	9
	MEA	3	12%	6	24%	16	64%	25
	Total	15	33%	14	30%	17	37%	46
Class 2	Positive	27	100%	.	.	.	.	27
	Negative	1	25%	3	75%	.	.	4
	MEA	3	30%	.	.	7	70%	10
	Total	31	76%	3	7%	7	17%	41
Class 2: Biosimilar	Positive	13	100%	.	.	.	.	13
	Total	13	100%	.	.	.	.	13
Class 3	Positive	30	100%	.	.	.	.	30
	Total	30	100%	.	.	.	.	30
Price	Positive	32	100%	.	.	.	.	32
	Negative	.	.	4	100%	.	.	4
	Total	32	89%	4	11%	.	.	36
Modification	No Proposal	2	50%	2	50%	.	.	4
	Positive	95	97%	3	3%	.	.	98
	Negative	.	.	10	100%	.	.	10
	MEA	4	25%	4	25%	8	50%	16
	Total	101	79%	19	15%	8	6%	128
Orphan	No Proposal	.	.	2	100%	.	.	2
	Positive	5	100%	.	.	.	.	5
	Negative	.	.	2	50%	2	50%	4
	MEA	1	9%	4	36%	6	55%	11
	Total	6	27%	8	36%	8	36%	22
Deletion	Positive	5	100%	.	.	.	.	5
	Negative	.	.	1	100%	.	.	1
	Total	5	83%	1	17%	.	.	6
Ind. Revision	Positive	13	100%	.	.	.	.	13
	Negative	.	.	16	100%	.	.	16
	Total	13	45%	16	55%	.	.	29
Import	MEA	.	.	1	100%	.	.	1
	Total	.	.	1	100%	.	.	1
Total	No Proposal	2	33%	4	67%	.	.	6
	Positive	232	99%	3	1%	.	.	235
	Negative	1	2%	44	92%	3	6%	48
	MEA	11	17%	15	24%	37	59%	63
	Total	246	70%	66	19%	40	11%	352

Table 69: Decisions of the Minister based on the CRM's proposal (unique files 2024)

Appendix 3: ART 111/112/113 conventions

METHODOLOGICAL NOTE ON THE CALCULATION OF COMPENSATION.

- **Introduction**

Managed Entry Agreements (MEAs), also known as Article 111 or formerly Article 81, are CRM procedures that make it possible to temporarily accept new pharmaceutical specialties to be reimbursed by the social security system if they offer a solution to unmet medical needs and there are still medical or budgetary uncertainties regarding the treatment and the sustainability of reimbursing the cost. During the period covered by the convention, further studies will have to be carried out to identify these uncertainties. Definitive listing for reimbursement will then be possible. Conventions with the NIHDI can be initiated in three different ways, defined in three articles of the Royal Decree of 1 February 2018:

- Article 111: The applicant may on their own initiative, in accordance with article 35bis, § 7 of the law, inform the Minister that they wish to enter into an agreement for the specialties for which the CRM has not been able to make a definitive proposal within the time limit referred to in article 35bis, § 3, paragraph 2, of the law. In this case, the final assessment report approved by the CRM will be the starting point for the working group's discussion.
- Article 112: The applicant may, following a proposal by the CRM to conclude a convention in accordance with Article 35bis, § 7, of the Law, inform the Minister that they wish to conclude a convention for the specialties for which the CRM has made a proposal for a convention as referred to in Article 35bis, § 7, of the Law.
- Article 113: The applicant may, following a reasoned proposal by the Minister to conclude a convention, in accordance with Article 35bis, § 7 of the Law, inform the Minister that they wish to conclude a convention with the NIHDI for specialties for which the CRM has issued a definitive negative proposal within the time limit referred to in Article 35bis, § 3, paragraph 2 of the Law.

Once the procedure has been initiated, a period of negotiation is opened to discuss the conditions for reimbursing the specialty and, more specifically, the terms of compensation. A distinction can be made between direct compensation (such as refunds of turnover generated by the manufacturer to the NIHDI) and indirect compensation (such as lower prices for other specialties already reimbursed by Social Security). These terms and conditions, contained in the appendices to notifications, are legally confidential and known only to the CRM and the manufacturer.

For each convention, a time window for access to reimbursement is specified, divided into different periods (usually, but not systematically, one year long) during which the calculations will take place for the compensation. The compensation mechanisms applied may vary from one period to another, and amendments may also be made that alter the time window or future compensation mechanisms.

