FRENCH HEALTHCARE PRODUCTS PRICING COMMITTEE

2014/2015 ANNUAL REPORT

September 2015

CONTENTS

ILLUSTRATIONS

INTRODUCTION

The French Healthcare Products Pricing Committee (CEPS), an interministerial and interinstitutional organisation under the joint authority of the French Ministries for Health, Social Security and the Economy, is primarily tasked by the law with the pricing of medicines and setting of tariffs for medical devices for single patient use as well as procedures reimbursed by compulsory health insurance.

Via its proposals, CEPS also helps to define the pricing policy concerning healthcare products.

Pursuant to Article D. 162-2-4 of the French Social Security Code, CEPS submits an annual report on its work to the French Ministries for Health, Social Security, the Economy and Industry. Article L. 162-17-3 of the French Social Security Code stipulates that this report must also be submitted to Parliament.

This report describes the Committee's main activities through 2014.

It contains a preliminary chapter addressing some topical issues and presents data sets over a long period. Mindful of providing ever more detailed information about how it works and its results, the CEPS presents an educational document in this chapter made up of FAQs, along with the corresponding answers.

Part One is devoted to describing the market (Chapter I) and trends concerning healthcare product expenditure (Chapter II).

Part Two looks at the measures regulating healthcare product expenditure and sanctions. Chapter I concerns the setting of healthcare product prices and tariffs and the affiliated clauses. Chapter II covers tariff reductions and changes to the reimbursement conditions.

Part Three presents statistics on the Committee's work, the case files processed in Chapter I and the processing times for these case files in Chapter II.

CEPS makes it decisions in a collegiate manner, in line with the guidelines it receives publicly from the Ministries. The guidance letter dated 2 April 2013 is attached in Appendix 1 hereto; it gives an account of how these guidelines have been put into practice.

Healthcare product price or tariff setting is preferably carried out via agreements signed with the companies marketing the products or, for some medical devices, with the professional organisations representing these companies.

The Committee's decisions are submitted for verification by the Administrative Judge.

The complete doctrine concerning the running of the Committee is presented in Appendices 4 and 5 hereto. The main clauses which may bear upon contractual pricing are also presented in Appendix 7.

The Committee has implemented its main mission guaranteeing patients' access to products by processing more than 500 case files in 2014 concerning reimbursable medicines issued in community pharmacies. 320 of the files closed in 2014 concerned listings with pricing, 124 re-listings and 20 extended medicine indications.

In the same way, the Committee made 122 medical device pricing decisions.

Mindful of presenting the principles of how it works and the results, since 2012 the Committee has published the list of products for which the Transparency Commission has not granted improvement in medical benefit, containing the prices set (see Appendix 9).

Efforts to bring prices down after they pretty much doubled in 2012[1] compared with the years before have continued at more or less the same level as in 2013 and 2014, accounting for almost a third of the savings planned to meet the National Health Insurance Expenditure Target (ONDAM). The resulting price changes placed a considerable burden on the activities of the Committee, which must continue to operate within its constant means.

Lastly, for the third year this report makes a contribution to international price referencing (or benchmarking, see Appendix 8). The national price trends, monitored by the French National Institute of Statistics and Economic Studies (INSEE), are also presented at the end of the introduction.

1 to more than EUR 900 million for the medicines sector

INTRODUCTION: TOPICAL ISSUES

CEPS is authorised to negotiate and set the prices of healthcare products. In this regard, it processes around **1,500 medicine case files every year**[2] and some **150 medical device case files.** CEPS aims to provide access to these products at the very best possible cost for the community.

Indeed, these often complex negotiations have enabled **access to all of the innovative medicines that have become available over the past three years**, for the benefit of patients: whether these concern anticancer drugs (e.g. Zelboraf®, Yervoy®, Jevtana®, Zytiga®, Xtandi®, Perjeta®, Kadcyla®, Imnovid®, and Adcetris®), orphan drugs (Kalydeco®, Soliris®) or antiviral drugs (e.g. Sovaldi®, Harvoni®, Daklinza® and Olysio®).

The **very best possible pricing conditions** have, in most cases, been met, with the lowest prices in Europe at face value, one example being the hepatitis C (HCV) medicines in 2014 and, what's more, these prices go hand in hand with significant clawback payments. This report (Appendix 8) provides new information regarding international price referencing. As for clawback payments, the negotiations held with companies can, where necessary, lead to the drawing up of clauses in agreements that are aimed at regulating reimbursement expenditure, either in terms of pricing or responsible use (Chapter 1, Part Two of this report).

Text box 1: Look back at the price negotiations for direct acting antiviral drugs treating HCV

Available under a temporary authorisation for use (ATU) since 27 September 2013, Sovaldi® (sofosbuvir) was awarded a marketing authorisation (MA) on 17 January 2014, with the indication "to treat chronic hepatitis C infection in adults". Laboratoire Gilead applied for eligibility for reimbursement on 23 January. The opinions of the Transparency Commission and the Public Health and Economic Evaluation Commission of the French National Authority for Health (HAS) were published in April and May 2014. After receiving a request from the Ministry for Health, the HAS college issued a recommendation on "Treating hepatitis C with direct-acting antiviral medicines" at the end of June. On the basis of all these documents, CEPS began a series of consultations in July with experts and patients' associations, who would be heard officially in September. The negotiations with Gilead got underway in July and were brought to a close in September and October. Sovaldi®'s inclusion on the list of products reimbursed to local authorities was published on 30 October. Reimbursement for the direct sale of medicines to outpatients by hospital pharmacies (*rétrocession*) was published on 4 November. The rider to the agreement setting the price was signed by the CEPS Chairman and Gilead on 17 November, and the price notice was published on 20 November.

Fundamentally, Sovaldi® was therefore available under a temporary authorisation for use (ATU), and then under "post ATU" terms (once the MA had been awarded) until it was listed as eligible for direct sale to outpatients by hospital pharmacies and its price was set, on the basis of a fee determined freely by Gilead, at EUR 18,667 a pack, i.e. a standard three-month treatment cost of EUR 56,000. Thanks to the negotiations that CEPS held, it was possible to bring the price of a pack down to EUR 13,666 (a 27% reduction on the initial fee), and the cost of a standard three-month treatment therefore fell to EUR 41,000. The French price thus reached is the lowest of the prices practised in the four countries usually taken for comparison: Spain (EUR 42,000), Italy (EUR 45,000), UK (EUR 44,660, at the GBP exchange rate in November 2014) and Germany (EUR 49,000). What's more, CEPS was also able to negotiate clawback payment clauses associated with sales volumes and product performance, monitored in real-world conditions on the basis of a single indicator (eradication of the viral load) and a large cohort of patients (Hépater-ANRS cohort), which guarantee a much lower net price than the price at face value.

Lastly, the reimbursement of Sovaldi is part of a broader movement of direct-acting antivirals (DAAs) entering the market; when such products are used in combination, they guarantee greater efficacy. Two distinct antivirals, Daklinza® (daclatasvir) by BMS, and Olysio® (simeprevir) by Janssen, were registered in May 2015. Gilead's Harvoni, the first once-daily fixed-dose combination therapy (sofosbuvir-ledipasvir), was listed for direct sale to outpatients by hospital pharmacies with a price set in June 2015. Like Sovaldi®, its price is the lowest in Europe (EUR 46,000 for three packs, versus EUR 47,000 in Spain, EUR 50,000 in Italy and EUR 54,345 in Germany – the product is still being assessed in the UK) and similar clawback payment clauses to Sovaldi's are applicable. The price of the second antiviral, combined with sofosbuvir to form Harvoni®, accounts for less than 11% of the whole price. By combining Exviera® and Viekirax® by Abbvie®, whose prices were published in August 2015, an already significant amount (around 10%) can be shaved off the price of combinations, compared with Harvoni®.

[2] first listings, re-listings, extended indications and price changes

In all, the new DAAs whose efficacy is well-established (sustained virological response/SVR rate of over 90% of cases according to the clinical trials) and which are well-tolerated, with a much shorter treatment duration than previous-generation products, nevertheless incur very high expenditure due to a high number of patients treated since 2014. Beyond the results of the negotiations held, CEPS is implementing two legislative mechanisms that are helping to significantly cut this expenditure:
- Firstly, pursuant to Article 48 of the French Social Security Financing Act (LFSS) for 2014, CEPS is calling for a clawback payment corresponding to the difference between the price set and the fee previously practised by the laboratory – applied to the volumes sold by the laboratory during the ATU/post ATU period,
- Secondly, CEPS is implementing the provisions of the LFSS for 2015 with application in the 2014 financial year so that, beyond a certain amount (set for 2014 at EUR 450 million and for 2015 at EUR 700 million), expenditure associated with hepatitis C treatment can be reined in. To this end, laboratories can choose to make clawback payments to CEPS instead of the progressive contribution provided for by the legal texts (see below).

Its primary mission aside, CEPS makes a significant contribution to responsible healthcare product use, assessment and forward-looking policies, to a richer and more transparent agreement framework and, more broadly, to drafting the healthcare product pricing policy and to balancing the accounts of *l'Assurance Maladie* (French national health insurance body).

Contribution to responsible healthcare product use

In 2014 CEPS signed a **new pharmaceutical promotion charter**, which is analysed in detail in this report and the purpose of which is to gain a clearer idea of promotional practices and, where necessary, to enable their control should a problem arise. An observatory in common with LEEM (the pharmaceutical companies' trade association in France) is currently being set up.

Moreover, some 200 medicines and 50 medical devices are regulated through **contractual clauses**, some of which explicitly concern responsible product use: particularly with respect to posology through the daily treatment cost, or compliance with the marketing authorisation indications through sales volume monitoring.

Lastly, over the past few years CEPS has developed **so-called performance contracts** aimed at checking that products are just as effective "in real life" as they are during clinical trials. If they are not, the prices are cut and clawback payments on the turnover achieved may be requested. An example of this kind of contract was signed in 2014 with Gilead (for Sovaldi® and Harvoni®, indicated in the treatment of hepatitis C), or with Celgene (for Imnovid®, medicine indicated to treat multiple myeloma) which will make clawback payments if the efficacy level demonstrated in clinical trials is not achieved in real life.

Contribution to assessment and forward-thinking policy in the field of healthcare products

In 2013, CEPS set up a **committee for monitoring real-world studies on medicines** in partnership with the HAS, so as to guarantee the successful completion of studies requested of laboratories. An equivalent committee for medical devices has been active since 2011. These particularly worthwhile initiatives provide a much more specific framework for the monitoring requirements of studies in progress. This report reports on how these committees are run.

Since the turn of 2014, CEPS has received opinions from the HAS assessing the **efficiency** of innovative products, and been able to use these opinions on several occasions to step up its requirements as regards companies and obtain lower prices at face value or more significant clawback payments.

Lastly, in early 2015, CEPS set up a **foresight committee on medical innovation**, making use of the appendices to agreements signed by laboratories and rounding this information off with hearings, which are still ongoing, with the main firms who have to present their research policies.

Contribution to the agreement framework and transparency of healthcare product policy

The agreement framework set up with the medicine and MD union spokespersons makes it possible to discuss most of the issues concerning pricing regulation in these sectors at regular intervals. CEPS has particularly overseen the **implementation of the framework agreement signed with LEEM in December 2012 and which is**

currently being renegotiated, as well as the framework agreement of December 2011, concerning medical devices.

The **annual report is constantly being added to** and now represents a public information document that goes a long way to ensuring the transparency of the work CEPS does. Since the 2012 report (submitted in 2013), CEPS thus now publishes the list of new ASMR 5 (improvement in medical benefit) products with their price[3], information on international price referencing of medicines[4], a summary of the pricing doctrine and a presentation of the main "product" clauses used. Long-term data is made available and this report now includes information that is often asked for about how CEPS is run, in the form of FAQs, for the first time (see below).

Lastly, in a context where vigilance is crucial, CEPS has long kept a **constant eye on public declaration of interest (PDI) procedures,** backed up by a specific legal text (L 162-17-3 French Social Security Code/CSS). These are monitored and updated at regular intervals by all CEPS members – people involved in the work, secretariat staff and rapporteurs. They can be found on the Ministry for Health's website. That said, given that the CEPS structure is primarily administrative in nature, it only lists a small number of conflicts of interest. A summary of the PDIs is traditionally appended to the annual report.

Contribution to drafting the healthcare product policy

Of course, pursuant to the guidance letter dated April 2013, **CEPS takes part in ministerial and interministerial work** within its means: it is thus a stakeholder in the March 2015 generics development plan, a member of the ONDAM steering committee, playing a part in the work of the Health Industries Strategic Council (CSIS) and has made a significant contribution to the discussions held by the mission entrusted to D. POLTON on healthcare product assessment.

Furthermore, the **MEDIMED database**, kept by CEPS and which had to be reconfigured in its entirety in 2014 as part of the decision to do away with the "vignette" price information sticker, is now the **national source for medicines prices.** This supplies information to the national public database on medicines (http://base-donnees-publique.medicaments.gouv.fr/). It is updated and forwards information daily to all of the software publishers, and community pharmacies use it as the basis for invoicing medicines.

Contribution to improving the balance of *l'Assurance Maladie*

This is a sizeable contribution.

Price and tariff reductions have doubled since 2012. CEPS has reduced the prices of medicines by EUR 400 to 500 million every year between 2007 and 2012. Since then, price reductions have reached 900 million, affecting both generic and original products as well as biological medicines. Since 2014, CEPS has developed a doctrine tailored to the pricing of biosimilars, presented below, aimed at guaranteeing not only substantial savings but also the viability of use of such products.

The reductions in medical device tariffs represent EUR 70 to 80 million, i.e. an annual total of **some EUR one billion**.

The **clawback payments due under "product" clauses** amounted to EUR 519 million in 2014.

Lastly, given the expenditure incurred by reimbursing HCV medicines (with ATU or post-ATU status) in 2014, CEPS called for exceptional legal clawback payments[5].

In total, the contribution CEPS makes to balancing out the accounts of *l'Assurance Maladie* amounted to almost EUR 1.4 billion in 2013, EUR 1.8 billion in 2014 and probably more than EUR 1.6 billion in 2015 – so almost **EUR 5 billion in three years.**

Dominique Giorgi

[3] Attesting that these enable the regulations to be followed ("savings in the treatment cost")

[4] Listing of the comparisons published and, in the 2014 report, price referencing for the main products on the community and hospital markets as well as price referencing for the main generic groups (Appendix 8)

[5] EUR 76.5 million for HCV regulation (excluding clawback payments collected when there was no agreement with CEPS) and EUR 205 million for ATU and post-ATU clawback payments (see Chapter 1, Part Two)

Table 1: CEPS' contribution to balancing out the accounts of* l'Assurance Maladie*: summary

€M	2013	2014	2015
Price reductions for medicines	844	913	895(p)
MD tariff reductions	85	90	74(p)
Product clawback payments	427[6]	519	500(p)
Other ATU/Post ATU clawback payments and contractual HCV rate and "L" rates[7]	0	76.5 (HCV) + 205 (ATU-post ATU)	200(p)
TOTAL	1356	1803.5	1669(p)

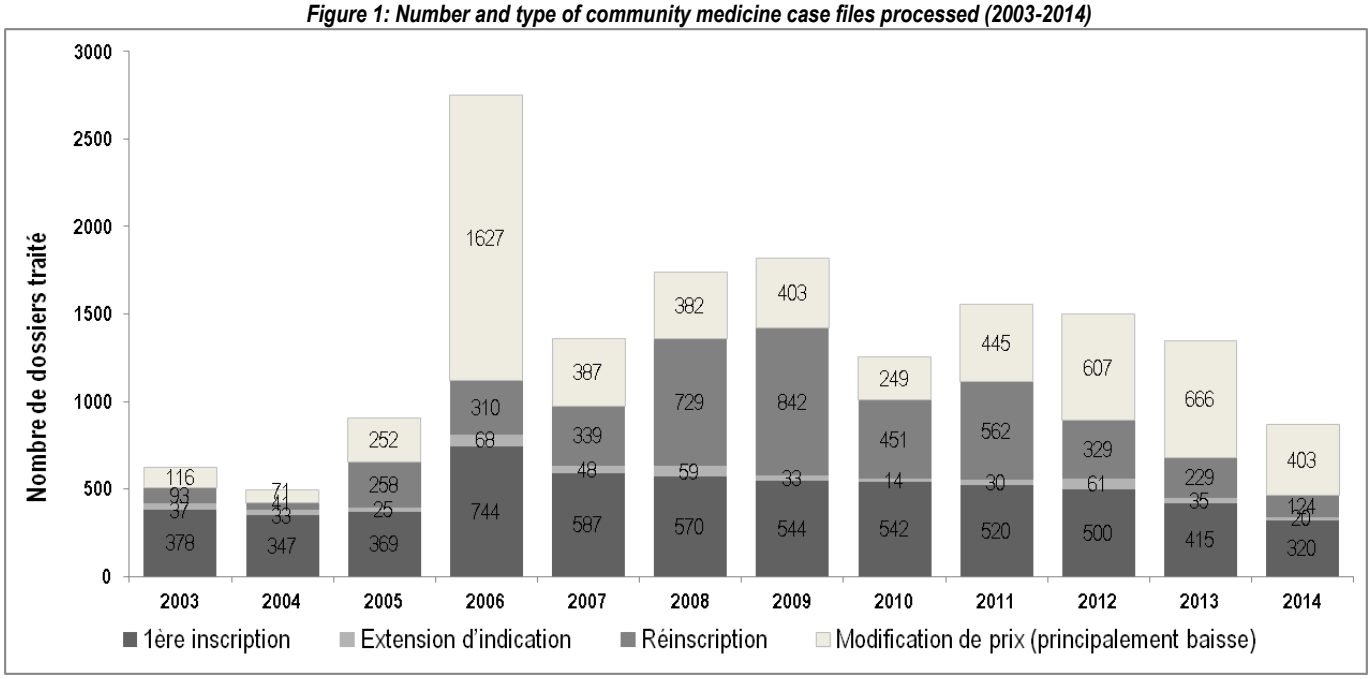
NB: The "other clawback payments for 2015" line is given for information only

[6]Incl. EUR 10 million for medical devices
[7]Excl. contributions collected where there was no agreement with CEPS. The "L" rate is the annual target growth rate for reimbursable medicine spending.

SIGNIFICANT STATISTICS CONCERNING THE RUNNING OF CEPS

DATA CONCERNING THE MEDICINES SECTOR

Figure 1: Number and type of community medicine case files processed (2003-2014)



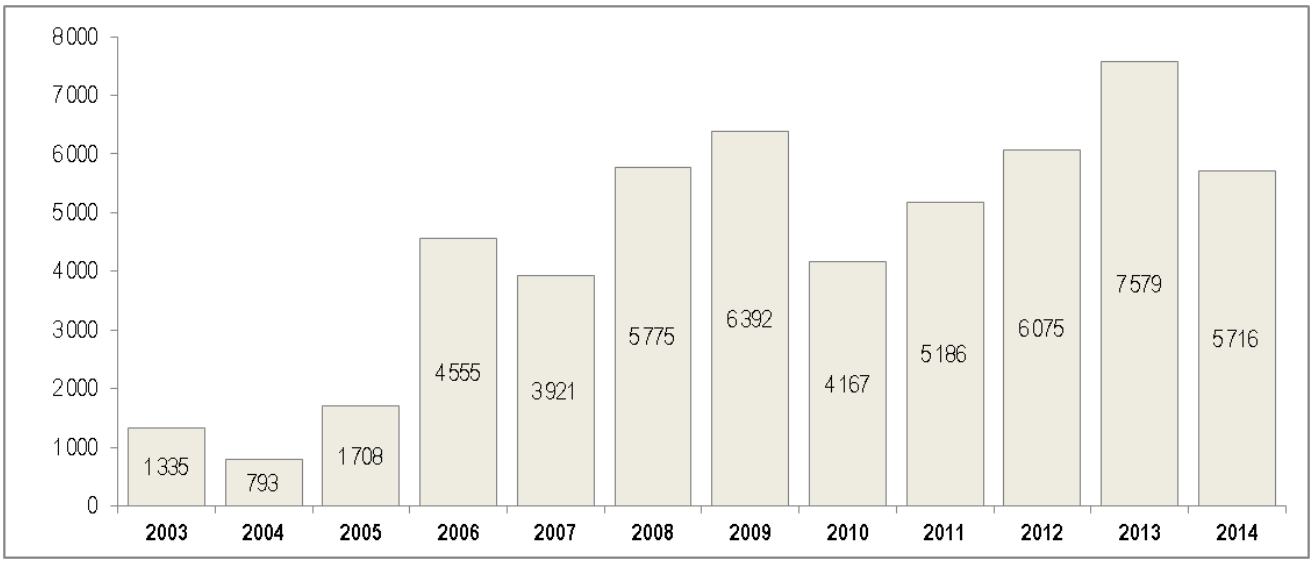
Source: CEPS

Note: 2006 was a particular year in that the list of generic medicines was extended, the number of generic-producing laboratories rose, there were many price reductions and quarterly packaging was introduced.

The number of community medicine case files processed by the Committee rose between 2003 and 2009 from 624 in 2003 to 1,822 in 2009. Since 2010, the number of case files processed per year has been falling. The changes made to the MEDIMED computer programme in 2014 meant that price reduction files could be generated that grouped together several proprietary medicines, and this is the primary explanation for the fall in the number of files observed.

The Committee's workload was increased by some members of the General Cabinet Office *(secrétariat général)* not being replaced, the secretariat moving offices and the problems encountered during some products' registration negotiations, and this may explain why fewer files were closed in 2014. The Committee has been working hard to make up for this backlog since the beginning of 2015.

Figure 2: Number of product formats associated with community-processed files per year since 2003



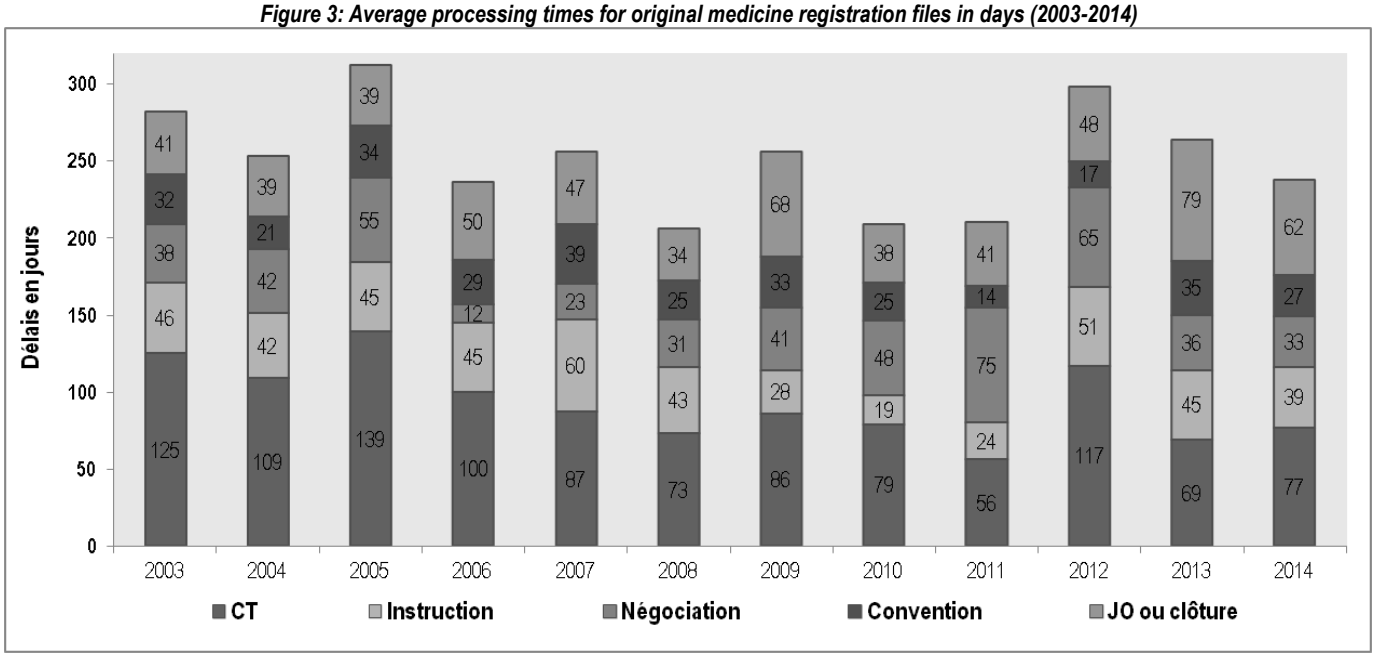
Source: CEPS

Although not as many files were processed, the number of product formats associated with these files has been rising steadily – up from 1,335 in 2003 to 7,579 in 2013. This increase is due to the fact that proprietary pharmaceuticals have more and more associated product formats, which comprise one or more variations in the presentation of the same molecule, depending on the dosage, packaging size and so on. The rise in the number of packaging items, with the introduction of large packaging in particular, along with price convergence operations per group (2012 and 2013), has brought about a much greater number of price changes.

See above for reasons why the number of files closed in 2014 fell.

CEPS lowered the price[8] of 3,386 product formats in 2012, 5,674 in 2013 and 4,459 in 2014, which means that around 30%[9] of product formats on the market were subject to a price change[10].

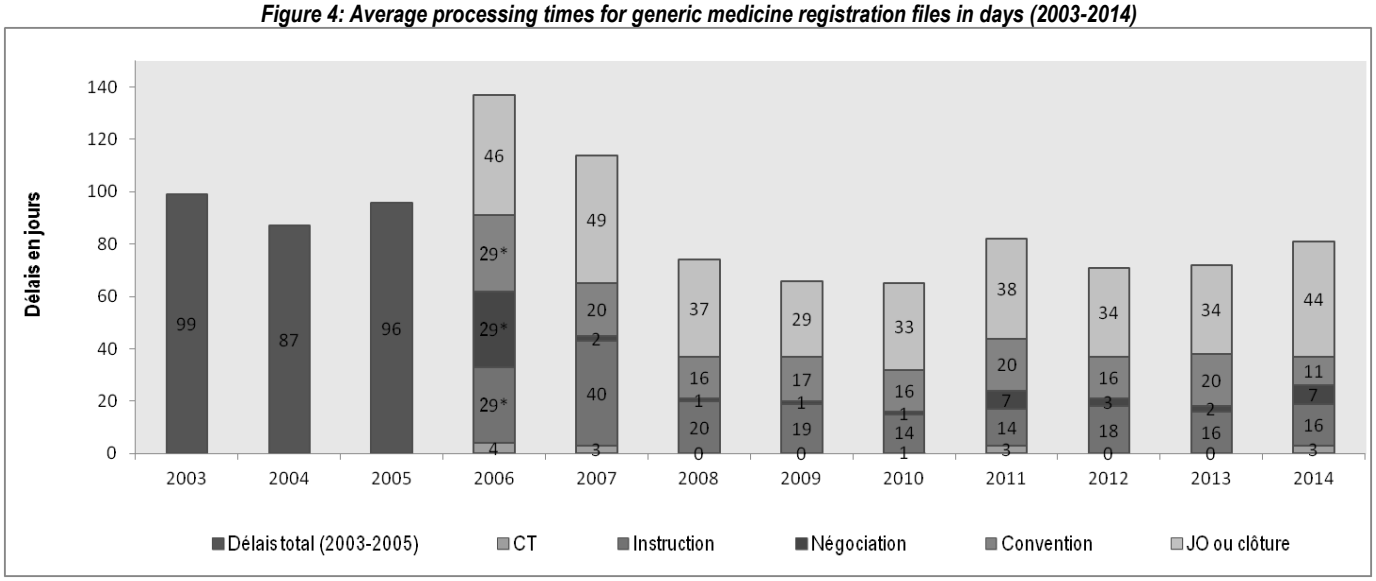
Figure 3: Average processing times for original medicine registration files in days (2003-2014)



Source: CEPS

[8] Change in the ex-manufacturer price (i.e. before tax) only (change in markup has not been taken into account)
[9] 15,401 medicine product formats are listed for reimbursement in the community sector (August 2015).
[10] The price revision rate will stay the same in 2015 (5,619 product formats were subject to price reductions between January and August 2015).

Figure 4: Average processing times for generic medicine registration files in days (2003-2014)



Source: CEPS

** in 2006 the total examination, negotiation and agreement time was 87 days. The different times spent on these separate stages are not listed.*

The processing times for non-generic medicine registration files varied between 206 days (2008) and 312 days (2005). The processing times for generic medicine registration files varied between 64 (2010) and 139 days (2006).

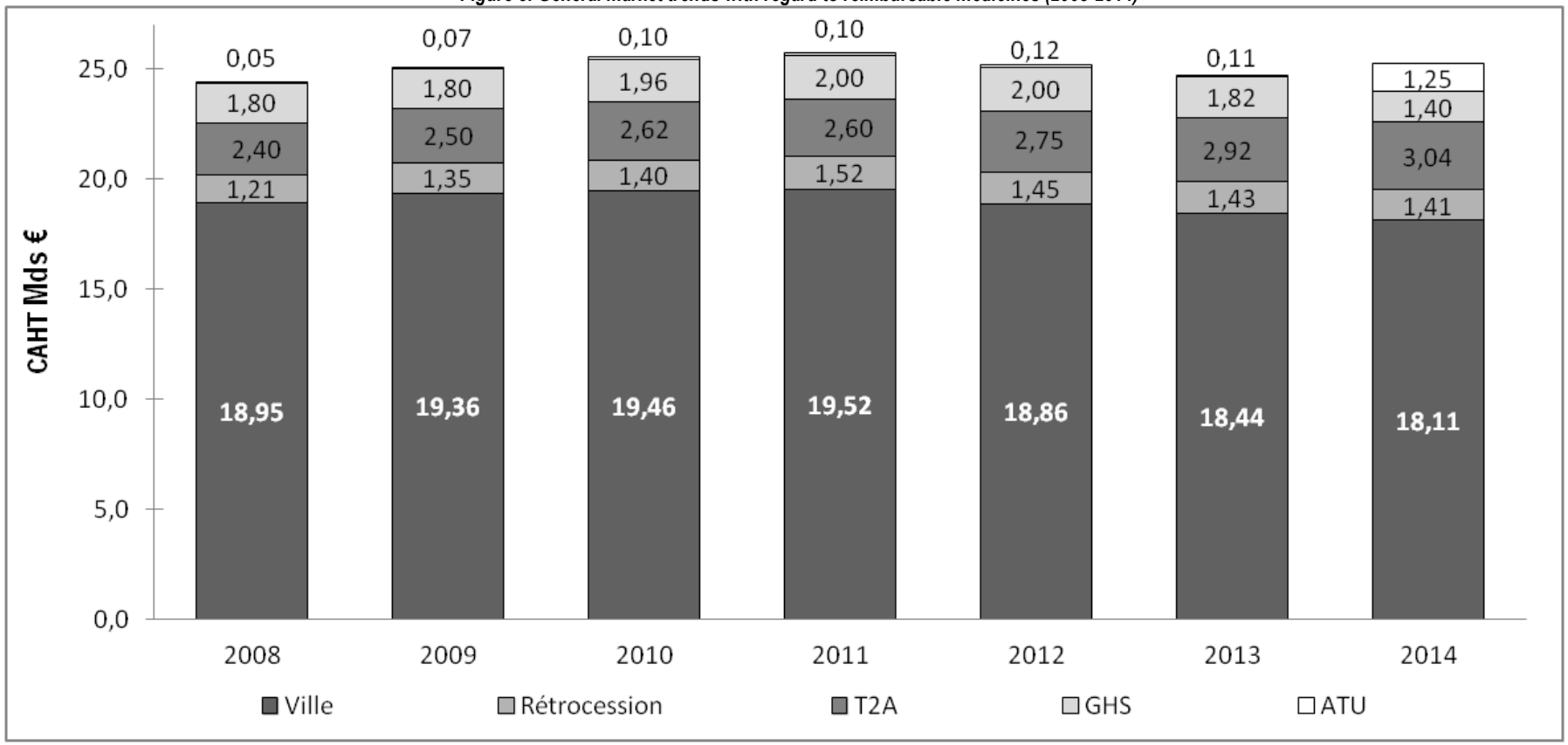
With regard to non-generic medicine files, between 2003 and 2013 the length of time each file processing stage took depended on the file's complexity and the number of files processed that year. On the whole, these times have remained stable overall since 2003 – at an average of 248 days.

The times taken to process generic registration files are much shorter on average than for non-generics, since the former do not have to be submitted to the Transparency Commission save in exceptional circumstances. What's more, the examination and negotiation stages do not take as long because there are already pre-established markdowns. The processing times for generic registrations fell between 2006 and 2009 and have since remained stable.

It is important to note that the vast majority of generics are registered before the reference molecule goes off-patent. Most of this processing therefore gets done before marketing becomes a possibility.

If it takes longer, the manufacturers' response times need to be factored in, and these may lengthen the processing times for some applications.

Figure 5: General market trends with regard to reimbursable medicines (2008-2014)



Source: GERS[11], ANSM[12], quarterly declaration, data processed by CEPS

The medicines market shrunk in 2012 (EUR 25.4 billion) and 2013 (EUR 24.7 billion). Only sales of medicines listed as able to be invoiced on top of "T2A" (diagnosis-related group [DRG]-based funding) fuelled market growth.

[11] Economic interest group of pharmaceutical companies, which produces market statistics
[12] French National Healthcare and Medicines Safety Agency

In 2014, sales of medicines dispensed in community pharmacies are still down, ever since 2012, after a stable year in 2011; sales of medicines intra-GHS (or intra-DRG) are down and direct sales to outpatients are stable (excluding those which are temporarily authorised for use). However, the overall market progressed in 2014 (EUR 25.2 billion) solely due to the skyrocketing sales of medicines which are temporarily authorised for use (i.e. with ATU status), borne along by HCV medicines.

Figure 6: Reimbursable market trends with regard to medicines dispensed in community pharmacies (2008-2014)

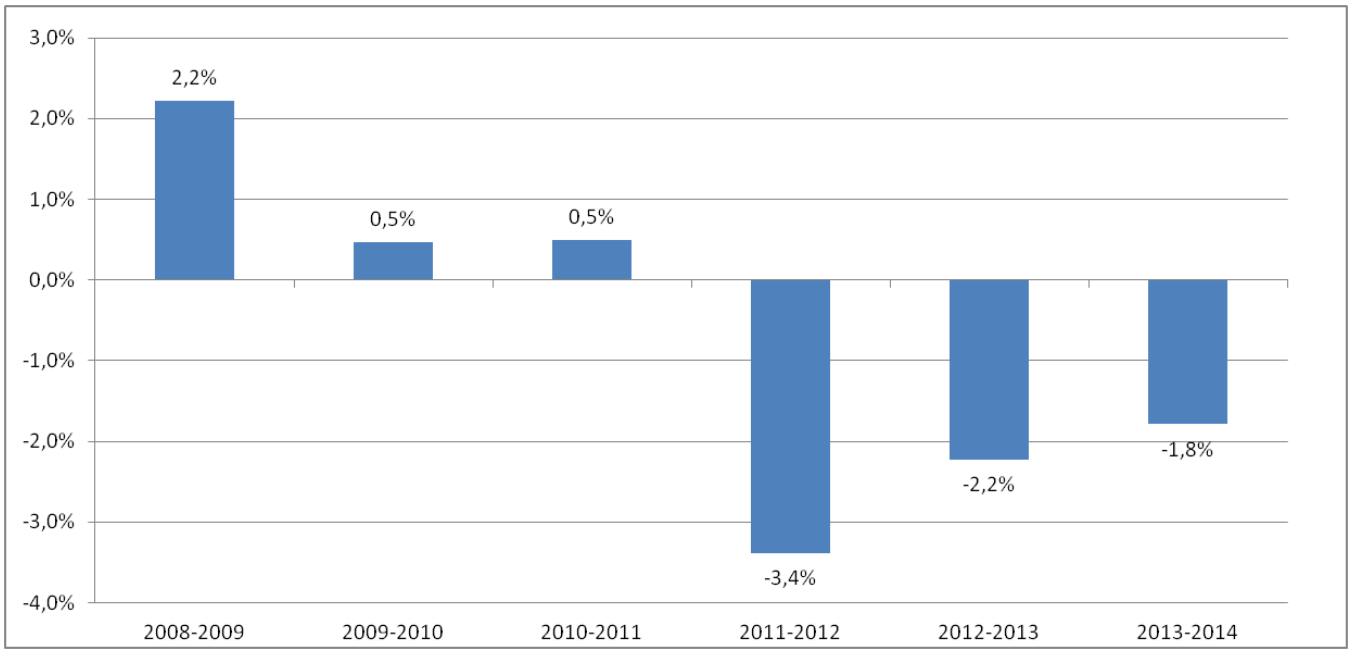


Figure 7: Market trends with regard to medicines listed as able to be invoiced on top of T2A (2008-2014)

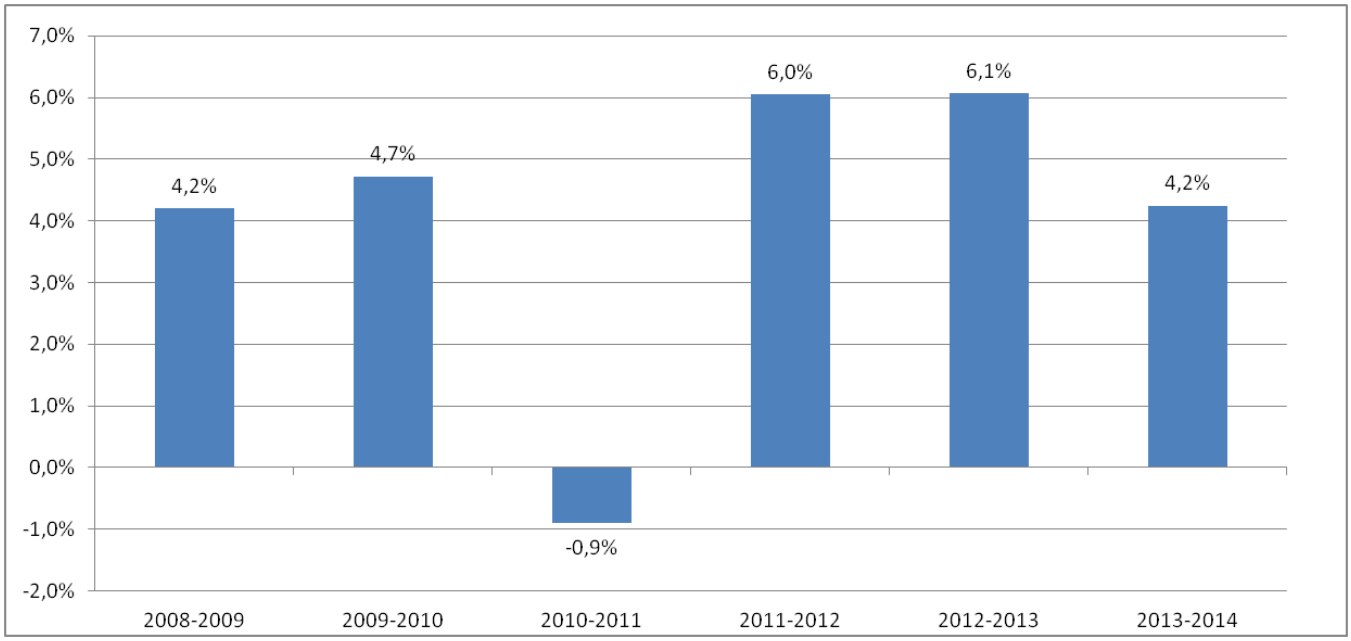
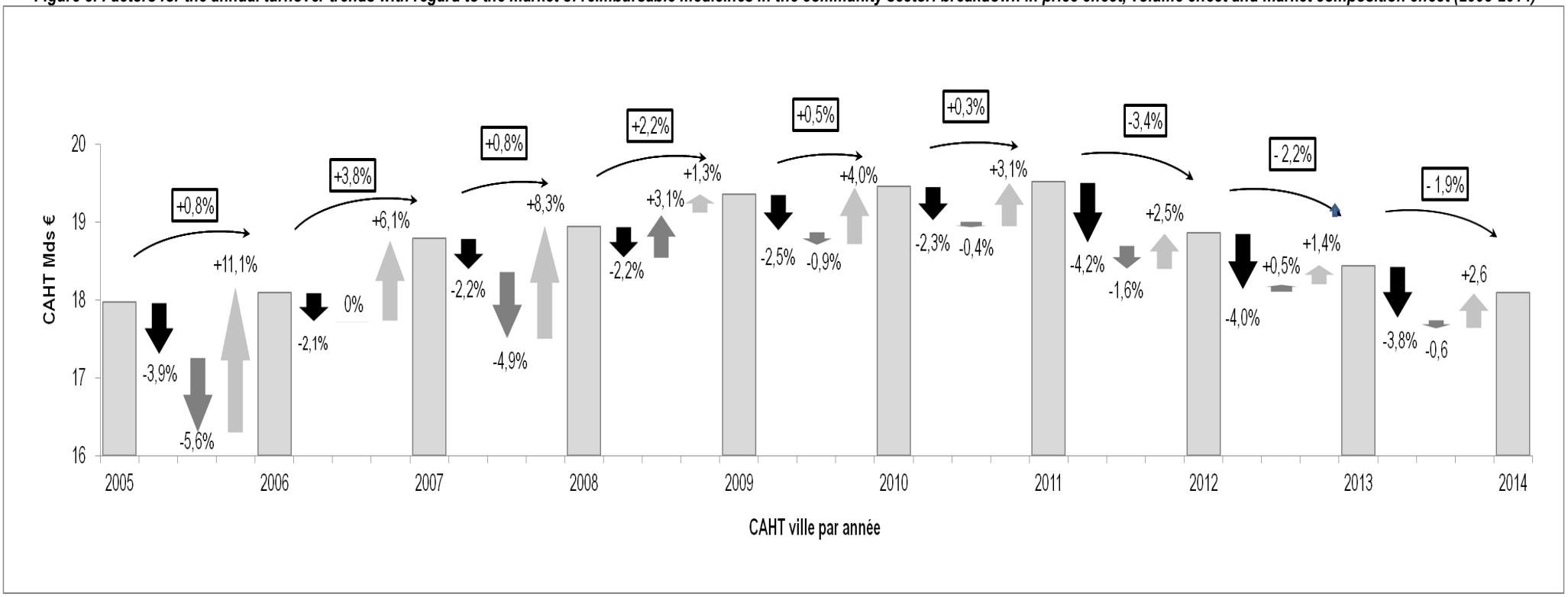
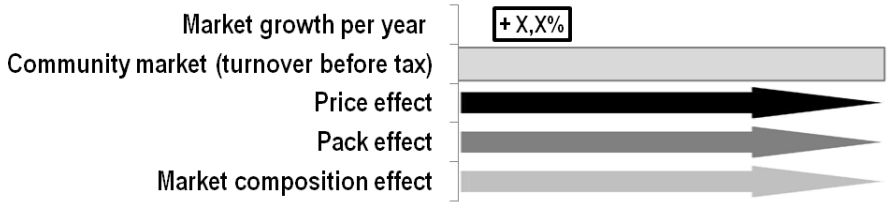


Figure 8: Factors for the annual turnover trends with regard to the market of reimbursable medicines in the community sector: breakdown in price effect, volume effect and market composition effect (2005-2014)



Source: GERS, data processed by DSS/6B



In a community market which slowed down (+0.5% in 2010, +0.3% in 2011) before losing ground (-3.4% in 2012, -2.2% in 2013, -1.9% in 2014), the various factors behind this are:

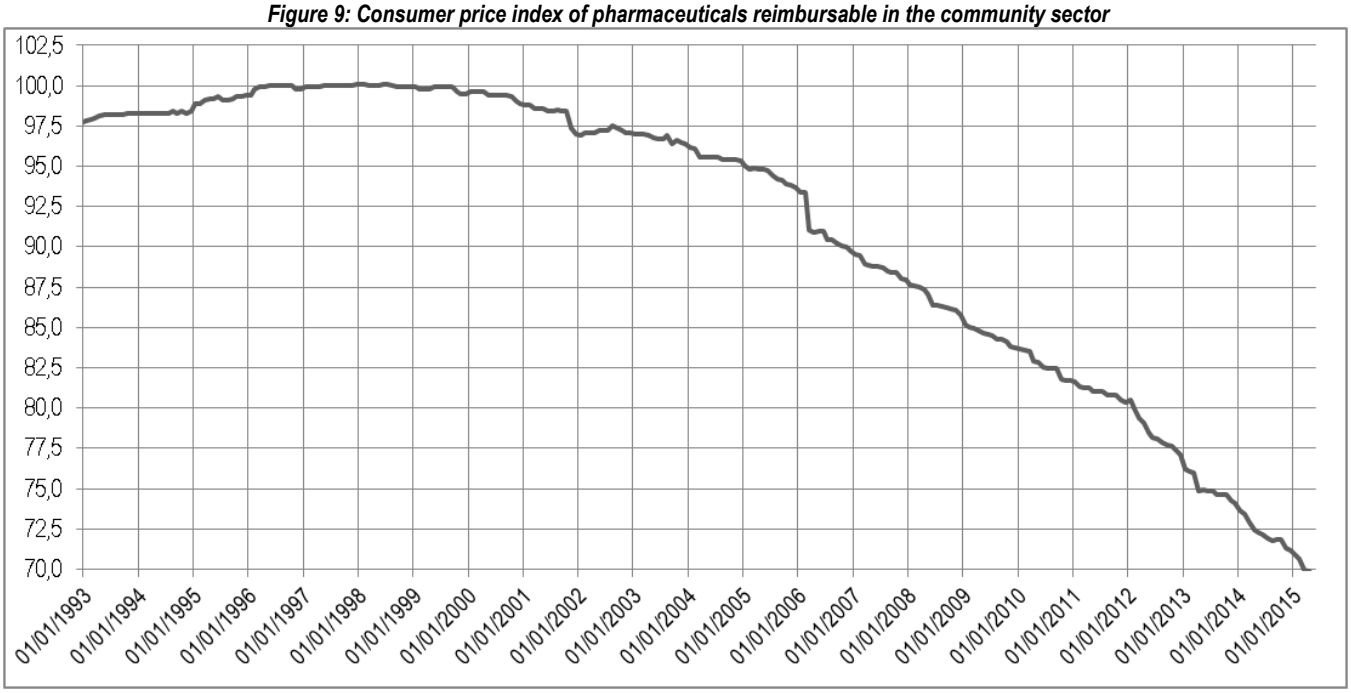
- The price effect, a direct reflection of CEPS' pricing work and the appearance of generics for blockbuster molecules, systematically plays a downward role; it is currently the main factor for controlling medicine expenditure, and its effect has been around -4% a year since 2012;

- The pack effect[13]: the rise in number of packs sold slowed so considerably in the second half of the 2000s, that it began to decline at the start of the next decade;

- The market composition effect is still the main factor influencing an upward market trend.