This note is intended to explain the general methodology for calculating direct compensation received in the context of MEAs. This will be accompanied by exemplary data. These will be fictitious data, since real data cannot be disclosed.

- **CALCULATION OF DIRECT COMPENSATION IN THE CONTEXT OF FINANCED-BASED AGREEMENTS**

Broadly speaking, there are two main types of budget mechanism: performance-based conventions, where the level of compensation paid by the company depends on the performance of the treatment, and finance-based conventions, where the level of compensation generally depends on the consumption volumes of the treatment. The latter are far more common than the former, which is why we will illustrate the calculation methodology for this type. Once again, there may be a variety of arrangements within this group of finance-based conventions: the amount of compensation, for example, may be fixed or depend on different parameters. A common approach is to set compensation linked to the turnover generated by the manufacturer per period with a tranche system (82% of the conventions signed according to the results presented in the report). When the convention is drawn up, the turnover figures are documented and estimated in order to plan the budgeting of expenditure and refunds. In our fictive case, let us imagine that a convention is signed for product X extending over two periods with the following estimated turnover figures:

	Period 1	Period 2
Period start date	01/05/2021	01/05/2022
Period end date	30/04/2022	30/04/2023
Estimated turnover for the period	€1,000,000	€1,200,000

Periods and estimated turnovers - Product X

with the following tranche and refund system:

Tranches	Definition of the tranche	Percentage of turnover refund
1	[0-50[% of estimated turnover	20%
2	]50-100] % of estimated turnover	30%
3	[100- ..[% of estimated turnover	85%

Definition of tranches and compensation terms - Product X

On the basis of these elements, total compensation can be calculated as a weighted sum, where p refers to the period, b to the tranche, x to turnover and r to the percentage of the refund relative to the tranche:

$$compensation = \sum_{p=1}^{P} \sum_{b=1}^{B} x_{pb} r_{pb}$$

Once established, the compensation would theoretically amount to €250,000 for period 1 and €300,000 for period 2, for a total of €550,000 for the entire convention.

Tranche	Turnover period 1	Turnover period 2	Tranche %	Comp. Est. Period 1	Comp. Est. Period 2
1	€500,000	€600,000	20%	€100,000	€120,000
2	€500,000	€600,000	30%	€150,000	€180,000
3	€0	€0	85%	€0	€0
Total	€1,000,000	€1,200,000		€250,000	€300,000

breakdown of estimated turnover and relative compensation by tranche - Product X

In the vast majority of conventions, these amounts per period are broken down into an advance due by December 31 of year T at the latest, and a balance to be paid at a later date when the actual figures are known, up to the amount of the difference observed. This makes it possible to regulate the compensation to a certain extent over a single budget year, whereas the flexibility of the contracts means that payments can technically be made over a variable number of budget years[17]. In the past, the conventions only stipulated payment at the end of the period.

At the start of each period, estimated advances and balances are calculated on the basis of estimated turnover pro rata to the number of months (m) in the period included in year T (for the advance) and year T+1 (for the balance). Either:

$$\widehat{advance}_p = \widehat{compensation}_p * (m_t / m_p)$$

$$\widehat{balance}_p = \widehat{compensation}_p * \frac{m_{t+1}}{m_p} = \widehat{compensation}_p - \widehat{advance}_p$$

In the example of product X, the advance always corresponds to a time window in year T running from 01/05/T to 31/12/T, i.e. 8 months out of the 12 months covered by a period, or two-thirds of the compensation linked to the period. Conversely, the time windows covered by the balance run from 01/01/T+1 to 30/04/T+1, i.e. 4 months out of the 12 of the period, or one third of the compensation.

	Period 1	Period 2
Estimated advance	Comp. Est. * 2/3 ≈ €166,667	Comp. Est. * 2/3 ≈ €180,000
Estimated balance	Comp. Est. * 1/3 ≈ €83,333	Comp. Est. * 1/3 ≈ €120,000
Estimated total	€250,000	€300,000

Estimates of advances and balances receivable

When periods straddle multiple budget years, it is possible to calculate several advances and balances per period. In this case, the periods cover identical time windows. This is likely not necessarily the case.

When the advance is paid at the end of the budget year, the NIHDI receives partial turnover figures, whereby it can adjust the amount to be paid on the basis of actual data rather than theoretical data. If, for example, the partial turnover figure for period 1 had been €800,000, in the absence of proof to the contrary, we can then deduce using the rule of three that the total turnover figure would then be higher than the millions of euros communicated, and therefore recalculate by extrapolation the hypothetical amount of the total compensation and, de facto, of the advance and the

[17] If, for example, the contract covers a 20-month period from 01/12/T to 01/07/T+2, the balance cannot be paid until two to three years after the start of the period.

balance. We will leave this as it is, and assume that the estimated amount of the advance corresponds to the actual amount to be paid.