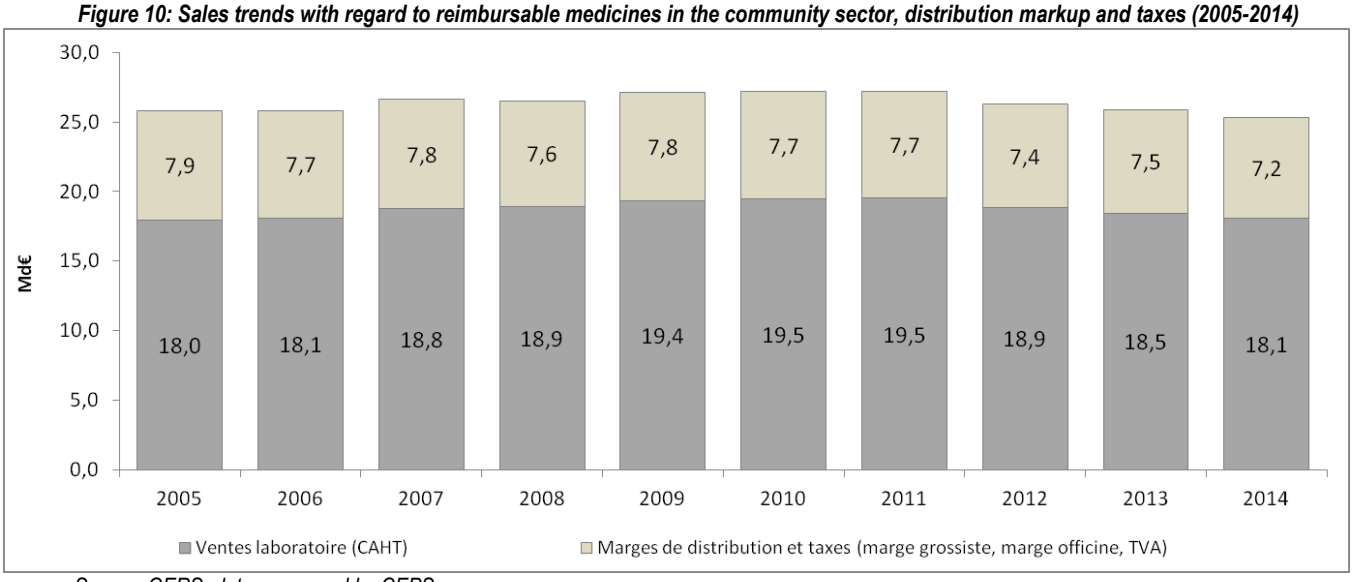
[13] The pack effect illustrated in this graph is not equivalent to a volume effect as it depends particularly on the size of packaging.

Figure 9: Consumer price index of pharmaceuticals reimbursable in the community sector



Source: INSEE[14] (monthly, all households, mainland France + overseas départements*, base 1998) - Nomenclature COICOP: 06.1.1.1 - Pharmaceuticals)*

Figure 10: Sales trends with regard to reimbursable medicines in the community sector, distribution markup and taxes (2005-2014)

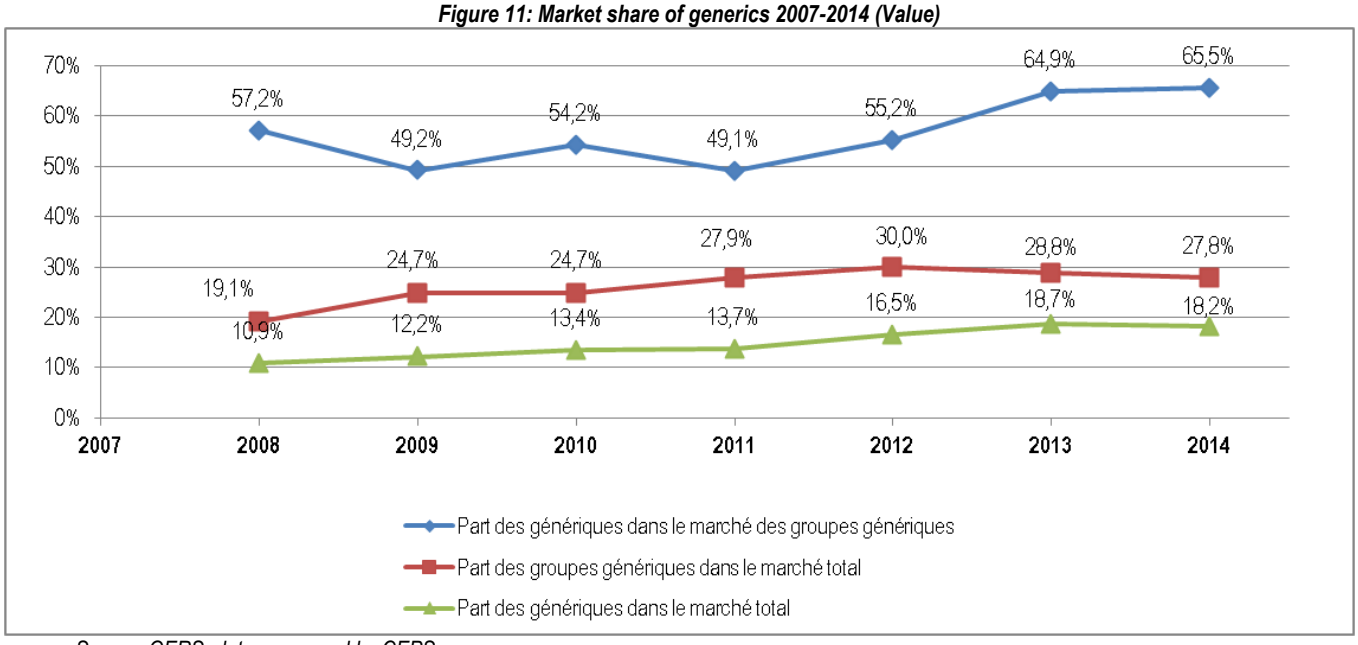


Source: GERS, data processed by CEPS

Expenditure attributable to distribution markup and VAT fell in 2014 as a result of price reductions and sales volumes.

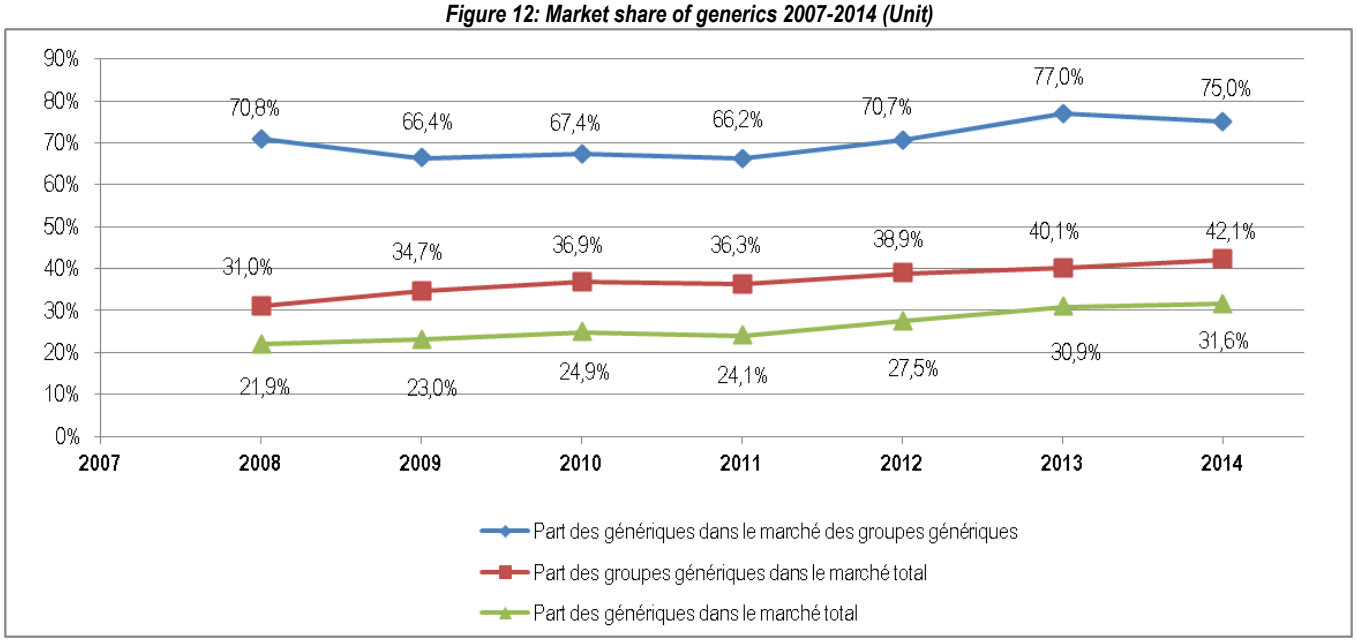
[14] French National Institute of Statistics and Economic Studies

Figure 11: Market share of generics 2007-2014 (Value)



Source: GERS, data processed by CEPS

Figure 12: Market share of generics 2007-2014 (Unit)



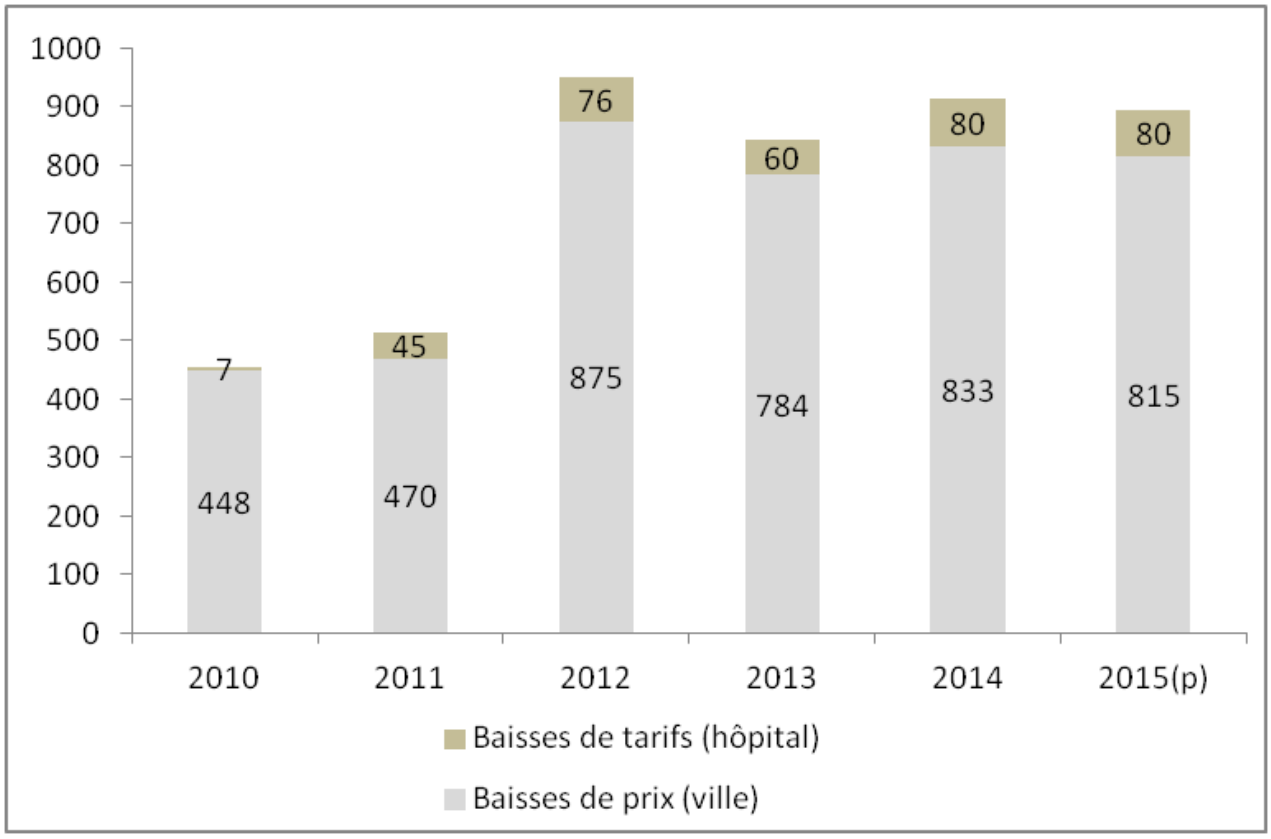
Source: GERS community pharmacy sales data, data processed by CEPS, in 2014 substitution list processed February 2015

After a dip between 2008 and 2011, the generics market share in value and unit has begun to pick up again since 2012. This upward trend can be explained by the introduction of "third-party billing for generics", which is based on a specific "performance-based' payment policy for community pharmacists.

Sales of generic groups account for 42.1% of medicine packs sold and 27.8% of the turnover in ex-manufacturer price made in community pharmacies in 2014. The generic share in generic groups reached its peak in 2014, at 65.5% in value, but in units there was a drop in 2014.

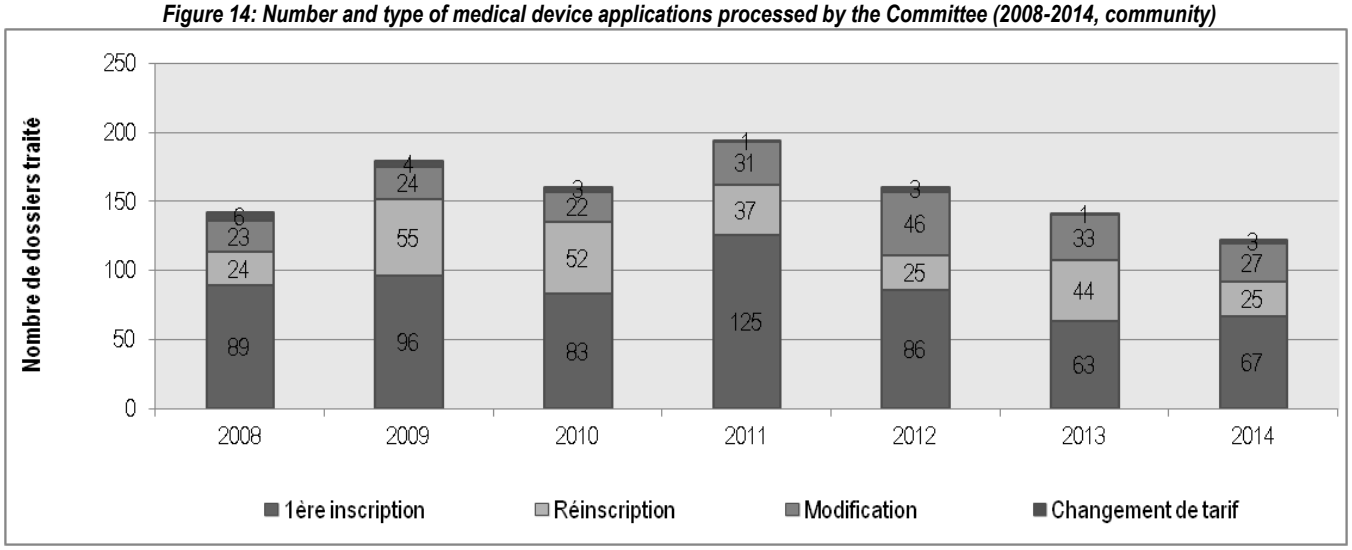
The generic share in the overall market climbed from 10.9% in 2008 to 18.2% in 2014 in value and from 21.9% in 2008 to 31.6% in 2014 in units. **Even if generics are continuing to creep up in units in the overall market, their market in terms of value has fallen in 2014, from 18.7% to 18.2% in the overall market – mainly as a result of the price reductions decided by CEPS.**

Figure 13: Savings linked to reductions in medicine tariffs and prices



DATA CONCERNING THE MEDICAL DEVICE SECTOR

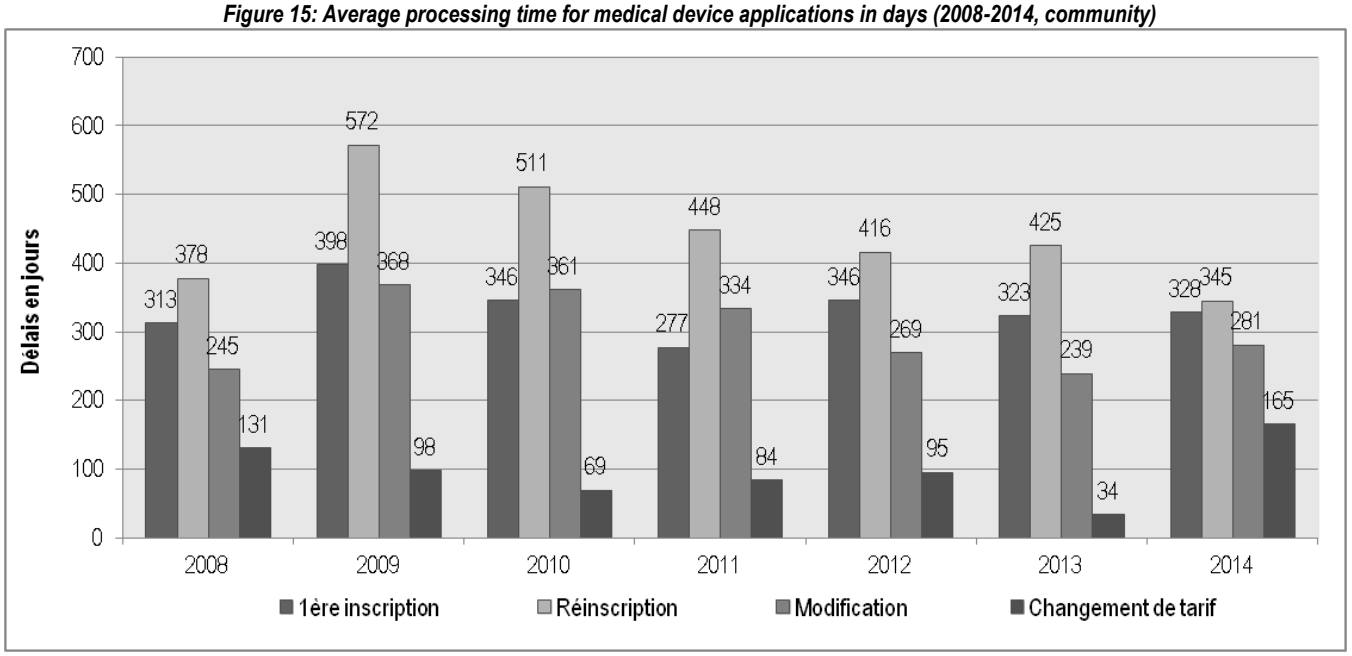
Figure 14: Number and type of medical device applications processed by the Committee (2008-2014, community)



Source: CEPS

The number of applications processed has fallen slightly in 2013 and 2014. An average of 156 applications are processed every year (122 in 2014).

Figure 15: Average processing time for medical device applications in days (2008-2014, community)



Source: CEPS

The processing times have fallen overall since 2009 and are continuing to get shorter in 2014.

HOW CEPS IS RUN AND ITS RESULTS: QUESTIONS & ANSWERS

What are the missions entrusted to CEPS?

Under the law CEPS is primarily tasked with the pricing of medicines and setting of tariffs for medical devices for single patient use reimbursed by *l'Assurance Maladie* (French national health insurance body). It is also responsible for implementing the ministerial guidelines it receives and for carrying out an annual price reduction programme through to completion, according to the remit the French Government and Parliament bestow upon it when the French Social Security Financing Act (LFSS) is passed. Lastly, CEPS promotes responsible product use, particularly through the adoption of the pharmaceutical promotion charter.
The Committee more generally lends a hand in drafting the healthcare product pricing policy and oversees the healthcare product agreement policy.

What is the setup at CEPS?

CEPS is an interministerial and interinstitutional committee made up of two sections – one dedicated to medicines and the other to medical devices. Since 2004, there has been a balance in the members sitting on the Committee[15] between representatives of the French State (directorate general for health, directorate for social security, directorate general for consumer affairs, competition and fraud control, directorate general for enterprise), and national health insurance funds and top-up health insurance bodies. The directorate-general for care provision and directorate for research (Ministry for Research) also sit on the Committee in an advisory capacity.
Trade unions – especially LEEM (the pharmaceutical companies' trade association in France) – or representatives of the medical device sector have never been, and never will be, members of CEPS.

Who are the members of CEPS and what is their remit?

The Committee members sit on it in an ex-officio capacity, as representatives of their ministry or institution which appoints them for this purpose. Beyond the vice-chairman of the "medicines" section, a university professor, hospital practitioner, as well as the chairman of the medical devices section, the inspector-general of finance, there are also several physicians, pharmacists, economists and legal experts sitting on the Committee who ensure that its remit is fully covered for carrying out its missions.

Are CEPS members independent as regards manufacturers in the medicines and medical device sectors?

Since 2005 CEPS has been subject to specific legal provisions (Article L 162-17-3, IV, Social Security Code) concerning the transparency of potential conflicts of interest with manufacturers. It goes without saying that CEPS members, its rapporteurs and any secretariat staff called to take part in the Committee's work fill out public declarations of interest which are updated and published at regular intervals (online on the Ministry for Health website).
In practice, given the way CEPS is set up, there are hardly any conflicts of interest. The rules ensuring that any member with a conflict of interest concerning an application being processed does not take part are applied in the same way as in all bodies subject to such rules.

What means does CEPS have at its disposal?

CEPS has a small standing administrative office tasked with drafting and implementing its decisions, made up of fifteen or so staff members including one general secretary and one general recording secretary, six people for the "medical devices" section (including the deputy general secretary in charge of this sector) and eight people for the "medicines" section. CEPS also calls on rapporteurs, who are usually consulting pharmacists for *l'Assurance Maladie*.

Why is pricing done by agreement?

[15] Article D162-2-1, French Social Security Code

Under the law (Article L. 162-16-4 of the French Social Security Code): "the public sales price for each of the medicines mentioned in Article L. 162-17, Paragraph 1, is set by agreement between the company selling the medicine and the French Healthcare Products Pricing Committee … or, if there is none, by decision of the Committee…". Similar provisions apply to medical devices.

This original system first came about in 1993 with the conviction that the methods practised previously for pricing medicines ran considerable risks in terms of legal and political safety.
Radical changes were called for, and the Committee was the instrument for these: it has become an interinstitutional forum where the prices of healthcare products are actually decided on through negotiation and agreement between CEPS and each company concerned, on the basis of independent regulatory powers.
If the negotiations process fails, CEPS can decide on a price unilaterally.

Of course, the final word on pricing is uttered through a policy and guidelines that the Committee helps to define, but which it is not up to the Committee to decide: the decision criteria and rules are set by law and the regulations, ministerial guidelines by Government.

What procedure do pricing negotiations typically go through?

In principle, negotiations are governed by statutory deadlines. The company submits an application for reimbursement that contains a medico-technical part examined by the Transparency Commission for Medicines (or CNEDiMTS for medical devices), and an economic part for CEPS. Once the TC (or CNEDiMTS) has forwarded its opinion to CEPS, the latter strikes up discussions with the company in question. In some cases, the French Public Health Economic and Evaluation Committee (CEESP) issues an opinion on efficiency. Discussions between CEPS and the manufacturer may be facilitated by appointing a rapporteur, depending on how complex the application is. CEPS deliberates and a proposal – based on the pricing criteria used (see question below) – is drawn up. A fair bit of to-ing and fro-ing with the company may be necessary, especially when special clauses need to be drawn up when setting the price.
CEPS' decision is made by majority vote and, if votes are split equally, the Chairman has the casting vote.

What happens if the negotiations fail?

Two solutions are possible. CEPS can set the price unilaterally, although such decisions are rare. For medicines, the ministries concerned can intervene and decide on a price themselves within two weeks. But what usually happens is that, for products that are not deemed essential as the therapeutic need is already met, the company concerned can decide not to market the product.

What are the criteria used for product pricing?

The product pricing criteria – when their price is first being set – derive from the law. In this respect, CEPS begins by taking account of the therapeutic added value of the product ("improvement in medical benefit"[16] for medicines or "improvement in expected service" for MDs), the price of comparable products and the foreseeable conditions of use, particularly the sales forecasts. As such, the price of medicines (or MDs) with the same indication or providing the same treatment is an essential reference. In some cases, the Committee may also have to heed the medico-economic opinions of the CEESP.

What do the ministerial guidelines say in terms of healthcare product pricing?

The last guidance letter is dated 2 April 2013 (see Appendix 1). This recalls the general objectives of the healthcare product pricing policy: access to high-quality care, responsible use, efficient expenditure and meeting the ONDAM target, transparent and consistent decisions, utilisation of innovations, support for the health industries.
It also indicates that CEPS is to contribute to

- drafting the medicine pricing policy.
- the policy concerning responsible use and suitable prescription of medicines,
- the policy concerning expenditure control, particularly for:

[16] As defined in the opinions of the Transparency Commission for Medicines, or CNEDiMTS for medical devices

    - generic pricing, price reductions and introduction of the TFR (fixed accountability tariff)
    - price reductions regarding medicines open to genericisation that have not been genericised,
    - price convergence within highly genericised groups
    - pricing medicines with no ASMR (improvement in medical benefit) rating
    - pricing innovative medicines
    - revising categories for the lists and generic lines of medical devices.
- the smooth performance of post-registration studies.

Is CEPS obliged to refer to existing European prices to set the prices of medicines in France?

Reference to European prices for pricing medicines has a very narrow scope. It does not apply to all medicines, only so-called "innovative" products which have a high "improvement in medical benefit" rating: this concerns no more than a handful of medicines every year.
For these products, France sets its prices by referring to those in the main comparable European Member States – Germany, the UK, Italy and Spain – and does not set the price below the lowest price observed in these countries. In practice, the prices set for such products are usually some of the lowest in Europe.
Lastly, the price is only set provisionally. If the product's indication is extended, or the prices or sales volumes observed in neighbouring European countries change significantly (which CEPS keeps a regular eye on), the price will be changed. It may be changed after five years on the market without taking the international references into account, in which case CEPS re-examines and possibly revises the price of innovative products after this length of time.

How does CEPS process medicines laying claim to a high price?

Price negotiations concerning expensive and innovative medicines usually go hand in hand with discussions on contractual clauses (clauses concerning matching use to need, volumes, performance and "real-world" surveillance, etc. - see below). These enable rebates to be obtained which limit the cost of the medicines for the local authority.

Moreover, CEPS has also sought to put a stop to the inflation of therapeutic innovation costs by determining set turnover budgets, particularly for orphan medicines or the orphan indications of some products: the price set enables the product to enter the French market, but for a set turnover budget. The laboratory undertakes to cover the whole of the target patient group for an average treatment cost, which may therefore be much less than the price at face value.
Lastly, CEPS is heavily involved in regulating medicine expenditure, especially through its annual price reduction programme which thus releases funding for innovations.

Is it possible to control the turnovers of some medicines or medical devices?

It is possible to control the turnovers of some medicines or MDs depending on the estimated number of patients to be treated, for public health and economic reasons.
If some sales volume thresholds are exceeded, the manufacturer must make clawback payments to the French National Health Insurance Fund (CNAM).

For well-defined rare indications or illnesses, for which availability of a product for a limited number of patients makes higher prices acceptable, this clawback payment can total 100% of the turnover beyond an upper limit. All of the patients in need of the product may be given it. The average cost for the local authority will fall if a budget set by agreement with the company is exceeded.

In total, in 2014, laboratories thus paid back 519 million under clauses signed per product (clauses concerning volume, posology or orphan medicines with a set budget, etc.). These clawback payments all concern a small number of products.

Can the "real-world performance" of a healthcare product be used to bring the price down?

The demonstrated therapeutic value in clinical trials used to obtain the marketing authorisation is a major pricing criterion. In exceptional cases, CEPS may sign a "**performance contract**" with the laboratory, especially when doubt remains over the product's efficacy. In this case the laboratory must prove that the real-world effectiveness of its medicine is at least equivalent to that demonstrated during clinical trials. If the demonstration

is not conclusive, the medicine price is revised downwards and the company may have to reimburse part of the turnover achieved.

Are prices set at the time of marketing re-assessed on the basis of medico-economic studies?

Since October 2013, medico-economic studies concerning the efficiency of medicines and medical devices have been attached to applications submitted to the Committee and assessed by HAS. These are only required for medicines or MDs with a high ASMR rating (1 to 3), characterising a so-called "innovative" medicine, with a forecasted annual turnover of more than EUR 20 million. In principle, such studies provide the Committee with worthwhile information when the initial price or tariff is being set – even if they can in this case only rely on models solely factoring in the results of clinical trials or price and cost hypotheses. They will also be very useful when examining a product's re-listing, for they may then take real-world data into account.

How is pricing carried out for medicines that do not have an improvement in medical benefit (ASMR V) rating?

The provisions of Article R. 163-5 of the French Social Security Code stipulate that medicines with an ASMR V rating are only included on the list of reimbursable medicines if they enable **savings to be made in the cost of the treatment** in question.

The difference in the price (or cost) of the new ASMR V medicine in relation to comparable medicines is generally around 5 to 10%. It may be greater if the product is expensive and the comparable medicines were listed a long time ago.

CEPS ensures that merely novel pharmaceutical products do not prevent market access for generics; for these "circumventions", the committee only approves registration at the price of the generics.

Since the 2012 annual report, the price of new ASMR V products has been mentioned and explained in a specific appendix to the report.

How are the prices of generic medicines set?

In principle, a markdown of -60% has been applied to the ex-manufacturer price, before tax, of the original medicine since 2012 (the markdown was more limited before this: -30% in 2002, and it has steadily doubled over ten years).

In exceptional cases, CEPS can approve a markdown that is less than 60% (in the event of high production costs, a low original price, no generic when the patent lapsed a long time ago, or of a market of little significance).

An "automatic" price reduction of 7% is applied after 18 months along with – where applicable – other subsequent price reductions in the event that the substitution is deemed insufficient compared with the original and CEPS believes that a fixed accountability tariff (TFR) is still not warranted.

Lastly, if substitution continues to be insufficient[17], CEPS can put the molecule under a TFR: reimbursement is then carried out on the basis of a fixed price equal to the price of generics.

Can the prices of medicines on the substitution list change, beyond reductions associated with a low substitution rate and then a possible TFR application?

The prices of medicines on the substitution list can still change in four situations

- Price convergence within a genericised group: the point of this is to even out the prices of generics on the one hand and original products on the other, by applying a target price to them – if necessary expressed in daily treatment cost. CEPS has followed the same procedure over recent years for proton pump inhibitors, statins, triptans, ACE inhibitors and sartans.
- European price referencing: this helps to reduce the differences with the prices of generics that are also sold on German, English, Italian or Spanish markets when the prices observed in these countries are lower.

[17] In this way, if the market share has not reached 60% of the generic group after 12 months, the group is put under TFR, in the same way as if substitution is less than 65% after 18 months, 70% after 24 months and 80% after 36 months.

- TFR trends: these may be reviewed to factor in the initial tariff level, which may be linked to a lower markdown level of generics than the level practised today. European prices are also compared.
- Lastly, on the basis of the legislation authorising it to do so, in 2015 CEPS set up a system for declaring the clawback payments manufacturers and distributors of generic medicines have granted to community pharmacists so as to ensure that the maximum authorised clawback threshold is complied with (40% of the ex-manufacturer price since 1 September 2014) and, where applicable, to base price reductions on this data.

Moreover, CEPS practises a policy of price consistency within one therapeutic group: on the basis of the ministerial guidelines (and provisions of the framework agreement), in the groups concerned the differences in price between the genericised original products on the list and the medicines providing the same treatment which are still on-patent are gradually reduced.

In all, what tools does CEPS have at its disposal to lower healthcare product expenditure?

For the Committee, **price reduction** is the main means for controlling expenditure. Attention is paid first to old medicines, no longer on-patent, whether or not they have been genericised. In 2014 for example, the price of statins across the board fell sharply, with reductions of 32% on average for original products and 28% for generics – and this accounts for EUR 130 million in savings. But in reality, there comes a time when all medicines are affected, for any number of reasons: when their sales shoot up, when lower prices in neighbouring European countries are spotted or when the products are no longer on-patent and generics make an appearance ... In this way, CEPS saved in the region of EUR 400 to 500 million a year between 2007 and 2011, and for 2012, 2013 and 2014 this figure has risen to around EUR 900 million a year – totalling almost three billion in price reductions in three years. For 2015, the price reductions will be similar.
In the MD sector, tariff reductions are around EUR 70 to 80 million a year.

Secondly, for each product requiring it, the Committee draws up **clauses** with companies for providing an economic framework regarding the sales volumes, posology or overall turnover of the product: these clauses lead to **clawback payments** to *l'Assurance Maladie*, which have totalled around EUR 400 million a year over the past three years[18].

Lastly, the Committee provides an **overall framework controlling the turnover** of medicines, stipulated by the law (Article L138-10 of the French Social Security Code) and implemented by the framework agreement signed between CEPS and LEEM. If a set turnover growth rate is exceeded, the pharmaceutical companies are asked to make a clawback payment (see below).

Does this mean that there are two major clawback categories, linked to "product" clauses on the one hand and end-of-year expenditure regulation on the other?

That's right, the first clawback category is based upon clauses agreed on a product-by-product basis. Of course, these clauses – which are sometimes complex to put into practice – are only agreed when absolutely necessary: control of sales volumes, posologies, overall turnover for an orphan medicine, etc.
For regulation clawback amounts, three mechanisms are now practised in the medicines sector (Chapter 1, Part Two of this report)

- Providing an overall framework for medicine turnover ("L" rate, which has now replaced the "K" rate: Article L 138-10, Social Security Code)
- Providing a specific framework for expenditure on antivirals intended to treat hepatitis C (Article L 138-19-1, Social Security Code)
- Recovery of the difference between the fee set by the manufacturer when a product has a temporary authorisation for use (ATU) or post-ATU status[19], and the final price negotiated with CEPS.

What is the logic behind an overall framework for controlling medicine turnover?

It is important to distinguish two types of measures used to control medicine expenditure:

[18] 310 million in 2012, 420 million in 2013 and 519 million in 2014
[19] Article 48 of the 2014 Social Security Financing Act

- one *a priori* regulation, which CEPS implements in the form of price or tariff reductions so as to keep to the ONDAM growth rate, adopted in the Social Security Financing Act (LFSS),
- and the other a *a posteriori* regulation, called a "safeguard clause" (Article L 138-10, Social Security Code) implemented in the form of contributions from pharmaceutical laboratories if the growth rate of the turnover before tax in reimbursable medicines dispensed in community pharmacies (L162-17 of the Social Security Code, and medicines dispensed to outpatients in hospital pharmacies L5126-4 of the Public Health Code) and in hospitals (medicines listed as able to be invoiced on top of "T2A", L162-22-7 of the Social Security Code) exceeds a certain rate[20] set in the LFSS.

Instead of legal contributions, companies can pay back slightly less in clawback payments if they opt to sign an agreement with CEPS.

Both forms of regulation are obviously linked.

Either price or tariff reductions, which constitute the major instrument of the a priori regulation, rounded off by medicalised prescription control, and generic development are likely to limit turnover growth to below the "L" rate, in which case the safeguard clause will not have to be applied,

Or the turnover progresses more quickly than the "L" rate, so the safeguard clause will apply.

Note that this double regulation is exceptional in nature and scope insofar as – with respect to the ministerial guidelines – it must lead to **stable medicine expenditure** in 2015, 2016 and 2017.

Has this mechanism been applied recently?

In 2011, and especially since 2012, prices have reduced to such an extent that the turnover growth has not exceeded the "k" rate (0.5% in 2012, 0.4% in 2013). Medicine turnover even lost ground in 2012 and 2013.

This means that the safeguard clause amount was nil. This happened in 2006, 2008 and 2010. The clause was last applied back in 2009.

2014 was marked by the arrival of new antivirals for treating hepatitis C, firstly with temporary authorisation for use (ATU) status and then post-ATU status. The considerable expenditure incurred was subject to a specific control framework, applied during the 2014 financial year (Article L 138-19-1, Social Security Code).

How can CEPS contribute to responsible medicine use?

CEPS is able to help through clauses agreed for medicines where there is a need. Volume and posology clauses for example are drawn up on economic grounds, but also, it goes without saying, on the basis of data concerning responsible use – especially the target patients per indication, normal posologies for the medicine's use, MA indications and so on.

Beyond these clauses, CEPS signs a promotional charter with the pharmaceutical companies. CEPS may declare financial sanctions if the undertakings are not complied with.

[20] formerly called the "K" rate, and now renamed the "L" rate in the 2015 Social Security Financing Act.

What does the promotional charter contain?

A new charter concerning information via door-to-door or canvassing methods to promote medicines, signed in October 2014, revises the provisions of the "medical visit" charter which has been in force since 2004. This factors in the changes observed in medicine promotion and the measures of the 29 December 2011 Act on reinforcing the safety of medicines and healthcare products.

The charter thus applies to everyone with a responsibility for promoting via door-to-door or canvassing methods, in any place and irrespective of the material format used. The provisions apply as regards any healthcare professional approached through such methods, across mainland France and the overseas territories.

New provisions have been introduced in this charter, particularly:

- specific rules for hospital visits,
- a clearer distinction has been drawn of the different advantages likely to be offered to people approached through such measures and the ban on handing out samples or on making special requests is underlined,
- the list of documents which may be presented at medical visits is reviewed,
- systematic assessment of the medical delegate's training.

There is also a provision on asking companies to communicate in a positive way with healthcare professionals, to recall the MA prescription framework and, where applicable, to communicate specific corrective messages if prescriptions outside of the MA framework have been observed.

Lastly, setup of a national promotional information observatory on the basis of which practices will become clear, will play a part in the initiative undertaken by the public authorities to better guarantee care quality and information transparency about medicines. Based on the information gathered, CEPS may, where applicable, provide a quantitative framework for controlling the promotional means used for a given medicine.

PART ONE – HEALTHCARE PRODUCT SALES AND EXPENDITURE IN 2014

CHAPTER I – SALES OF REIMBURSABLE HEALTHCARE PRODUCTS

1. The medicines market

The analysis presented here concerns the market of reimbursable medicines in 2014[21]. It looks at manufacturers' [22]sales for the French market and does not factor in the clawback payments made to *l'Assurance Maladie*.

The sales made are expressed in ex-manufacturer price (i.e. before tax). These concern sales of reimbursable medicines in community pharmacies (source: GERS) on the one hand and sales of medicines to healthcare establishments on the other (source: hospital purchase and company declarations) made between 1 January and 31 December 2014. Sales of reimbursable medicines to community pharmacies are those made at the price set by the Committee. In hospitals, sales are made at the price negotiated directly by healthcare establishments. For medicines sold to hospitals, the Committee is responsible for setting the outpatient prescription fee (medicines sold to outpatients in hospital pharmacies, Article L.5126-4 of the Social Security Code) and/or accountability tariff (medicines that can be invoiced on top of hospital services, Article L.162-22-7 of the Social Security Code). Medicines which are funded via hospital service tariffs are bought by establishments at a free rate and are not examined by the Committee.

1.1. General market trends concerning reimbursable medicines

In 2014, at odds with the two years before, **the reimbursable medicine market grew (+2%)**. The overall turnover generated by this market amounted to EUR 25.2 billion, versus EUR 24.72 billion.

This market growth concerning reimbursable medicines does not include those issued in community pharmacies (-1.9% to EUR 18.1 billion in 2014), only those bought by hospital establishments[23] (+11.6% up to EUR 7.1 billion in 2014).

Table 2: Sales growth rate in ex-manufacturer price of reimbursable medicines 2000-2014

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Growth rate	7.7%	7.7%	5.7%	6.5%	6.9%	5.0%	1.8%	3.9%	2.8%	2.8%	1.3%	0.7%	-2.2%	-1.8%	2.0%

Source: GERS community pharmacy sales data, declarations from companies and establishment purchases for hospitals, data processed by CEPS

[21] The market breakdown presented in this report takes account of any changes in status or reimbursement of medicines. Sales trends therefore reflect the individual progression of products on the one hand and changes in scope on the other. Accordingly, a medicine attributed orphan status in 2013 may, after an exclusivity period of ten years, have lost this status in 2014. Sales of this product in 2013 are therefore considered within the sales of orphan medicines for 2013, but this will no longer be the case in 2014. An increase in this product's sales may go hand in hand with a fall in orphan medicine sales – all other things being equal. The same applies for medicines that can invoiced on top of hospital services, which would be considered within GHSs (DRGs).

[22] The distinction between sales, reimbursement basis and amounts reimbursed by *l'Assurance Maladie* was explained in the 2012 CEPS annual report.

[23] Medicines bought by healthcare establishments include those listed as able to be invoiced on top of hospital services, those on the list of products that can be sold to outpatients in hospital pharmacies and those with temporary authorisations for use.

1.2. **Detailed analysis of the reimbursable medicines market**

Sales of reimbursable medicines are expressed in ex-manufacturer price (i.e. before tax) and amounted to EUR 25.2 billion in 2014.