Once the actual turnover figures are known and communicated to the NIHDI, it is then possible to calculate the actual compensation to be paid on the basis of the tranche system previously established. As a result, the actual balance is also known, and is the difference between the actual compensation linked to declared turnover and the advance paid.

$$balance_p = compensation_p - advance_p$$

Assuming that actual turnover declared in T+1 is €1.2 million for period 1 and €1 million for period 2, the actual compensation would be €420,000 for period 1 and €240,000 for period 2, i.e. a total of €660,000, a difference of €110,000 on the amounts initially estimated in the convention.

Tranche	Turnover period 1	Turnover period 2	Tranche %	Comp. Est. Period 1	Comp. Est. Period 2
1	€500,000	€600,000	20%	€100,000	€120,000
2	€500,000	€400,000	30%	€150,000	€120,000
3	€200,000	€0	85%	€170,000	€0
Total	€1,200,000	€1,000,000		€420,000	€240,000
Advance paid in T				€166,667	€180,000
Balance in T+1				€253,333	€60,000

Breakdown of actual turnover and relative compensation by tranche and calculation of balance - Product X

The actual balance payable at the end of period 1 would then be €253,333 for period 1 (€420,000 - €166,667), and €60,000 for period 2 (€240,000 - €180,000). Depending on the budget mechanism used, actual turnover may be declared one or two months after the end of the period, or several years later if inter-mutual data is used (AMI/IMA).

- **Rescheduling of turnover over the budget year**

The turnover figures of the companies are therefore communicated to the NIHDI after the close of the previous period. As periods cover different lengths of time, and start and end dates can fall at any time of the year, in order to make calculations based on budget years, the declared turnover figures need to be adjusted.

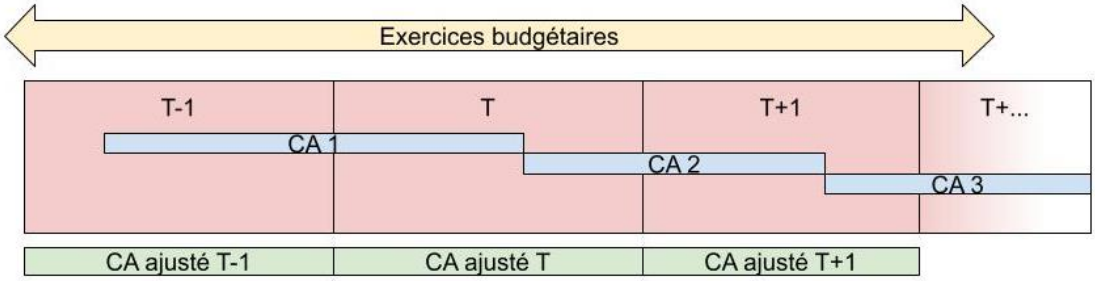

Diagram of declarations of turnovers and turnovers adjusted to the budget year

Turnovers adjusted to the budget year are therefore the sum of the portions or turnovers falling within the year in question. The declared portions of turnovers are turnovers multiplied by a ratio of the number of months falling within the budget year divided by the total number covered by the period to which the turnover relates.

The turnover figures used and summarised in this report are all turnover figures rescheduled to the budget year.

- **Use of dates**

Producing the various statistics on conventions means that a lot of different dates have to be used for reference. Theoretically, the conventions stipulate the deadlines by which advances and balances are supposed to be paid and turnovers declared. The actual dates on which these operations are carried out come after that. Finally, depending on the requirements, other dates may be used, such as the start and end dates of periods, the dates on which requests for reimbursement are submitted to the CRM, the date on which the convention is signed, the date on which the convention comes into force, or the date on which the convention expires.