The reimbursable medicines market is analysed as follows:

- based on the type of buyer

Community pharmacy	Hospital
reimbursable medicines dispensed in community pharmacies	medicines listed as able to be invoiced on top of "T2A" (DRG-based funding)
	medicines that can be sold to outpatients in hospital pharmacies
	GHS (DRG) medicines
	medicines with a temporary authorisation for use (ATU)

- based on the ONDAM scope concerned

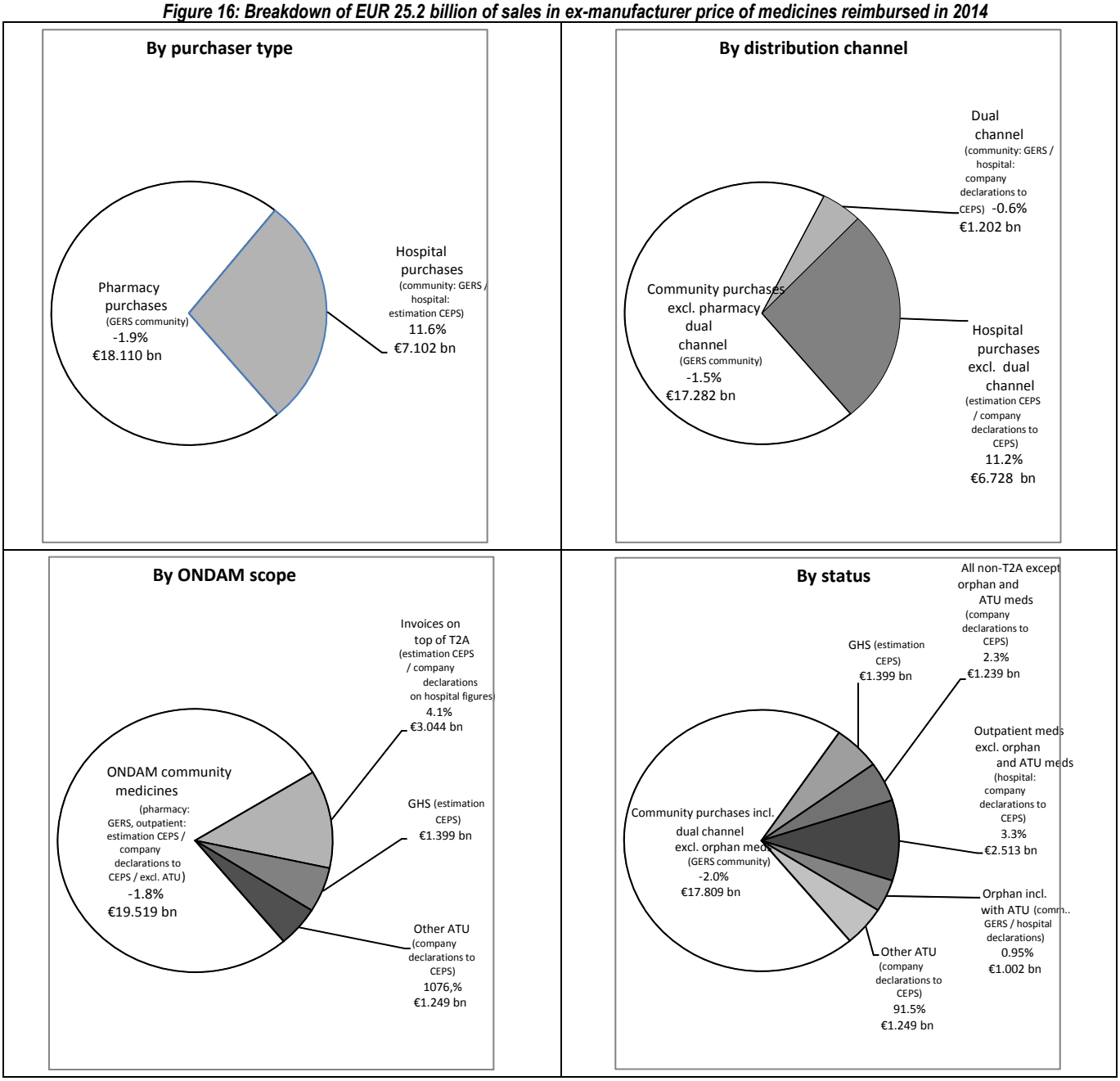
ONDAM community target	ONDAM hospital target
reimbursable medicines dispensed in community pharmacies	medicines listed as able to be invoiced on top of "T2A" (DRG-based funding)
medicines sold to outpatients in hospital pharmacies	GHS (DRG) medicines
medicines with an ATU sold to outpatients in hospital pharmacies	medicines with an ATU that are not sold to outpatients in hospital pharmacies

Company sales declarations are sent to CEPS and the ANSM [24]. For medicines listed as sellable to outpatients in hospital pharmacies or as able to be invoiced on top of "T2A" (DRG-based funding), CEPS estimates the breakdown of sales concerning medicines that can be sold in hospital pharmacies between those which are actually sold in hospital pharmacies and those that are invoiced on top of GHS (DRG) services for inpatients on the basis of the type of product and of what it might know of outpatient sales practices (from CNAMTS and ATIH[25] data).

[24] Turnover declarations forwarded to CEPS and the ANSM for establishing the tax collected pursuant to Article L5121-18 of the French Public Health Code (CSP) are not exhaustive (they do not cover medicines with a temporary authorisation for use (ATU) or those orphan medicines with less than EUR 20 million turnover before tax). Regarding sales to wholesaler-distributors, these include medicines exported under what it has been agreed to call parallel trade. This explains the difference between sales to community pharmacies and hospitals presented in the ANSM report and those in the CEPS annual report.

[25] French Technical Agency for Hospitalisation Information

Figure 16: Breakdown of EUR 25.2 billion of sales in ex-manufacturer price of medicines reimbursed in 2014



Comment: because this concerns the breakdown of sales depending on ONDAM target scope, note that almost all sales of medicines with a temporary authorisation for use (ATU) in 2014 were dispensed to hospital outpatients, and they are therefore attached to the ONDAM community target. As such, the ONDAM community target for medicines amounts to EUR 20.8 billion in 2014 – an increase of 3.8% from 2013. This increase is solely due to the arrival of new medicines with ATU status intended to treat HCV (Sovaldi®, Olysio®, Daklinza® and Harvoni® at the end of the year)

1.3. **Sales within the scope of the ONDAM community target**

1.3.1. ***Breakdown of the growth in sales of medicines dispensed in community pharmacies***

The downward market trend over the last three years concerning reimbursable medicines dispensed in community pharmacies has been such that it largely offsets the growth observed over the years before. These sales trends bring the turnover for these medicines – before tax and for the retail price after tax alike – back down to 2006 levels. The -1.9% dip in turnover before tax is mainly the result of policies implemented in terms of price reductions or the development of generics on the one hand and a continuing upward market composition trend on the other.

Table 3: 2013-2014 sales trends for reimbursable medicines through community pharmacies

	Sales in ex-manufacturer price (€bn)	Sales in retail price after tax (€bn)
2013	18.44	25.83
2014	18.11	25.32
Growth	-1.9%	-2.0%

Source: GERS community pharmacy sales data, data processed by CEPS

1.3.1.1. ***Price, pack and market composition effects***

The overall growth rate for medicine expenditure between two years n-1 and n is broken down into three effects and calculated as follows:

Overall growth rate = (1 + price effect) x (1 + pack effect) x (1 + market composition effect) - 1

The price effect corresponds to the unit price trends between n-1 and n for proprietary medicines marketed over the last two years (constant scope).

The pack effect is defined as the ratio between the number of packs sold in n and the number of packs sold in n-1.

Lastly, the market composition effect reflects the market share trends between n-1 and n: when it is upward (or downward respectively), this effect corresponds to the deformation of sales towards expensive product formats (or less expensive respectively). Innovation and development concerning generics are reflected in the market composition effect; the former wields an upward influence on the composition effect, while new generics bring this effect down.

The pack and composition effects are the two components of the volume effect.

Table 4: Breakdown of sales trends before tax in community pharmacies, 2000-2014

Year	Price effect	Pack effect	Market composition effect	Total growth
2000	-0.9%	2.9%	6.8%	8.9%
2001	-1.3%	1.2%	7.3%	7.2%
2002	-1.6%	0.7%	5.1%	4.1%
2003	-0.4%	0.6%	5.5%	5.7%
2004	-0.4%	-1.1%	7.8%	6.2%
2005	-1.0%	3.4%	4.4%	6.8%
2006	-3.9%	-5.6%	11.1%	0.8%
2007	-2.1%	0.0%	6.1%	3.8%
2008	-2.2%	-4.9%	8.3%	0.8%
2009	-2.2%	3.1%	1.3%	2.2%
2010	-2.5%	-0.9%	4.0%	0.5%
2011	-2.3%	-0.4%	3.1%	0.3%
2012	-4.2%	-1.6%	2.5%	-3.4%
2013	-4.0%	0.5%	1.4%	-2.2%
2014	**-3.8%**	**-0.6%**	**2.6%**	**-1.9%**
Effects combined 2000-2014	-27.7%	-5.9%	98.0%	34.7%

Source: GERS community pharmacy sales data, data processed by DSS/6B

The 1.9% dip in sales expressed in ex-manufacturer price (i.e. before tax) of reimbursable medicines dispensed in community pharmacies is for the most part the result of price reductions (price effect: -3.8%). The number of packs sold – which was slightly up in 2013 (+0.5%) – is now slightly down (-0.6%). The market composition effect is still on an upward trend.

This was only 2.5% in 2012 and 1.4% in 2013, and is continuing at this rate in 2014 (+2.6%). Since fewer new molecules reached the community market in 2014 – above all innovative and more expensive medicines likely to be prescribed instead of older medicines (sometimes genericised) – the scope of the composition effect is limited.

In all over the 2000-2014 period, the price effect (which directly reflects CEPS' work) is -27.7%. Over the same period, the pack effect was also on a downward trend, albeit much less pronounced (-5.9%). The total market composition effect is 98.0%. The only factor driving the growth of the turnover achieved for medicines dispensed in community pharmacies over the past thirteen years is the deformation in the composition of sales from cheaper medicines to more expensive products.

1.3.1.2. *Average price of medicines dispensed in community pharmacies*

The average ex-manufacturer price of one pack of reimbursable medicine dispensed in a community pharmacy began dropping in 2012, and this trend is continuing in 2014. It has fallen from €7.58 to €7.15 between 2011 and 2014. Likewise, the average retail price after tax is also on a downward spiral – down from €10.58 in 2011 to €10.00 in 2014.

The average distribution markups are still dropping too (-2.22% compared with 2013).

Table 5: Trends in average pack price and distribution markup on reimbursable medicine sales between 2005 and 2014

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Pre-tax sales (€bn)	17.97	18.10	18.79	18.94	19.36	19.46	19.52	18.86	18.44	18.11
Post-tax sales (€bn)	25.83	25.83	26.61	26.53	27.11	27.19	27.23	26.29	25.83	25.32
No. of packs (millions)	2,817	2,658	2,656	2529	2607	2582	2574	2529	2545	2531
Average ex-manufacturer price of pack (€)	6.38	6.81	7.08	7.49	7.43	7.54	7.58	7.46	7.25	7.15
Growth / year n-1	*3.20%*	*6.70%*	*3.89%*	*5.90%*	*-0.85%*	*1.44%*	*0.63%*	*-1.68%*	*-2.81%*	*-1.38%*
Average retail price after tax of pack (€)	9.17	9.72	10.02	10.49	10.40	10.53	10.58	10.39	10.15	10.00
Growth / year n-1	*2.70%*	*6.00%*	*3.05%*	*4.73%*	*-0.86%*	*1.25%*	*0.47%*	*-1.77%*	*-2.33%*	*-1.47%*
Average markup (€)	2.60	2.71	2.74	2.78	2.76	2.78	2.78	2.72	2.70	2.64
Growth / year n-1	*1.20%*	*4.10%*	*1.10%*	*1.72%*	*-0.88%*	*0.76%*	*0.02%*	*-2.02%*	*-1.02%*	*-2.22%*
Markup rate	43.80%	42.70%	38.70%	37.13%	37.12%	36.87%	36.65%	36.52%	37.19%	36.94%

Source: GERS community pharmacy sales data, data processed by CEPS

1. distribution markups i.e. wholesale markup + pharmacist markup (ex-manufacturer price + markup + VAT = retail price after tax)

2. markup rate = average markup / average ex-manufacturer price

Table 6: Prices and distribution markups of medicines on the substitution list and those not on the list in 2014

Market	Average ex-manufacturer price	Average retail price after tax	average markup [1]	markup rate [2]
Generics [3]	€4.12	€6.82	€2.56	62.1%
Original products	€6.51	€9.31	€2.61	40.0%
Whole substitution list	**€4.72**	**€7.45**	**€2.57**	**54.5%**
Non-substitution list	€8.92	€11.87	€2.70	30.3%

Source: GERS community pharmacy sales data, data processed by CEPS

1. distribution markups i.e. wholesale markup + pharmacist markup (ex-manufacturer price + markup + VAT = retail price after tax)

2. markup rate = average markup / average ex-manufacturer price

3. ANSM substitution list, processed in 2013: 10 February 2015

The average markup rate (relative to the ex-manufacturer price) stands at 54.5%, when it was 46.5% in 2012 and 53.5% in 2013 for medicines on the list. For on-patent medicines, the average markup rate is now 30.3% compared with 32.6% in 2012 and 31.1% in 2013.

1.3.1.3. ***Market share of generics***

The "**third-party billing for generics**" policy, involving a specific performance-based payment policy for community pharmacists, very quickly led to a **rise in the substitution rate in 2012 which continued in 2013 before levelling out in 2014**. The proportion of generics within generic groups has not continued to grow. Generics accounted for 71% of the substitution list in units sold in 2012, 77% in 2013, but only 75% in 2014.

The turnover before tax achieved on generics sales amounted to EUR 3.3 billion in 2014, down from 2013 (-3.8%) when the market had been worth EUR 3.4 billion, having grown by 13.3% compared with 2012. This downward trend is due to price reductions.

Sales of generic groups account for 42% of medicine packs sold and 28% of the turnover in ex-manufacturer price made in community pharmacies in 2014. Sales of generic or similar generic medicines alone account for 31.6% of units dispensed in community pharmacies.

Table 7: Market share of generic medicines 2013-2014

	2013 [1]		2014 [2]	
	Units	**Value**	**Units**	**Value**
Proportion of generic groups in overall market	40.14%	28.78%	42.15%	27.82%
Proportion of generics in generic groups market	77.01%	64.88%	75.01%	65.52%
Proportion of generics in overall market	30.91%	18.67%	31.61%	18.23%

Source: GERS community pharmacy sales data,
1. 2013 substitution list processed (29 January 2014) 2. 2014 substitution list processed (10 February 2015)
These include all the generic groups listed in the Journal Officiel *in which generics were actually sold during the year in question*

1.3.1.4. ***Analysis of growth by category of pharmacotherapeutic groups***

The overall decline in the market of reimbursable medicines dispensed in community pharmacies (-EUR 350 million) is the result of widely differing trends depending on product category.

The market segmentation into categories of pharmacotherapeutic groups that CEPS carries out as part of the financial regulation of reimbursable medicines enables it to fine-tune its analysis. The trends regarding the different sub-markets which correspond to each therapeutic group are very disparate.

Table 8: The main contributions (positive and negative) to growth in 2014

Group	Pre-tax turnover in 2014 (in €M)	growth in pre-tax turnover 2014/2013 (in €M)	Contribution to growth	Proportion of pre-tax turnover
sub-total of the top five positive contributions	3,777	265	1.4 pt	20.9%
sub-total of the growing groups	6,780	398	2.2 pt	37.5%
sub-total of the top five negative contributions	2,849	-397	-2.1 pts	15.7%
sub-total of the declining groups	11,321	-748	-4.1 pts	62.5%
Total	**18,102**	**-350**	**-1.9 pts**	**100.0%**

The turnover before tax of pharmacotherapeutic groups that are growing is EUR 6.8 billion, which corresponds to a sales increase of EUR 398 million (2.2 point growth) compared with 2013, while the fall in declining pharmacotherapeutic groups is EUR 748 million (-4.1 point growth) compared with 2013, making the pre-tax turnover amount EUR 11.3 billion in 2014.

Concerning groups whose pre-tax sales are rising, the five groups whose pre-tax turnover is growing the most account for 20.9% of the market for reimbursable medicines dispensed in community pharmacies, and 1.4 points in growth, while the five groups declining most sharply account for 15.7% of this market and -2.1 points in growth.

Table 9: The top five pharmacotherapeutic groups contributing to sales growth in 2014

Group	Pre-tax turnover in 2014 (in €M)	growth in pre-tax turnover 2014/2013 (in €M)	Contribution to growth	Proportion of pre-tax turnover
anticancer drugs	1,307	88	0.5 pt	7.2%
disease-modifying anti-rheumatic drugs	767	77	0.4 pt	4.2%
anticoagulants	540	41	0.2 pt	3.0%
antidiabetics	1,028	32	0.2 pt	5.7%
orphan drugs - €30M	136	28	0.1 pt	0.7%
sub-total of the top five contributions	***3,777***	***265***	***1.4 pt***	***20.9%***

Source: GERS community pharmacy sales data, data processed by CEPS

Anticancer drugs are the pharmacotherapeutic group whose ex-manufacturer price sales are growing the most. They have made more than EUR 1.3 billion in turnover and contributed up to EUR 88 million to overall growth (so 0.5 points).

Some therapeutic groups have been characterised by steady medicine sales growth for several years now. This is the case for **disease-modifying anti-rheumatic drugs, the second largest contributor to market growth** (+EUR 77 million, or 0.4 points in overall growth), indicated in inflammatory rheumatism, chronic inflammatory diseases of the intestines (such as Crohn's disease) and plaque psoriasis.

Anticoagulant sales amounted to EUR 540 million in 2014 (EUR 499 million in 2013). They account for 3% of the market for reimbursable medicines dispensed in community pharmacies and are the **third largest contributor to this market's growth**. They are up by EUR 41 million, i.e. 0.2 points in overall growth. The growth of this group is due solely to the rising sales of Xarelto® and Pradaxa®, and then Eliquis® following the extended therapeutic indication to prevent stroke and systemic embolism in people with non-valvular atrial fibrillation, obtained in the middle of 2012 and 2013.

Antidiabetics are still achieving 0.2 points in overall growth in terms of reimbursable medicines dispensed in community pharmacies.

Table 10: Top five pharmacotherapeutic groups contributing to downward growth in 2014

Group	Pre-tax turnover in 2014 (in €M)	growth in pre-tax turnover 2014/2013 (in €M)	Contribution to growth	Proportion of pre-tax turnover
treatment of hypercholesterolaemia	905	-122	-0.7 pt	5.0%
renin-angiotensin-system (RAS)-acting agents	841	-91	-0.7 pt	4.6%
antidepressants	381	-68	-0.5 pt	2.1%
hepatitis C	19	-67	-0.4 pt	0.1%
antihypertensives	704	-49	-0.3 pt	3.9%
sub-total of the top five negative contributions	***2,849***	***-397***	***-2.1 pts***	***15.7%***

Source: GERS community pharmacy sales data, data processed by CEPS

RAS-acting agents are continuing their downward trend (which began in 2009) this year as a result of the particularly strong price regulation in 2014. In the same way, the decline in the group of medicines indicated to treat **hypercholesterolaemia** is continuing after atorvastatin went off-patent, leading to an impact on its price. Lastly, the marketing of new hospital treatments for hepatitis C has led to a collapse in the sales of all medicines already marketed through community pharmacies.

1.3.2. ***Medicines issued to outpatients by hospital pharmacies (excluding those that are temporarily authorised for use)***

The Committee has sales declarations completed by companies for medicines on either the list for sale to outpatients or the list for invoicing on top of hospital services. For medicines included on both these lists, it is not possible from the declarations to distinguish the proportion actually dispensed to outpatients from the proportion invoiced on top of hospital services. Thanks to the CNAMTS' publication of Rétrocéd'AM data, sales can be compared to reimbursements made by the General Health Insurance Scheme. Establishment invoicing data submitted by the ATIH can be used to check – when a medicine is on both lists – whether they are primarily dispensed to outpatients or subject to invoicing on top of DRG-based payments. That said, since none of these three sources exactly covers the same scope or period (sales or invoicing dates), it is only possible to estimate the sales of medicines dispensed to outpatients.

The Committee puts this figure (excluding medicines with a temporary authorisation for use) at EUR 1.4 billion in 2014, based on sales that have been declared stable since 2013.

1.3.3. ***Medicines issued to outpatients by hospital pharmacies with temporary authorisations for use (ATU)***

Since a rider thereto was signed on 7 October 2010, the CEPS-LEEM framework agreement has provided for the declaration by companies of quarterly sales of medicines with a temporary authorisation for use (ATU) – irrespective of whether or not they can be dispensed to outpatients. The overall turnover of medicines dispensed to outpatients with ATU status[26] amounts to some EUR 1.2 billion in 2014 (versus EUR 106 million in 2013), with the major growth observed mainly due to new medicines for treating HCV(Sovaldi®, Daklinza®, Olysio® and Harvoni® at the end of the year).

Purchases of medicines that cannot be dispensed to outpatients but which have ATU status are estimated on the basis of the budget for education, research, reference and innovation missions (MERRI), which stood at EUR 43 million for 2014.

1.3.4. ***The dual channel[27]: medicines for hepatitis and HIV/AIDS***

Sales of so-called "dual channel" medicines, expressed in ex-manufacturer price (i.e. before tax), are stable compared with 2013, at EUR 1.2 billion.

This market covers medicines dispensed to patients to treat HIV, AIDS and hepatitis B and C, either by hospital pharmacies or by community pharmacies. Although CEPS has shed light in a global manner on such treatments in the past because of their specifics and shared trends, in 2013 the sales trends for HIV and AIDS medicines were not the same as those for hepatitis treatments.

Sales expressed in ex-manufacturer price of medicines indicated to treat HIV and AIDS are stable. Lapses in patent and associated reductions in treatment costs have offset the arrival of new molecules on this market.

Sales of dual channel medicines dispensed to hepatitis sufferers are clearly declining. In 2013, these medicines only accounted for 12% of the overall turnover for dual channel treatments. The marketing of new treatments for hepatitis C has led to a collapse in sales for all medicines that were already on the market, especially the most recent – Victrelis and Incivo. The new products are not available in the dual channel for the time being, but are reserved for sale to outpatients.

Table 11: 2013-2014 dual channel sales trends

	2013	2014	Growth
Sales in ex-manufacturer price (€M)	1,209	1,202	-0.6%
Proportion of sales made in hospitals	25%	31%	24.1%

Source: GERS community pharmacy sales data and sales declarations, data processed by CEPS

1.4. Sales within the scope of the ONDAM hospital target

1.4.1. ***Medicines financed on top of hospital services***

Sales of medicines on the list of proprietary products financed on top of hospital services are estimated on the basis of companies' declarations, factoring in the establishments' invoicing data (ATIH source), at a little over EUR 2.9 billion. Their growth is buoyant: +3.6% compared with 2013. The top three products (Avastin®, Remicade® and Herceptin®) on the list account for a total expenditure of EUR 950 million[28].

[26] Since declarations made to the Committee are grouped in six-month terms, the amount partly includes sales made after the MA had been obtained when this happens during the quarter.
[27] Medicines issued either by a community pharmacy or a hospital pharmacy to outpatients.
[28] Source ATIH expenditure, excluding extended therapeutic indications.

1.4.2. ***Medicines financed on the basis of GHS (DRG) hospital service tariffs***

By cross-linking data from different sources – establishments' purchases (ATIH source) and laboratories' sales declarations forwarded to CEPS and the ANSM – it is possible to estimate the market of medicines financed in GHS (DRGs). Since this data does not exactly cover the same scope (as it is based on different coding and does not exactly correspond to the same period – invoicing data vs sales data), this estimation process is complicated, but CEPS has fine-tuned its 2012, 2013 and 2014 estimates for all that, and believes that sales of medicines financed on the basis of GHS (DRG) hospital service tariffs are down for the third year in a row. The 2014 figure of EUR 1.4 billion presented in this report may well be under-estimated compared with other data sources (Directorate-General for Public Finances/DGFIP data for 2014).