129 - Appendix 3: ART 111/112/113 conventions

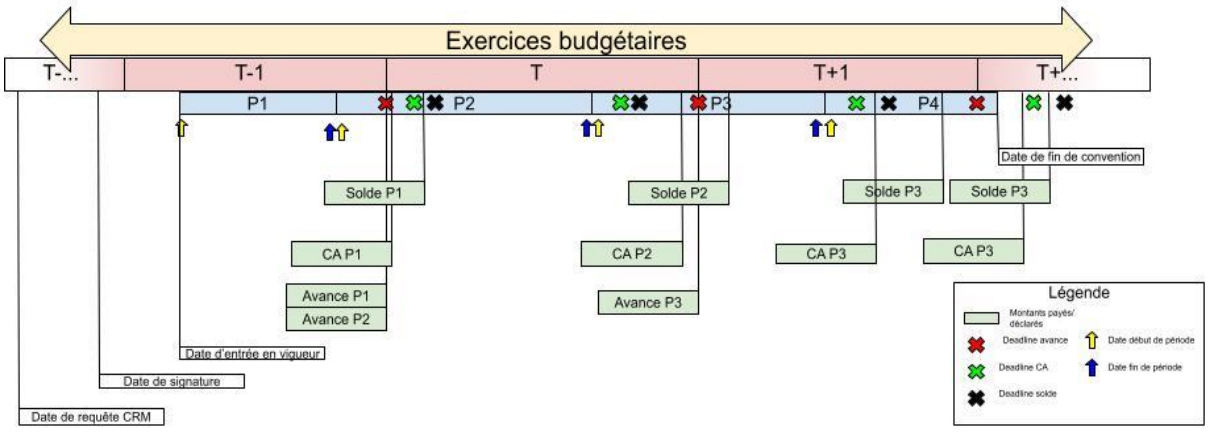

Diagram of the different dates within conventions

When the compensation is calculated, we refer to the actual dates of receipt/declaration of the amounts, not the expected deadlines. As shown in the diagram above, late declaration of turnover, for example, can lead to late payment of the balance. As such, if certain amounts are expected to be paid in a given year, we consider the amount to be allocated to the budget year of the actual payment date. When tables relating to the number of procedures are drawn up, depending on the question asked or the interest, the dates used may vary according to the date the MEA request was submitted to the CRM, the date of signature, the date of entry into force, any period dates or the end date of the convention. The statistics produced are therefore highly sensitive to the dates used, and a change in the grouping variable is likely to alter the results obtained to a greater or lesser extent.

LIST OF PHARMACEUTICAL SPECIALTIES UNDER CONVENTION IN 2024

The number of pharmaceutical specialties does not necessarily correspond to the number of current conventions, as a pharmaceutical speciality may have several conventions simultaneously. The dates associated with each pharmaceutical speciality represent, respectively, the lowest (old) and highest date among the conventions if a speciality has more than one.

Drug Name	first_date	last_date
ADTRALZA	01NOV2022	31MAY2026
AIMOVIG	01JUN2021	29FEB2024
AJOVY	01JUL2021	29FEB2024
ALECENSA	01SEP2022	31MAR2028
ALUNBRIG	01SEP2021	31AUG2025
ARIKAYCE	01JUL2022	30JUN2026
ASPAVELI	01APR2023	31MAR2026
BAVENCIO	01APR2021	31OCT2024
BESPONSA	01AUG2019	30APR2026
BLENREP	01JAN2022	30APR2024
BRAFTOVI	01NOV2019	30APR2026
BRILIQUE	01MAR2020	31AUG2024
BRUKINSA	01OCT2022	31AUG2026
BYLVAY	01OCT2022	30SEP2026
CABOMETYX	01JAN2018	31DEC2025
CALQUENCE	01NOV2021	31MAR2026
CIBINQO	01MAY2023	30APR2026
CUPRIOR	01JUL2021	28FEB2025
DACOGEN	01MAY2020	30APR2026
DARZALEX	01MAY2021	31OCT2026
DUPIXENT	01JUN2020	31MAY2026
ELIQUIS	01MAY2020	31OCT2026
EMGALITY	01JUL2021	29FEB2024
EMPLICITI	01SEP2017	30APR2024
ENHERTU	01JUL2023	30JUN2026
EPCLUSA	01JAN2017	31DEC2025
ERLEADA	01SEP2021	30APR2027
ESBRIET	01DEC2022	31MAR2025
EVRYSDI	01JUN2022	31DEC2025
EYLEA	01JUN2022	31MAR2025
FAMPYRA	01FEB2022	31JUL2026