1.5. Orphan medicines

To draw up its 2014 annual report, the Committee has taken on board all of the products removed from the European orphan medicine register and any MA repeal that arose before this report was published. Accordingly, medicines that the Committee considered to have orphan status in 2013 no longer do in this report, either because they obtained their MA before the European regulation and were indicated for treating orphan diseases, or because they had orphan status based on inclusion in the European register or a specific mention in the Transparency Commission's opinion, and an MA of at least ten years[29].

Thus defined, the orphan medicine market, all distribution channels combined, amounted to EUR 1.002 billion in 2014, up from 2013.

2. The market for medical devices covered by the reimbursable products and services list (LPPR)

CEPS does not receive any systematic declaration of sales of medical devices, and at present there are no complete statistics available on sales figures. The market analysis presented here is therefore an analysis of the expenditure amounts concerning medical devices covered by the reimbursable products and services list (LPPR) presented for reimbursement in 2014 for codes I, II, and IV. The amounts presented for code III are based on establishments' purchasing data supplied by the ATIH.

In 2014, the breakdown of expenditure per LPPR category is based on the categories for the lists adopted since the 2010 report. The three main compulsory national health insurance schemes (UNCAM) have been consistent in transferring the expenditure data concerning them. Some data concerning 2013 expenditure has been corrected.

2.1. General market trends concerning medical devices covered by the reimbursable products and services list (LPPR)

The reimbursable amounts presented in the table below correspond to quantities costed at the reimbursement tariffs set by CEPS. The actual sale prices can be higher than these tariffs, and even much higher for code II items, especially adult opticianry and hearing aids. However, the table presents services associated with the LPPR.

Total reimbursable spending on medical devices listed in the reimbursable products and services list (LPPR) amounted to EUR 8.4 billion in 2014, up by 5.1% compared with 2013 but just over 2 points slower compared to 2013.

[29] When the report was being written, so in 2014.

Table 12: 2013-2014 trends concerning reimbursable spending on products and services reimbursed under the LPPR (€M)

Service title		2013 reimbursable total	2014 reimbursable total	growth rate
CODE I	**EQUIPMENT AND DRESSINGS**			
	Aerosol generating equipment	69.0	66.8	-3.2%
	Home breathing aids and oxygen therapy equipment (other)[1]	713.1	722.0	1.2%
	CPAP	567.9	619.1	9.0%
	Nutrition	475.5	507.0	6.6%
	Beds (purchase, hire and accessories), mattresses and extras, cushions	389.9	408.4	4.7%
	Diabetic self-treatment and self-testing equipment, incl. pumps	835.0	863.4	3.4%
	Hired chairs	89.2	95.9	7.5%
	Infusion equipment	252.4	270.3	7.1%
	Misc. items and services related to Code III	0.0	0.0	
	Other home treatment equipment	195.8	216.0	10.3%
	Casting and support equipment and devices	38.7	47.3	22.2%
	Other equipment and devices for misc. treatments[2]	483.7	497.6	2.9%
	Dressing items	670.9	724.5	8.0%
	Sub-total CODE I	**4,781.1**	**5,038.5**	**5.4%**
CODE II				
	ORTHOTIC DEVICES			
	Small devices (chap. 1)	440.2	472.0	7.2%
	Other orthotic devices	202.3	228.2	12.8%
	MEDICAL OPTICIANRY (chap. 2)			
	Medical opticianry proper	1.1	1.5	36.4%
	Frames (incl. those covered by universal health cover)	97.4	95.2	-2.3%
	Glass (incl. that covered by universal health cover)	213.5	213.8	0.1%
	Lenses	9.7	9.5	-2.1%
	EXTERNAL PROSTHETIC DEVICES			
	Electronic hearing devices (chap. 3)	166.1	176.8	6.4%
	Non-orthopaedic external prosthetic devices (chap. 4)	15.1	16.0	6.0%
	Eye and face prosthetic devices (chap. 5)	10.9	11.1	1.8%
	Orthopaedic shoes (chap. 6)	99.1	102.2	3.1%
	Orthotic prosthetic devices (chap. 7)	246.1	256.2	4.1%
	Medical device reimbursed on an exceptional basis	0.2	0.2	0.0%
	Sub-total CODE II	**1,501.7**	**1,582.6**	**5.4%**
CODE III	**INTERNAL PROSTHETIC DEVICES**			
	ORTHOPAEDIC IMPLANTS			
	Orthopaedic hip implants	284.0	276.3	-2.7%
	Orthopaedic knee implants	257.0	275.6	7.2%
	Other orthopaedic implants	233.2	222.7	-4.5%
	VASCULAR IMPLANTS			
	Bare-metal stents	35.7	28.7	-19.6%
	Drug-eluting stents	122.9	146.3	19.0%
	Peripheral stents	73.5	78.8	7.2%
	Percutaneous valve replacement	73.2	101.0	38.0%
	Implantable cardiac stimulators (incl. for probes for stimulators)	273.9	276.2	0.8%
	Other vascular implants	129.3	122.4	-5.3%
	IMPLANTABLE NERVE STIMULATORS	52.5	54.4	3.6%
	OTHER IMPLANTS	73.4	97.8	33.2%
	Sub-total CODE III	**1,608.6**	**1,680.1**	**4.4%**
CODE IV	**Mobility equipment**	**123.6**	**126.6**	**2.4%**
Other expenses		**3.2**	**3.2**	**0.0%**
	TOTAL	**8,018.2**	**8,431.0**	**5.1%**

Data from all health insurance schemes for the whole of France

Sources: *CNAMTS (General scheme, with local mutual sections – mainland France), RSI, MSA (all of France) and ATIH for code III (implantable devices) Estimated timeframes between purchase and reimbursement low*

1. "Other home breathing aids and oxygen therapy equipment" includes fixed fees associated with oxygen therapy equipment with CPAP. The detailed analysis in point 2.2.1. factors in these associated fixed fees.

(Oxygen therapy alone, short-term, alone, long-term gas, long-term liquid - Breathing: spacer devices, stimulators, implants and other - Tracheal devices, ventilation service, breathing and voice prosthetic devices - Breathing treatments, other services alone, ventilation - Breathing treatments, services with oxygen)

2. The section "equipment and devices for misc. treatments" includes genital-urinary devices (urinary catheterisation and incontinence), digestive ostomy equipment and viscoelastic injections.

2.2. **Detailed analysis of the market concerning medical devices covered by the reimbursable products and services list (LPPR)**

2.2.1. ***Home breathing aids and oxygen therapy equipment***

Building on the analyses performed in previous years, the Committee is continuing to analyse the home breathing equipment market. In 2014, the estimated amounts presented for reimbursement (service providers' turnover after tax) reached EUR 1.339 billion (+ 4.9% compared with 2013) and the compulsory national health insurance (CHI) reimbursement amount: EUR 1.121 billion (+ 4.1%). These upward trends are smaller than what was observed between 2012 and 2013.

The different fixed fees for breathing equipment are divided into three main categories: oxygen therapy (fee categories 1 to 3 + fixed fees for "alternative devices to liquid oxygen" which continued to develop – three new devices were listed in 2014 – in view of the savings agreements signed at the start of 2015 with service providers and manufacturers, and fixed fee categories 28 and 29, for cluster headaches, ventilation (fee categories 4 to 6) and continuous positive airway pressure/CPAP (fee category 9). Added to these are two specific fixed fees, category 7 (chest mobilisation and assisted coughing) and category 8 (tracheotomy without ventilation). Fee categories 4 to 9 can be combined with some oxygen therapy categories (10 to 27 and 30 to 129 for fee categories listed at the end of 2014). For the analysis below, combined fees were added to the basic fees, with their corresponding allowance margin. The data shown was extrapolated from data gathered by CNAMTS, excluding local mutual sections, and accounts for between 68 and 74% depending on the year (74% in 2014) of CHI expenditure for the whole of France.

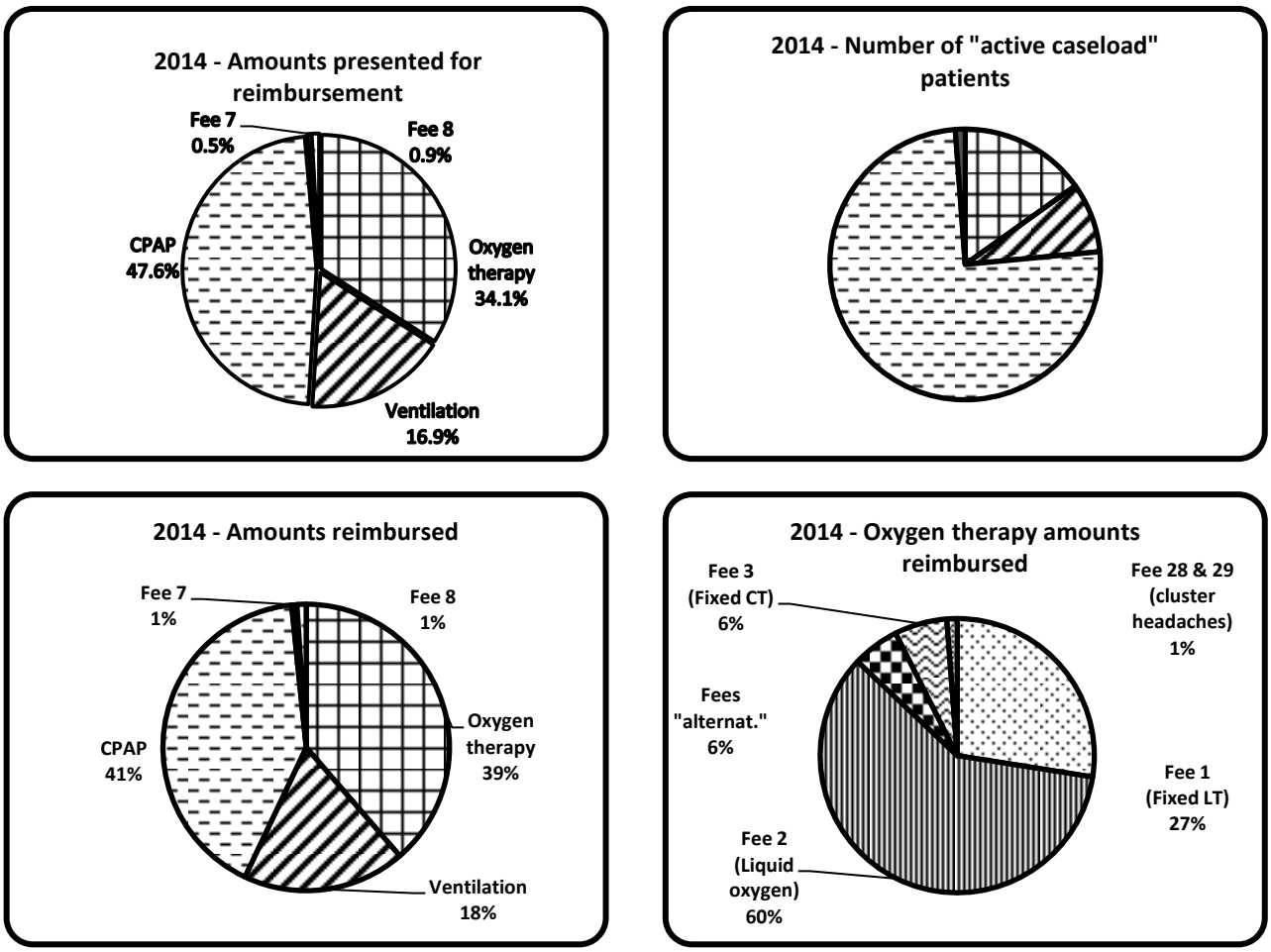
In 2014, based on the decisions of the Council of State, the CPAP fixed fees varied enormously. From the beginning of the year until 14 February 2014, four fees applied (three for remotely-monitored patients and one for patients who were not monitored in this way). Following the suspension of the 22 October 2013 ruling, the fee that was applicable from 1 October 2011 (€21.25 per week) came back into force. This significant increase generated an additional cost of around EUR 12 million given the fact that no precautionary measures in pricing terms were taken alongside the suspension decision. Through the statutory procedures it took almost three months for the rate applicable previously for patients who were not remotely monitored to be restored, from 6 May 2014 (EUR 19.00). Lastly, the 28 November 2014 decision to partially cancel the 22 October 2013 ruling brought the 9.4 fee category back to EUR 18.00. In all CEPS only recorded EUR 9.9 million in savings on this fee category, so around a third of what had been expected for this fee, whose CHI cost in 2014 was EUR 463.4 million.

The reimbursement rate is still around the 100% mark, except for fee categories 6 (90%), 9 (73%) and 28 and 29 (73%).

The number of patients who received breathing equipment, averaged out over the year (active caseload), was almost 800,000: a 9.2% increase on 2013 (this is the number obtained by dividing the number of weekly fees recorded during the year by 52) and some 37,800 of these patients benefited from the two-fee combination (+ 4.7%). Approximately 631,000 patients were on CPAP, which is around 66,000 more than in 2013 (+ 11.7%). More than 66,400 patients (+ 1,400) were on fee category 6, 54,400 (+ 500) category 1 (long-term fixed oxygen) and over 48,800 (- 1,500) category 2 (liquid oxygen). In all, in 2014 there were almost 109,800 patients receiving long-term oxygen therapy on average: 2,200 patients more than in 2013. Patients concerned by alternative fees to liquid oxygen increased from 3,400 to 6,600 – a significant rise in view of the aim to substitute liquid oxygen fees with this type of fee. That said, part of this increase has been to the detriment of fixed oxygen fees, as the proportion of this fee category in long-term oxygen therapy has fallen from 50.1% to 49.5%.

In all, oxygen therapy (including short-term oxygen therapy and cluster headaches) has concerned an average 126,800 patients in 2014 (+ 1.7%) and non-invasive ventilation 70,000 patients (+ 1.9%).

Figure 17: Home breathing aids and oxygen therapy equipment in 2014



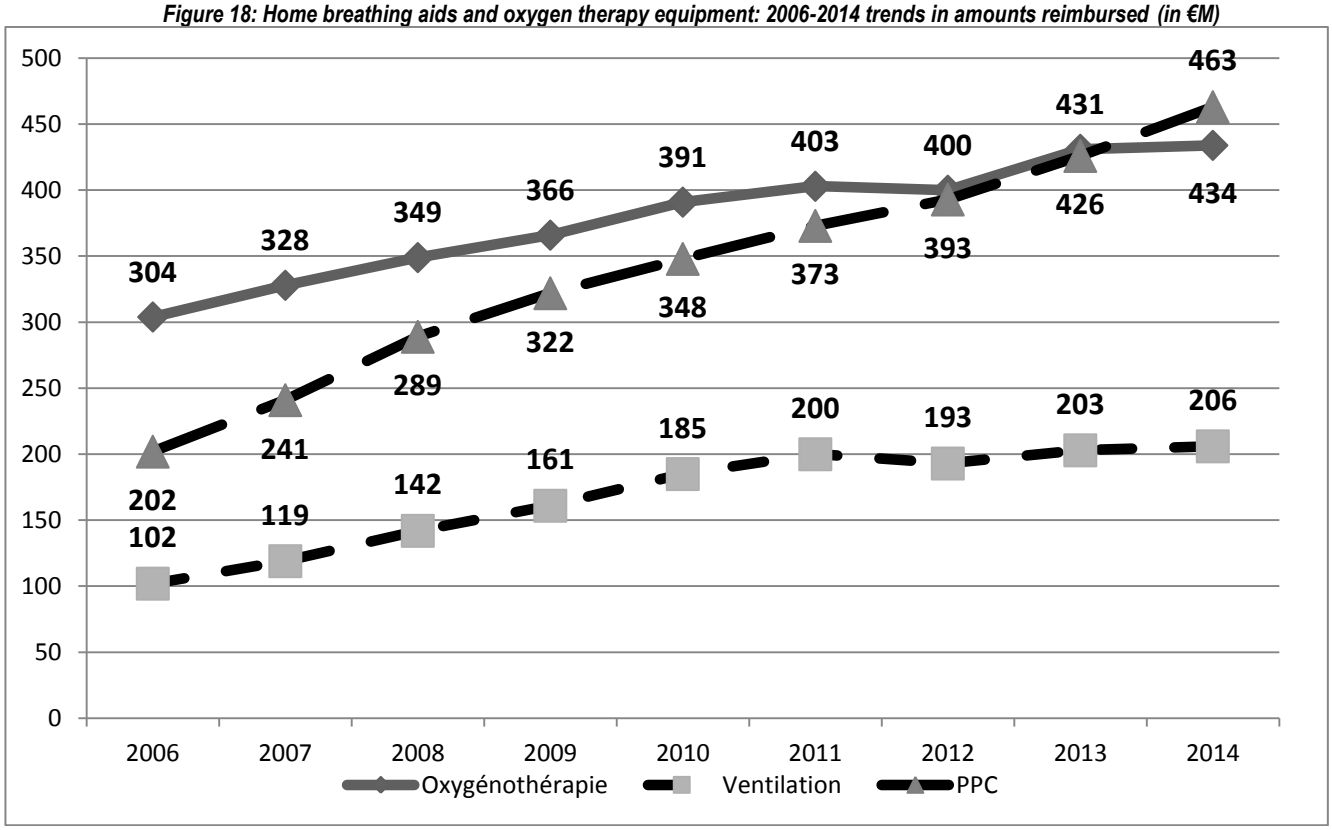
Source: CNAMTS, data processed by CEPS

The graph below shows the breathing equipment cost trends for *l'Assurance Maladie*. It is clear that, since 2006, overall expenditure has risen, in eight years, from 81.4%, despite the tariff reductions introduced in 2010, 2011, 2013 and 2014. Volume growth has in fact been very strong with a 48.3% increase in patients receiving oxygen therapy, triple the number of patients receiving CPAP (+ 212.3%) and more than double the number of patients receiving ventilation (+ 121.4%).

While oxygen therapy expenditure has jumped by 42.8%, CPAP spending has more than doubled (+ 129.6%) and ventilation expenses have doubled (+ 102.0%).

Note that, for the first time, *l'Assurance Maladie* spending for CPAP exceeded its expenditure on oxygen therapy in 2014, when it only accounted for 2/3 of this in 2006 and the tariff had fallen by 24.1%.

Figure 18: Home breathing aids and oxygen therapy equipment: 2006-2014 trends in amounts reimbursed (in €M)



Source: CNAMTS, data processed by CEPS

2.2.2. ***Drug-eluting stents***

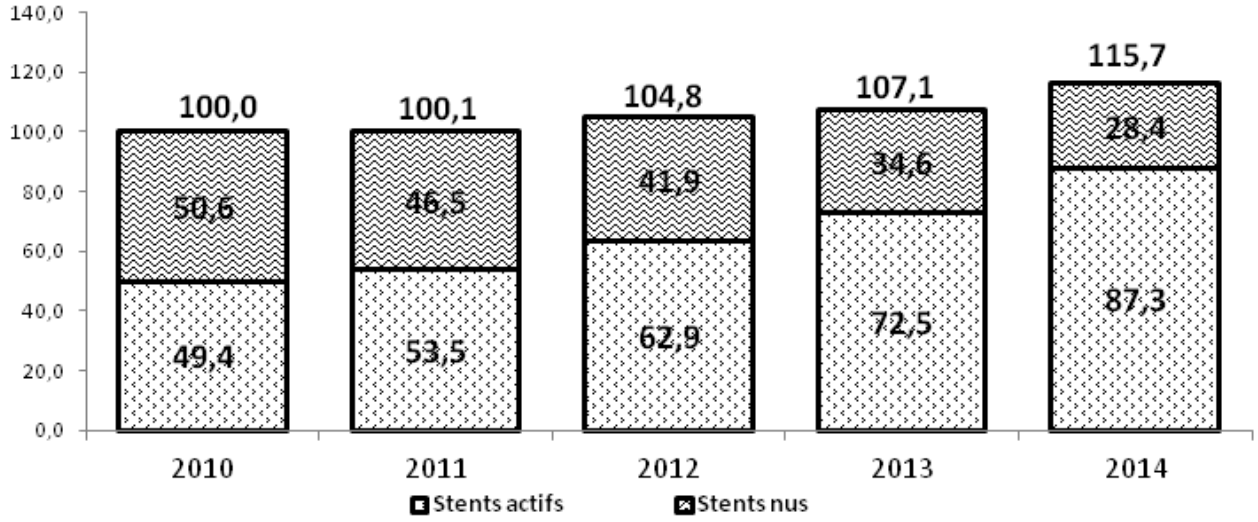
Thanks to data it now has from the ATIH, the Committee has extended its market analysis concerning coronary stents by including data about bare-metal stents and drug-elating stents. In the analysis below, the data used comes from the ATIH as well as companies. It is important to clarify, however, that the ATIH records reimbursements when they are made by compulsory national health insurance, which may result in a difference of a few months with companies' invoices. This explains why some ATIH data is presented in index form.

2.2.2.1. ***Significant change in the bare-metal/drug-eluting stents ratio***

In 2014, growth in the number of coronary stents was strong (8.0%), when this totalled 7.1% for the 2010-2013 period (graph below).

Also apparent is a swift and significant change in the ratio between non-active bare-metal stents and drug-eluting stents: the proportion of bare-metal stents has fallen from 50 to 25% overall in just four years. This downward trend follows on from the guidelines of the European Society of Cardiology which indicate that, irrespective of the therapeutic grounds for implantation, it is preferable to implant a drug-eluting stent.