FARYDAK	01DEC2016	30APR2024
FORXIGA	01FEB2022	31JAN2027
GAVRETO	01JAN2023	31AUG2024
GIVLAARI	01JUL2021	30JUN2027
HARVONI	01DEC2015	31DEC2025
HEMLIBRA	01MAR2020	28FEB2027
HOLOCLAR	01MAY2017	31OCT2025
IDEFIRIX	01JUN2023	31MAY2026
ILARIS	01JUL2018	30JUN2025
IMBRUVICA	01DEC2021	30NOV2024
IMFINZI	01APR2021	31DEC2026
IMNOVID	01SEP2018	31MAR2024
INVOKANA	01AUG2021	30JUN2025
JAKAVI	01MAR2018	31AUG2025
JARDIANCE	01JUN2022	31JAN2027
KADCYLA	01AUG2022	31JUL2026
KAFTRIO	01SEP2022	31AUG2026
KALYDECO	01OCT2019	31AUG2026
KERENDIA	01FEB2023	31JAN2026
KEYTRUDA	01APR2021	31DEC2026
KIMMTRAK	01NOV2023	31OCT2026
KYMRIAH	01JUN2019	31MAY2024
KYPROLIS	01NOV2016	31MAR2024
LEQVIO	01MAY2022	31JAN2024
LIBTAYO	01APR2021	31DEC2026
LIXIANA	01MAY2020	31DEC2026
LOKELMA	01SEP2021	31MAR2024
LORVIQUA	01JAN2021	31AUG2026
LUXTURNA	01APR2021	31MAR2027
LYNPARZA	01MAY2020	30SEP2027
MAVENCLAD	01AUG2018	30JUN2024
MAVIRET	01JAN2018	31DEC2025
MAYZENT	01NOV2021	30APR2026
MEKTOVI	01NOV2019	30APR2026
MINJUVI	01NOV2023	31OCT2026
NINLARO	01OCT2017	30APR2024
NUBEQA*	01OCT2021	30APR2026
NUSTENDI	01FEB2022	28FEB2025
OBIZUR	01NOV2017	31AUG2024
OCREVUS	01JUL2019	31MAY2024
FOEN	01JUL2022	30JUN2025
OLUMIANT	01JUN2022	30APR2026
ONIVYDE	01MAY2019	31MAR2024
ONPATTRO	01DEC2019	30NOV2026
OPDIVO	01APR2021	31DEC2026
ORKAMBI	01APR2021	31AUG2026
OXLUMO	01JUN2023	31MAY2026
PADCEV	01MAR2023	28FEB2026
PALEXIA	01APR2022	31AUG2024
PEMAZYRE	01JUL2022	30JUN2028
POTELIGEO	01MAY2021	30APR2025
PRADAXA	01MAY2020	31OCT2024
PRALUENT	01APR2022	28FEB2027
PREVYMIS	01DEC2022	30NOV2025
PROCYSBI	01FEB2020	31JAN2027
QARZIBA	01APR2020	31MAR2026
RAVICTI	01MAY2023	30APR2026
RAXONE	01SEP2019	31OCT2024
REPATHA	01MAY2017	29FEB2028
RETSEVMO	01MAR2022	31DEC2027
REVESTIVE	01JUN2021	31MAY2025
SARCLISA	01APR2022	31MAR2024
SOLIRIS	01AUG2022	31OCT2027
SOVALDI	01JAN2015	31DEC2025
SPINRAZA	01SEP2018	31JAN2024
SPRAVATO	01JUN2021	31MAY2024
TAFINLAR	01MAY2021	30APR2026
TAGRISSO	01SEP2021	30JUN2027
TAKHZYRO	01JUL2022	30JUN2026

TALZENNA	01JUL2021	30JUN2025
TARGAXAN	01DEC2018	30NOV2025
TECARTUS	01DEC2022	30NOV2025
TECENTRIQ	01APR2021	31DEC2026
TECVAYLI	01SEP2023	31AUG2026
TRODELVY	01JAN2023	31DEC2025
TUKYSA	01OCT2023	30SEP2025
UPSTAZA	01NOV2023	31OCT2026
VENCLYXTO	01JAN2022	30JUN2024
VERZENIOS	01JUN2019	30APR2026
VOSEVI	01JUN2018	31DEC2025
VOTUBIA	01AUG2016	31DEC2024
VYNDAQEL	01OCT2021	31AUG2025
XARELTO	01APR2020	30APR2024
XTANDI	01MAY2022	30JUN2027
YERVOY	01JAN2020	31DEC2025
YESCARTA	01MAR2021	30NOV2025
ZEPATIER	01JAN2017	31DEC2024
ZEPOSIA	01DEC2021	30NOV2027
ZOLGENSMA	01DEC2021	30NOV2027

Table 70: List of specialties reimbursed under art 111/112/113 conventions in 2024

Appendix 4: List of savings measures applied in 2024

MEASURES APPLIED FOR OLD DRUGS/BIOLOGICAL DRUGS

01.01.2024: (30621)