Figure 19: Breakdown of coronary stents reimbursed (base 100: total 2010)

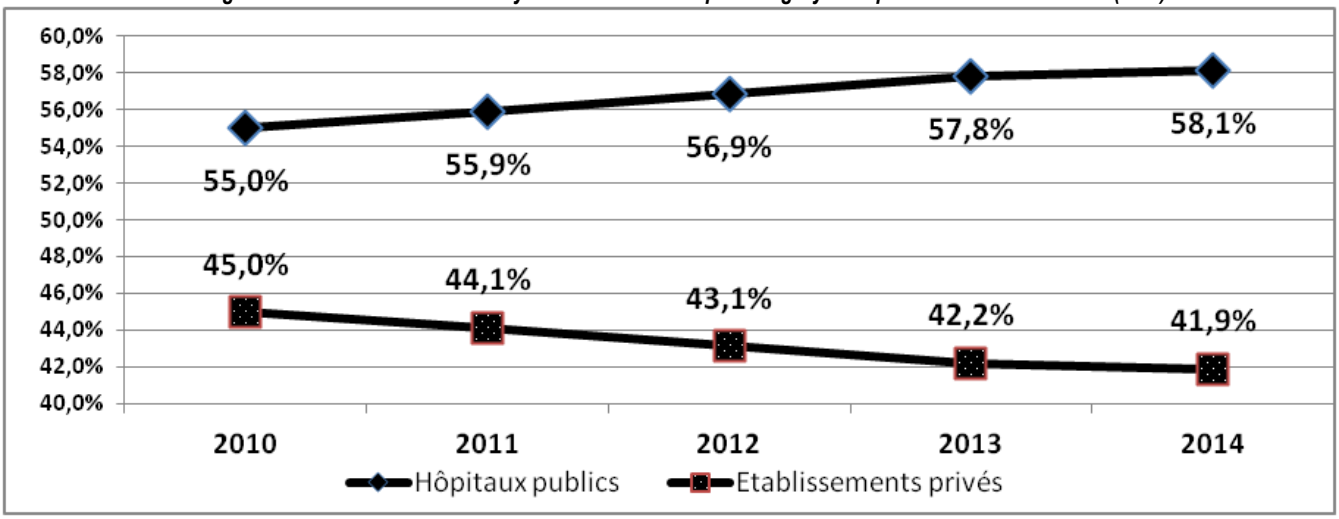


Source: ATIH, data processed by CEPS

2.2.2.2. *Growth that is beneficial to public hospitals*

Over four years, it can be seen that the 15.7% growth in the number of stents reimbursed has primarily benefited public hospitals, which have been behind a 12.2 point growth, while private establishments have only marked 3.5 points in growth (graph below). In 2014, the breakdown more in private establishments' favour since the 8.0% increase was split 4.9% and 3.1% respectively – with private establishments losing 0.3% of the market share.

Figure 20: Breakdown of coronary stents reimbursed per category of implantation establishment (in %)



Source: ATIH, data processed by CEPS

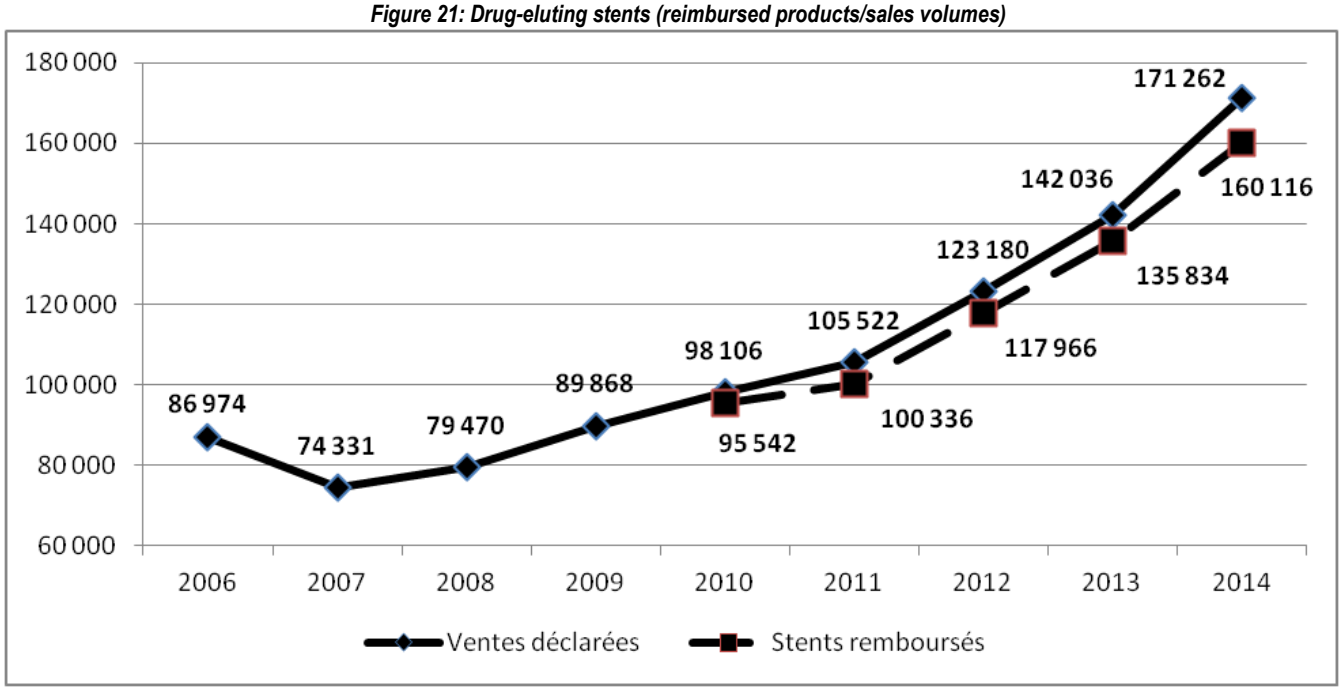
2.2.2.3. ***Booming drug-eluting stent sales in terms of volume***

The increase in the number of drug-eluting stents sold was around 9.2% on average between 2008 and 2011. 2012 growth was 16.7%[30]. This strong growth continued in 2013 (+ 15.3%) and above all in 2014 (+ 20.6%, graph below).

The growth in drug-eluting stents since 2010 is also shown. 2013/2014 growth was 17.9%.

The buoyant drug-eluting stent sales are due both to the increase in the coronary market and the transfer of sales of bare-metal stents to drug-eluting stents.

Figure 21: Drug-eluting stents (reimbursed products/sales volumes)



Source: sales declarations and ATIH, data processed by CEPS

[30] and not 20.3% as indicated in the 2012 annual report, following a transcription error

2.2.3. ***External insulin pump therapy***

The rise in the number of type 1 diabetics using external insulin pumps has slowed through 2014, even if it is still fairly steady (+ 8.1%).

The service associated with this equipment has, since the start of 2012, comprised three daily fixed fees for the pump hire, catheters and consumables for the service proper. There is also a fixed fee for the initial technical training. With the introduction of the fee on catheters and consumables, service providers have been asked to monitor these products' actual consumption. From the results it is possible to note that the bases observed before the fixed fee was introduced no longer matched up with reality and the fee was able to be lowered in early 2014 with account taken of the average number of catheters supplied to patients.

Following the adjustment of the 2012 annual report data, the table and graph presented for the past two years could be updated with 2014 data.

2.2.3.1. ***Volume trends from 2010 to 2014***

Table 13: 2010-2014 trends regarding volumes of external insulin pumps reimbursed by compulsory national health insurance/CHI (in thousands)

LPP code	List category	CHI volumes (in thousands)				
		2010 (/0.71)[1]	**2011 (/0.72)[1]**	**2012 (/0.73)[1]**	**2013 (/0.72)[1]**	**2014 (/0.74)[1]**
1121332	Infusion, portable active system, programmable pump hire, insulin.	9,614.9	11,187.4	13,025.2	15,310.0	16,553.4
		29.0%	16.4%	16.4%	17.5%	8.1%
1146183	Infusion, portable active system, initial technical training fee	6.4	6.2	7.1	7.3	7.3
		20.4%	-3.5%	14.3%	2.6%	-0.1%
1110908	Infusion, active system, catheter and associated consumables for pump, insulin	3,997.7	4,429.1	710.8	26.4	0.5
		20.2%	10.8%	-84.0%	-96.3%	-98.2%
1120663	Infusion, active system, catheter and associated consumables for pump, insulin, daily fixed fee			11,271.2	15,393.7	16,579.9
					36.6%	7.7%
1188069	Infusion, active system, external insulin pump, monthly fixed fee	363.8	409.5	84.1	2.5	0.1
		16.7%	12.5%	-79.5%	-97.0%	-98.0%
1130058	Infusion, active system, external insulin pump, weekly fixed fee			11,125.8	15,422.7	16,615.4
					38.6%	7.7%
Estimated average number (in thousands) of "active caseload" patients *(no. of catheters/142 up to 2011, no. of days under hire/366 in 2012 and/365 in 2013 and 2014*		*~ 28.2*	*~ 31.2*	*~ 35.6*	*~ 41.9*	*~ 45.4*
		+ 20%	*+ 11%*	*+ 14%*	*+ 18%*	*+ 8%*

Source: CNAMTS, data processed by CEPS

1. Correspondence table general scheme excluding local mutual sections and overseas départements *- all schemes (compulsory national health insurance)*

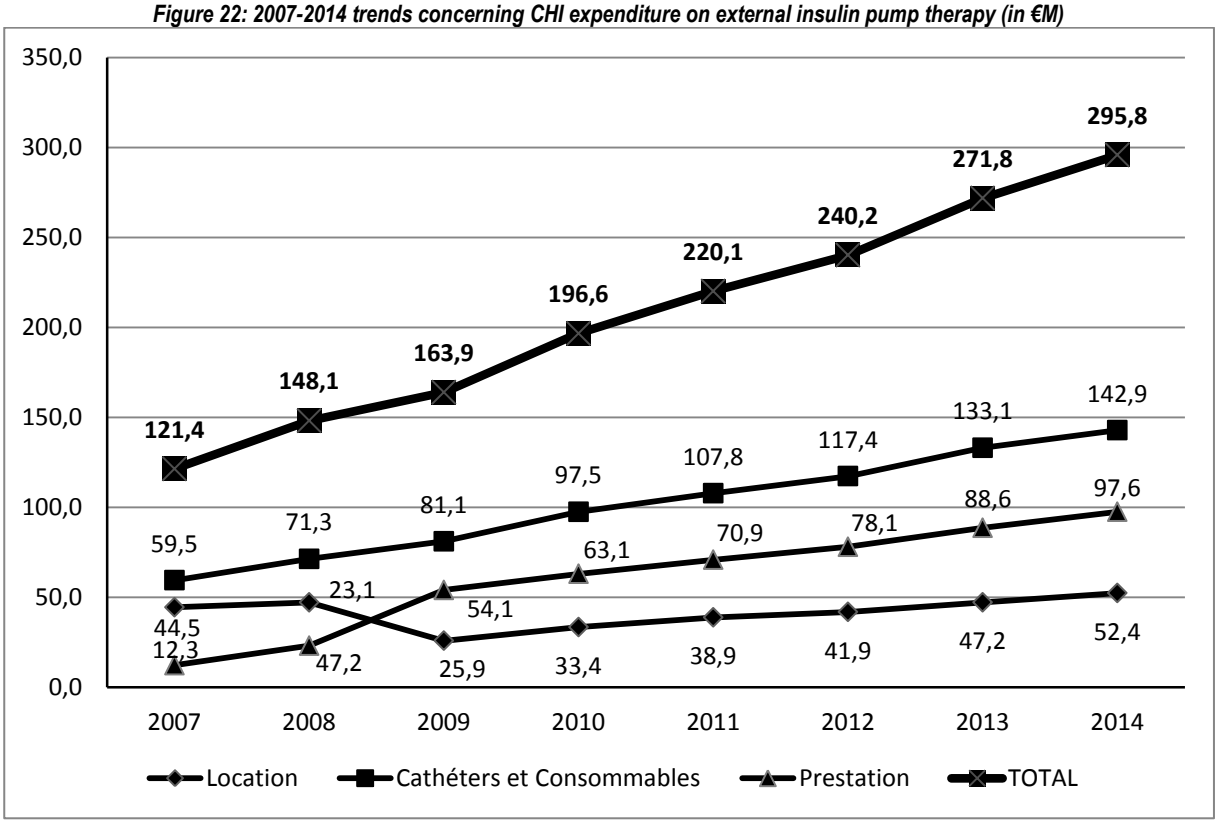
2.2.3.2. ***Reimbursed expenditure trends 2007 – 2014***

In 2014, reimbursements – which amounted to 99.3% on average relative to the expenditure presented for reimbursement (almost all patients have chronic conditions) – were worth EUR 295.8 million (+ 8.8% compared with 2013). They break down into EUR 142.9 million (+ 7.4%) for catheters and consumables (so 48.3% of

overall expenditure); EUR 97.6 million (+ 10.1%) for the service (33.0%), EUR 52.4 million (+ 11.0%) for pump hire (17.7%) and EUR 3.0 million (+ 2.5%) for the initial fixed fee (1.0%).

The graph below shows the different expenditure trends (in €M). The total factors in the installation fixed fee and the reimbursements for pump purchases.

Figure 22: 2007-2014 trends concerning CHI expenditure on external insulin pump therapy (in €M)



Source: CNAMTS, data processed by CEPS, extrapolation all schemes

It can be noted that reimbursements grew by 34.4% between 2011 and 2014 and the estimated increase in the number of patients is over 45.5%. The savings measures taken in early 2012 have therefore borne fruit, but must be continued.

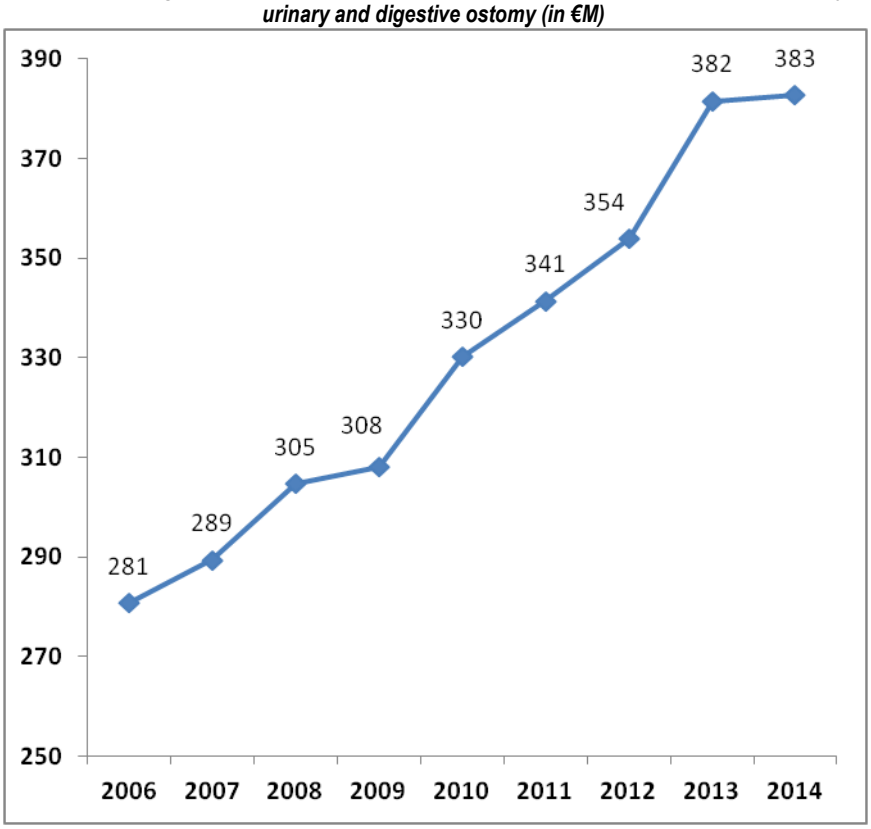
2.2.4. ***The urinary or faecal incontinence and urinary and digestive ostomy market***

This market analysis on urinary or faecal incontinence and urinary and digestive ostomy, as well as colorectal problems caused by neurological disorders, only concerns the part associated with direct reimbursement by compulsory national health insurance (CHI). For the record, the market for these products is much larger since it takes into account consumption in hospitals and care homes for dependent elderly people (EHPADs), and absorbent protection products, which represent a significant share of the incontinence market, at home and in establishments, are not reimbursed by CHI.

Reimbursement tariffs for medical devices covered by the LPP were cut by 5% as of 1 September 2013, and a maximum purchase price was introduced at the amount of these new tariffs.

CHI spending for the whole of France on these MDs – estimated by extrapolating data from the CNAMTS general scheme, excluding local mutual sections in mainland France – amounted to EUR 382.76 million in 2014, which shows that the growth observed since 2006 is levelling out, even though the 3% increase in 2014 of the overall volume of these MDs (factoring in the number of units depending on code) was equal to the average increase in volumes observed between 2006 and 2013.

Figure 23: 2006-2014 trends concerning CHI reimbursed expenditure for the whole of France on MDs for urinary or faecal incontinence and urinary and digestive ostomy (in €M)



source: CEPS according to CNAMTS data

CHAPTER II – FROM SALES OF REIMBURSABLE MEDICINES TO ACTUAL REIMBURSEMENTS WITHIN THE SCOPE OF THE ONDAM COMMUNITY TARGET

1. Medicine reimbursements

Total sales after tax of reimbursable medicines within the scope of the ONDAM community target, i.e. community pharmacy sales plus sales of medicines dispensed in hospital pharmacies to outpatients (including products with temporary authorisations for use/ATU), rose in 2014 to EUR 28 billion (EUR 27.5 billion in 2013).

To translate the growth in sales into the growth in expenditure within the scope of the ONDAM community target, we need to know what changes there were in the average reimbursement percentage. The theoretical average reimbursement percentage, i.e. the percentage that would emerge if none of the insured patients were on the chronic conditions rate, does not generally increase much year on year. That said, it was 67.5% in 2013 and rose to 68.9% in 2014. This fairly clear increase reflects the increasing share in overall medicine sales, whose cover level is 100%, and above all the growth of products available to outpatients with ATU status, which are 100% reimbursed (HCV medicines).

The CNAMTS indicates an actual reimbursement percentage of 79.5% in 2014, versus 78.4% in 2013[31]. The proportion of 100% reimbursements for medicines within the scope of the ONDAM community target for patients with chronic conditions[32] is up from 33.5% in 2013[33] to 34.1% in 2014.

Table 14: 2013-2014 trends concerning sales in community and hospital pharmacies and theoretical reimbursements (in €M) according to the cover level

	2013			2014		
Cover level (theoretical reimbursement)	**Sales after tax**	**Theoretical reimbursements**	**Theoretical average reimbursement percentage***	**Sales after tax**	**Theoretical reimbursements**	**Theoretical average reimbursement percentage**
15%	1,033	155		1,091	164	
30%	1,829	549		1,802	541	
65%	19,344	12,574		18,566	12,068	
100%	3,629	3,629	**67.5%**	3,855	3,855	**68.9%**
Hospital sales to outpatients	1,669	1,656		2,710	2,683	
Total under ONDAM community target	**27,504**	**18,563**		**28,024**	**19,311**	

Source: CNAMTS and GERS community pharmacy sales data and tax declarations of hospital sales; data processed by CEPS
**average cover level for products, weighted by sales after tax. This can differ from the actual reimbursement level, as patients with chronic conditions receive 100% reimbursement regardless of the stated cover level*

2. Reimbursements of medical devices covered by the reimbursable products and services list (LPPR) within the scope of the ONDAM community target

2.1. Overview

Products and services covered by the LPPR list (all schemes) were reimbursed for an amount of EUR 7.4 billion in 2014, up by 5% from 2013. This growth is comparable to the growth in expenditure of the general scheme alone, which was not quite as swift.

The overall average reimbursement percentage is 87.2% of reimbursable expenditure – i.e. that which is costed at the tariff rates. The average reimbursement percentage of code I is 87.1% and 72.8% for code II. The other products and services reimbursed under the LPPR list were reimbursed at 100% of the tariff.

[31] Monthly statistics from the general health insurance scheme. Total expenditure for 2013, December, incl. medical insurance excess and extemporaneous preparations.
[32] Chronic conditions and other co-payment exemptions
[33] Erratum in the 2103 annual report: the proportion of patients with chronic conditions was 34%

Table 15: 2013-2014 trends concerning reimbursements of products and services covered by the LPPR list (€M)

	Service title	2014 reimbursements	2014/2013 growth rate	2014 reimbursement percentage	Proportion of the total amount in 2014
CODE I	**EQUIPMENT AND DRESSINGS**				
	Aerosol generating equipment	53.8	-2.5%	80.5%	0.7%
	Home breathing aids and oxygen therapy equipment (other)1	670.1	1.4%	92.8%	9.1%
	CPAP	443.2	9.1%	71.6%	6.0%
	Nutrition	439.8	6.6%	86.7%	6.0%
	Beds (purchase, hire and accessories), mattresses and extras, cushions	376.6	4.6%	92.2%	5.1%
	Diabetic self-treatment and self-testing equipment, incl. pumps	836.3	3.4%	96.9%	11.4%
	Hired chairs	84.5	7.1%	88.1%	1.1%
	Infusion equipment	260.7	6.8%	96.4%	3.5%
	Misc. items and services related to Code III	0.0	0.0	0.0	0.0%
	Other home treatment equipment	174.9	9.5%	81.0%	2.4%
	Casting and support equipment and devices	36.8	24.3%	77.8%	0.5%
	Other equipment and devices for misc. treatments²	447.7	2.7%	90.0%	6.1%
	Dressing items	565.1	7.8%	78.0%	7.7%
	Sub-total CODE I	**4,389.5**	**5.1%**	**87.1%**	**59.7%**
CODE II					
	ORTHOTIC DEVICES				
	Small devices (chap. 1)	319.4	7.3%	67.7%	4.3%
	Other orthotic devices	148.9	13.1%	65.2%	2.0%
	MEDICAL OPTICIANRY (chap. 2)				
	Medical opticianry proper	0.7	16.7%	47.4%	0.0%
	Frames (incl. those covered by universal health cover)	57.4	-1.9%	60.3%	0.8%
	Glass (incl. that covered by universal health cover)	130.6	0.5%	61.1%	1.8%
	Lenses	5.8	-1.7%	61.1%	0.1%
	EXTERNAL PROSTHETIC DEVICES				
	Electronic hearing devices (chap. 3)	116.2	6.1%	65.8%	1.6%
	Non-orthopaedic external prosthetic devices (chap. 4)	14.5	5.8%	90.5%	0.2%
	Eye and face prosthetic devices (chap. 5)	11.0	2.8%	98.5%	0.1%
	Orthopaedic shoes (chap. 6)	93.3	3.2%	91.2%	1.3%
	Orthotic prosthetic devices (chap. 7)	253.7	4.0%	99.1%	3.5%
	Medical device reimbursed on an exceptional basis	0.2	0.0%	99.4%	0.0%
	Sub-total CODE II	**1,151.8**	**5.4%**	**72.8%**	**15.7%**
CODE III	**INTERNAL PROSTHETIC DEVICES**				**0**
	ORTHOPAEDIC IMPLANTS				
	Orthopaedic hip implants	276.3	-2.7%	100.0%	3.8%
	Orthopaedic knee implants	275.6	7.2%	100.0%	3.7%
	Other orthopaedic implants	222.7	-4.5%	100.0%	3.0%
	VASCULAR IMPLANTS				
	Bare-metal stents	28.7	-19.6%	100.0%	0.4%
	Drug-eluting stents	146.3	19.0%	100.0%	2.0%
	Peripheral stents	78.8	7.2%	100.0%	1.1%
	Percutaneous valve replacement	101.0	38.0%	100.0%	1.4%
	Implantable cardiac stimulators (incl. for probes for stimulators)	276.2	0.8%	100.0%	3.8%
	Other vascular implants	122.4	-5.3%	100.0%	1.7%
	IMPLANTABLE NERVE STIMULATORS	54.4	3.6%	100.0%	0.7%
	OTHER IMPLANTS	97.8	33.2%	100.0%	1.3%
	Sub-total CODE III	**1,680.1**	**4.4%**	**100.0%**	**22.9%**
CODE IV	**Mobility equipment**	**126.3**	**2.4%**	**99.7%**	**1.7%**
Other expenses		**3.2**	**7.8%**	**100.0%**	**0.0%**
	TOTAL	**7,350.9**	**5.0%**	**87.2%**	**100%**

Data from all health insurance schemes for the whole of France

Sources: CNAMTS (General scheme, with local mutual sections – mainland France), RSI, MSA (all of France) and ATIH for code III (implantable devices)
Estimated timeframes between purchase and reimbursement low

1. Home breathing aids and oxygen therapy equipment (other): Oxygen therapy alone, short-term, alone, long-term gas, long-term liquid - Breathing: spacer devices, stimulators, implants and other - Tracheal devices, ventilation service, breathing and speech prosthetic devices - Breathing treatments, other services alone, ventilation - Breathing treatments, services with oxygen

2. The section "equipment and devices for misc. treatments" includes genital-urinary devices (urinary catheterisation and incontinence), digestive ostomy equipment and viscoelastic injections.