- Rufinamide (2058) 19.75% partial reduction EU6
- Tadalafil (2054) 19.75%

01.02.2024: (-)

- Perflutren, human albumin microspheres (42534) 20% no reduction because EU6

01.03.2024: (30636)

- Fingolimod (2064) 25% (partial reduction EU6 for GILENYA 0.25 mg 01541286) (complete reduction 01.04.2024 (R))
- Fondaparinux (1637) 20% partial reduction EU6

01.04.2024: (30649)

- Etravirine (1991) 20%

01.05.2024: (30657)

- Follitropin-alpha (biosynthetic follicle-stimulating hormone)(650) 20%
- Rivaroxaban (2000) 35% partial reduction EU6 (complete decrease on 01.06.2024 (R))

01.06.2024: (30668)

- Canakinumab (2070) 25% no reduction because EU6
- Velaglucerase alpha (2069) 20%

01.08.2024: (30684)

- Ustekinumab (2038) 35% partial reduction EU6 (complete reduction on 01.09.2024 (R))

01.09.2024: (30693)

- Romiplostim (1999) 25% partial reduction EU6

01.11.2024: (30708)

- Certolizumab pegol (2023) 25%
- Saxagliptine (2024) 20%

01.12.2024: (30715)

- Asenapine (2108) 20% no reduction because EU6
- Moroctocog alpha (2109) 20% partial reduction EU6

REFERENCE REIMBURSEMENT APPLIED:

01.01.2024: (30623)

- Risperidon (inj). (1821) 27,90% (end of exception)

01.02.2024: (30630)

- Calcipotriol + Betamethason (1929) 44.75% (ENSTILUM discontinued)

01.04.2024: (30650)

- Atosiban (52) 44.75%

- Fingolimod (2064) 44.75% + end of EU6 exception for GILENYA 0.25 mg 01541286
- Paliperidone (inj.)(1975) 27.90% (end of exception)

01.05.2024: (30662)

- Carteolol (107) 44.75%

01.06.2024: (30669)

- Rivaroxaban (2000) 44.75% + end of EU6 exception (deferred phasing out of XARELTO except for 2.5 mg dosage)

01.07.2024: (30676)

- Plerixafor (2013) 51.52%

01.09.2024: (30688)

- Ustekinumab (2038) 26.60% + end of EU6 exception (13.30% + end of exception EU6 for STELARA 130 mg). STELARA ORIFARM discontinued

01.11.2024: (30705)

- Bosutinib (2146) 63.64% (R + OLD)
- Dabigatran etexilate (2002) 44.75%

Tiotropium (1658) 44.75% (deferred phasing out of SPIRIVA)

01.12.2024: (30714)

- Levodopa + Carbidopa (1863) 27.82% (exception)

MO INDEX (ENTRY INTO FORCE: 1 JANUARY 2024)(30620)

- The basic fee for pharmacists was indexed as of 1 January 2024. The amount increased from €4.77 to €5.06 (excluding VAT).
- The wholesaler's margin was also indexed by 6.05%.
- The pharmacist's margin was not indexed.
- The ceilings for the personal intervention were not indexed.

MO MEASURES (ENTRY INTO FORCE: 1 JANUARY 2024)(30622)

A reference reimbursement system set up for biological medicines (8.25% reduction with no EU6 price floor)

- Adalimumab (1667) 8.25% (R biological)
- Bevacizumab (1809) 8.25% (R biological)
- Eculizumab (1992) 8.25% (R biological)
- Enoxaparin (249) 8.25% (R biological)
- Epotin alpha (r-HuEPO alpha) (1143) 8.25% (R biological)
- Etanercept (262) 8.25% (R biological)
- Filgrastim (286) 8.25% (R biological)
- Infliximab (383) 8.25% (R biological)
- Pegfilgrastim (1651) 8.25% (R biological)
- Ranibizumab (1762) 8.25% (R biological)
- Recombinant growth hormone (somatropin) (651) 8.25% (R biological)
- Rituximab (666) 8.25% (R biological)
- Teriparatide (1687) 8.25% (R biological)
- Trastuzumab (756) 8.25% (Biological R)

Change in tranches of turnovers and reduction percentages for the "old medicines" measure (with regularisation and EU6 floor price)

REVISION OF THE "JAK INHIBITORS' GROUP' (1 JULY 2024 – MB STANDARD 20240701 (30677))

Changes in reimbursement conditions (with some price reductions)