2.2. **Examination per code**

2.2.1. ***Code I: Medical devices for home care and daily living aids, dietary foods and dressing supplies***

Code I includes homecare equipment and products and services for patients who are elderly, disabled, require post-operative care or have chronic conditions.

This code accounted for 59.7% of total expenditure on medical devices in 2014, at an amount of EUR 4.4 billion. Expenditure growth for this code (+5.1%) remains buoyant, even if it is slowing down (-3 points) compared with the year before. This slowdown is the result of various measures taken regarding certain services.

Indeed, expenditure on breathing services excluding CPAP has stabilised with a growth of just 1.4%. The same applies for diabetic self-treatment and self-testing equipment, with regards to which the measures taken in 2013 and 2014 have had an effect, since growth was only 3.4% in 2014.

2.2.2. ***Code II: External prosthetic and orthotic devices***

External prosthetic and orthotic devices accounted for 15.7% of total expenditure on medical devices reimbursed by compulsory national health insurance in 2014, a 5.4% increase on 2013.

The average reimbursement percentage of reimbursable expenditure (i.e. sales costed at the tariff rate) for code II is stable (72.8%).

Growth of the orthotic devices item (small devices and orthotic devices) has picked up, rising from 7.3% in 2013 to 9.1% in 2014.

Overall, there continues to be marked growth for most of the items in this code.

2.2.3. ***Code III: Implantable medical devices (IMDs), human-derived implants and human-derived tissue grafts***

For implantable medical devices listed under Code III of the LPPR, CEPS sets maximum purchase prices identical to the reimbursement tariffs. The reimbursement percentage for these devices is 100%.

Expenditure on implantable medical devices amounts to EUR 1.7 billion and accounts for 22.9% of total expenditure on medical devices reimbursed by compulsory national health insurance (CHI). It is up by 4.4% compared with 2013.

The ATIH has supplied the Committee with data concerning establishment purchases. Since all products under Code III have tariffs plus a maximum purchase price (MPP) in euros after tax and are reimbursed at 100%, the only factor that might be causing the deviations between the purchasing amounts incurred by private establishments (e.g. OQN) and the reimbursements made in any given year is the invoicing time.

Implantable vascular implants account for 44.8% of reimbursements under Code III. This reimbursement item grew by 6.3% in 2014. Its growth is mainly borne along by coronary stents (bare-metal and drug-eluting), up by 10% in 2014, and by percutaneous valves which grew by 38% in 2014.

Orthopaedic implants represent 46.1% of reimbursements under this code. This expenditure item's growth was offset in 2014 by the tariff reductions introduced in 2013. This stabilising factor was the result of an increase in "hip and other orthopaedic implants" items which also offset the sustained growth of the "knee" item.

2.2.4. ***Code IV: Purchases of mobility equipment***

Growth in terms of mobility equipment purchases under Code IV has been somewhat sluggish in 2014 (+2.4%), bringing this expenditure item to EUR 126 million.

In addition to spending associated with purchases of mobility equipment under Code IV, spending on the hire of this equipment under Code I, Chapter II: “medical devices for home care and daily living aids for people with medical conditions and disabilities” was almost EUR 85 million in 2014 (up by 7.1% compared with 2013) and accounted for 40% of the overall expenditure on mobility equipment.

PART TWO – FRAMEWORK AGREEMENTS AND EXPENDITURE CONTROL MEASURES

CHAPTER I – HEALTHCARE PRODUCT TARIFF AND PRICE SETTING WORK AND AFFILIATED CLAUSES

1. Tariff and price setting methods

The way in which medicine prices are set is presented in Appendix 4, which is unchanged from the 2012 annual report save for the addition of information on the pricing of generics in 2012, which featured under 1.1 and 1.2 of the latter annual report.

In 2014, the Committee clarified the method it uses to set the prices and tariffs for so-called "biosimilar" medicines.

In hospitals, where medicines listed as able to be invoiced on top of hospital services ("T2A" DRG-based payment model) are bought through calls for tender by hospital pharmacies, the Committee has decided to set the same tariff for biosimilars as for its reference biological medicine, in line with its generics pricing doctrine. This is because any biosimilar with a tariff lower than the reference biological medicine would be at an irreparable disadvantage given the rule whereby hospitals recover 50% of the difference between the price obtained after the call for tenders and the tariff set by CEPS.

For infliximab and its biosimilars, the tariff has been reduced by 10% compared with the initial tariff of Remicade. The aim of this relatively modest markdown is to leave biosimilars enough time to adapt under open calls for tenders. From this point of view, CEPS notes that only those intended to treat so-called "naive" patients, i.e. who are just beginning their treatment, are accessible to biosimilars for this initial call for tenders campaign. The Committee intends to report any differences that have arisen between the tariff and prices obtained so as to once again bring the tariff of infliximab down as a result.

For the community sector, the Committee is not yet able to present a reference markdown for the reference biological medicine and its biosimilars. At present it intends to take on board the potential known constraints in terms of development, production and substitution of biosimilars in community medicine, which imply a tariff-based policy that combines the requirement for savings from the local authority's point of view, and product viability. Regarding reference biological medicines, there is no reason why the lapsing of patents should, for all that, lead to an immediate markdown similar to the one applied for other products. For a biological medicine, this should not be less than 15%, and should reach the usual markdown of 20% in time. As for biosimilars, the Committee has adopted a minimum markdown of 30% from the initial price of the reference biological medicine for the time being.

2. Contractual clauses

2.1. Financial regulation of healthcare products

2.1.1. ***Financial regulation of medicines***

The net clawback payments to *l'Assurance Maladie* (2.1.1.3) correspond to gross amounts (2.1.1.1) after deduction of used clawback credits (2.1.1.2).

2.1.1.1. ***End-of-year clawback payments under agreements concerning medicines***

There are three types of clawback payment:

- specific clawback payments for certain products (a)
- annual regulation clawback payments including the new regulation specific to HCV products (b)

- clawback payments due in the event of a deviation between the fee paid for products with temporary authorisations for use (ATU) or post-ATU status, and the price set by CEPS (c).

a) ***Product-based clauses***

Companies can be liable for clawback payments under specific clauses for some of their products, pursuant to Article L.162-18 of the French Social Security Code (clauses concerning daily treatment cost, posology or volume, see pro-forma clauses in Appendix 7).

Clawback payments made by pharmaceutical companies to the compulsory national health insurance body (CHI) correspond to the sums due under clauses concerning products provided for in the agreement framework between CEPS and these companies. The corresponding gross clawback amount, before companies' clawback credits have been used, calculated on the basis of sales made in 2014, is EUR 711 million. This has grown significantly compared to the clawback amounts due in 2013 (EUR 546 million), despite the overall downward turn in the market.

These high clawback amounts concern a limited number of companies and products only. The top five contributing laboratories owe 46% of total clawback payments due between them; 36% of these payments concern a dozen or so products reducing the actual cost paid by CHI for these treatments.

Contractual clauses can be agreements drawn up on economic or public health grounds, such as price/volume agreements, following the posology indicated in the MA or the average daily treatment cost (DTC). Some volume undertakings, drawn up on economic grounds, with payback of part of the turnover before tax to *l'Assurance Maladie* depending on how far different thresholds are exceeded, may also factor in responsible use. Such clauses can thus provide for major clawback payments if the target patient group determined in the Transparency Commission's opinion, or a maximum active ingredient volume determined on the same basis, is ignored. One product may be subject to several different clauses, such as a DTC clause to bring the product's daily treatment cost down to the target daily treatment cost set for its reference medicine, and a volume clause to encourage the laboratory to limit prescription to the target patient group.

Price/volume type undertakings account for 68% of clawback payments due. So-called "first pack" clawback payments represent 13% of sums due and correspond to payment of the differential between the price at face value and the net price sought by the Committee when the risk of parallel exports calls for these prices to be separated. Clauses concerning DTC, posology or limitation of the number of units by delivery, account for 8% of the total, and agreements on orphan medicines 10%.

Table 16: 2014 clawback payment amounts per type of medicine clause

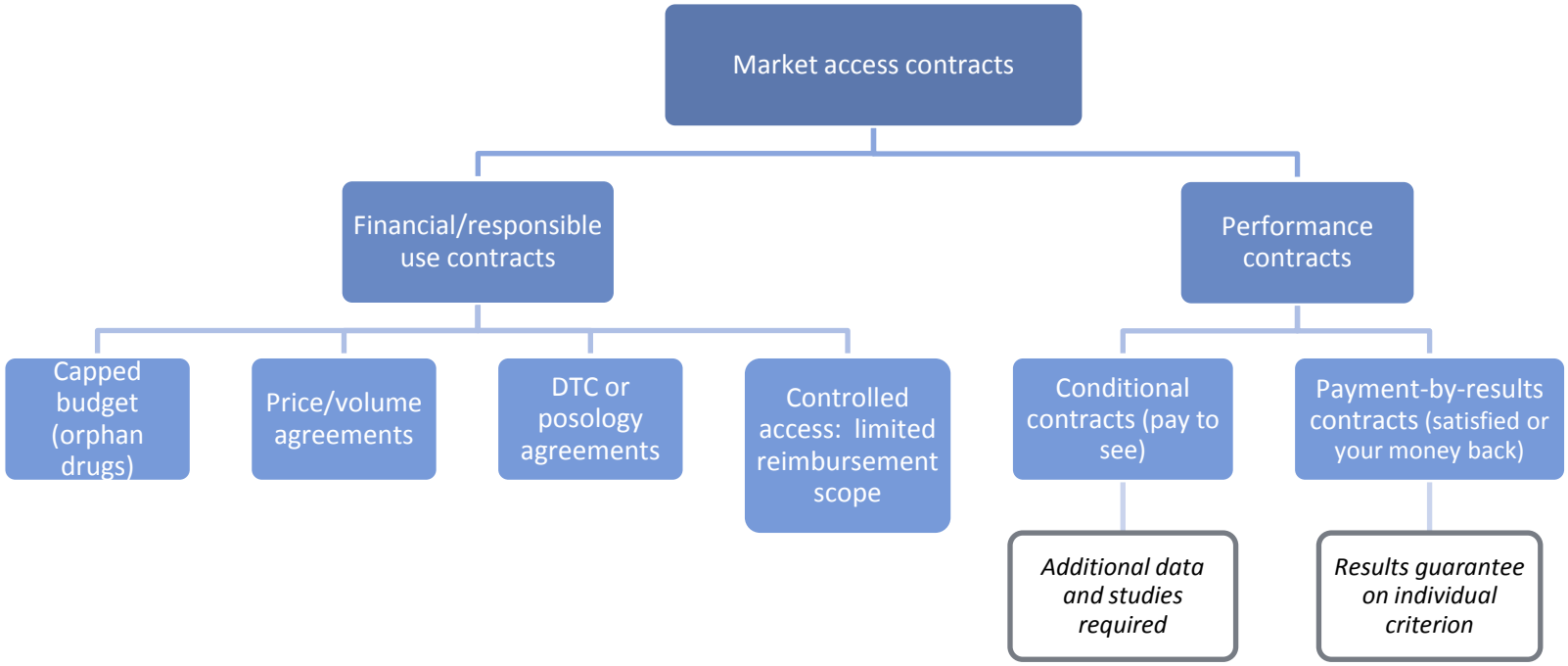
Type of clauses	2014 gross clawback amounts (in €M)	In % of total
Treatment cost clause (DTC, posology)	54	8%
Volume clause	484	68%
First-pack clawback clause	96	13%
Capped pre-tax turnover clause ("orphan" clauses)	69	10%
Other	8	1%
TOTAL	**711**	**100%**

Source: CEPS

Text box 2: The different types of contracts for market access

CEPS draws a distinction between "conventional" clauses and clauses that address product performance. Price-volume type agreements are the most common for the former. Likewise, CEPS sets closed budgets fairly often for orphan products, or posology clauses, if there is an identified risk in this respect. Lastly, limited reimbursement scopes can be defined, but these usually stem from regulations governing registration of a product on the reimbursable medicines list, as was the case for HCV products in 2014.

As for clauses addressing product performance, CEPS distinguishes between, on the one hand, clauses leading to one or more real-world studies being set up so as to confirm the clinical trial findings and, on the other, performance-related pay clauses based on one or more (as the case may be) performance indicators and individual register-based monitoring.



b) ***Collective financial regulation***

The framework agreement between CEPS and LEEM provides that the companies sign a multiannual agreement stating, for each of them, the list of reimbursable medicines that it markets and the affiliated clauses in part one; then the company's undertakings concerning promotion in part two; and finally, in part three, the company's participation in the agreement-based scheme that exempts it from the safeguard clause. These agreements can be amended by riders and are updated yearly, by the end of semester one, to factor in any changes in the companies' budgets that may affect the first two parts, and by 31 December for the third part.

In 2014, 175 companies marketing reimbursable medicines dispensed in community or hospital pharmacies signed an agreement exempting them from the safeguard contribution, proposed by CEPS[34].

Given the sales trends halfway through 2014 and the growth forecasts for the rest of 2014, the Committee has begun to question the implementation of collective financial regulation since expenditure associated with products for treating HCV with temporary authorisations for use (ATU status) has shot up.

The target for reimbursable medicine sales growth ("K" rate) has thus been exceeded in 2014. That said, the decision was made to apply the new regulation mechanism specific to expenditure incurred by the new products Sovaldi®, Daklinza®, Olysio® and Harvoni®, set up by the 2015 Social Security Financing Act (LFSS), with application to 2014 financial year spending.

For the 2014 financial year, clawback payments due under this new mechanism were EUR 76.5 million[35].

Text box 3: Presentation of the mechanism regulating expenditure associated with HCV treatments

Article 3 of the 2015 LFSS added the following provisions to Article L138-19-1 of the French Social Security Code (CSS):

"When the pre-tax turnover achieved in mainland France and overseas *départements*, over the calendar year, for medicines intended for treating chronic hepatitis C infection, minus the clawback payments mentioned in Articles L. 162-16-5-1 and L. 162-18, is over an amount W determined by the law and has increased by more than 10% compared with the same turnover achieved the year before, minus the clawback payments mentioned in Articles L. 138-19-4, L. 162-16-5-1 and L. 162-18 and the contribution stipulated herein, the companies holding the rights to sell these medicines are subject to a contribution.

The list of medicines mentioned in Paragraph 1 herein is drawn up and published by the French National Authority for Health (HAS). Where applicable, this list is updated after each marketing authorisation or temporary authorisation for use with the medicines covered thereby."

This legislative mechanism is subsidiary in practice for companies that have signed an agreement with CEPS, as specified in Article L 138-19-4:

"Companies liable to pay the contribution which, pursuant to Articles L. 162-16-4 to. 162-16-5 and L. 162-16-6, have signed with the French Healthcare Products Pricing Committee (CEPS), for all of the medicines on the list

[34] Article 31 of the Social Security Financing Act (LFSS) for 1999 introduced a permanent safeguard clause. The aim of this mechanism is to regulate healthcare expenditure via accountability on the part of pharmaceutical companies. It involves the pharmaceutical laboratories paying a contribution to *l'Assurance Maladie* when their overall turnover before tax, achieved in France, for reimbursable proprietary products, has grown faster than a growth rate defined by the Social Security Financing Act.
Known as the "K" rate, this brings the safeguard clause into effect. Pursuant to Article L.138-10 of the French Social Security Code, this corresponds to the ONDAM growth rate that results from a comparison of the Social Security Financing Act from the year in question and the years previously. The contribution rate (50%, 60%, 70%) varies depending on the extent to which the "K" rate has been exceeded, and applies successively to a determined band of additional turnover observed compared with what the result would have been had the "K" rate been followed.
Companies can be exempt from paying this contribution if they choose to take an agreement out with CEPS. They then settle contractual clawback payments in return, which are only due if the "K" rate is exceeded.

[35] Excl. contributions collected where there was no agreement with CEPS

mentioned in Paragraph 2 of Article L. 138-19-1 they sell, an agreement that is valid until 31 December of the calendar year under which the contribution is due and according to the arrangements defined by an agreement signed, where applicable, pursuant to Paragraph 1 of Article L. 162-17-4, can sign with CEPS, by 31 January of the year following the calendar year under which the contribution is due, an agreement providing for the payment in the form of a clawback payment, to one of the bodies mentioned in Article L. 213-1 appointed by the Head of the Central Agency for Social Security Bodies (ACOSS), of all or part of the contribution amount due.
Companies selling the medicines on the aforementioned list that are authorised pursuant to Article L. 5121-12 of the French Public Health Code or reimbursed pursuant to Article L. 162-16-5-2 herein – for which the representative association has signed the agreement mentioned in Paragraph 1 of Article L. 162-17-4, can also sign with CEPS an agreement providing for the payment of clawback payments.

A company that signs an agreement mentioned in Paragraph 1 herein is exempt from the contribution if the clawback payments it makes are over or equal to 90% of the contribution amount for which it is liable."

c) ***ATU/Post-ATU clawback payments***

Article 48 of the 2014 Social Security Financing Act added the following provisions to Article L162-16-5-1 of the Social Security Code:

"The laboratory holding the rights to sell a medicine with a temporary authorisation for use (ATU) provided for in Article L. 5121-12 of the French Public Health Code or reimbursed pursuant to Article L. 162-16-5-2 declares to the French Healthcare Products Pricing Committee (CEPS) the maximum fee amount it demands from healthcare establishments for the product. If no laboratory holds such rights, any hospital pharmacy interested in buying this medicine declares to CEPS the fee amount that it has been asked to pay to acquire the product if said fee has not already been declared to the Committee. The Committee makes these declarations publicly available.

Either the laboratory selling the proprietary product, or the hospital pharmacies which have acquired said product, annually communicate(s) the turnover corresponding to said proprietary products to CEPS, along with the number of units supplied or received.

If the reimbursement tariff or price set subsequently by CEPS for the medicine during its registration on the reimbursable medicines list for a marketing authorisation is less than the fee amount declared to CEPS, the laboratory pays back to the bodies mentioned in Article L. 213-1 appointed by the Head of the Central Agency for Social Security Bodies (ACOSS), in the form of a clawback payment, the difference between the turnover invoiced to healthcare establishments on the basis of the fee and what the turnover would have been if the units sold had been costed at the reimbursement tariff or price set by CEPS. The product of this clawback payment is assigned to the health insurance schemes as provided for in Article L. 138-8."

In this regard, and for the first time, CEPS has calculated the clawback payments due for the 2014 financial year. Six products are concerned, including SOVALDI®.

The total clawback payments due on these grounds amount to EUR 205 million for the 2014 financial year.

2.1.1.2. ***Clawback credits***

Pursuant to Article 18 of the framework agreement, clawback credits are granted which can be deducted from the various clawback payments to *l'Assurance Maladie*, pursuant to product-specific clauses and clawback payments due in the event the "K" rate is exceeded.

Any clawback credits that have not been used in a given year can be carried over to the next year, and there is no time limit on their use. The amount of credits carried over in 2014 reached EUR 386 million.

Some of the credits were awarded to partially offset the price reductions introduced in 2014, for the reductions that qualify for these credits. These credits are generally equal to 50% of the price reduction applied to the volumes over the twelve months preceding the reduction. They are only granted in the context of contractual reductions for products dispensed in community or hospital pharmacies. Price reductions concerning medicines on the generics substitution list do not entitle companies to such clawback credits. Reductions pursuant to contractual clauses are not concerned either. In 2014, these clawback credits amounted to EUR 115 million.

Credits were also awarded under the Health Industries Strategic Council (CSIS) system to companies who have made investments in Europe that will create, maintain or boost research and production activities in the pharmaceutical sector. An example of this is companies who had entered into agreements with third party manufacturers to produce generics locally before the original medicines went off-patent. They were awarded special clawback credits. The total amount of CSIS credits granted in 2014 was EUR 44.2 million. No credits were granted under an agreement providing for the early transfer of rights to a French third party manufacturer to enable part of the production of generics to be transferred.

Companies who can prove they have produced patient information leaflets in Braille also receive clawback credits to compensate for all of the expenditure they have incurred for the purpose. In this respect, EUR 0.26 million of clawback credits were granted in 2014.

As such, in 2014, the total amount of clawback credits at companies' disposal was EUR 546 million. EUR 192 million of clawback credits were actually used in 2013, and the remainder (EUR 354 million) has been carried over to the 2015 financial year.

2.1.1.3. ***Actual clawback payments***

The amount of "product" clawback payments notified to pharmaceutical laboratories in the second quarter of 2014 was EUR 519 million. This corresponds to the net amount to pay, so the gross amount of clawback payments, EUR 711 million, after deduction of the EUR 192 million worth of used clawback credits.

In addition to this amount are the EUR 76.5 million notified to the regulation mechanism for expenditure linked to HCV treatments[36], as well as the EUR 205 million notified for ATU/Post-ATU clawback payments.

The amounts actually paid to URSSAF[37] were being checked when this report was being written.

Table 17: Rundown of contractual clawback payments for the 2014 financial year

Clawback type	**2014 amount in €**
Product clawback amounts, net	519
Clawback payments L. 162-16-5-1 Social Security Code (post ATU)	205
Clawback payments L138-19-4 (HCV)	76.5
Total	800.5

2.1.2. ***Clawback payments under agreements concerning medical devices***

Clawback payments owed by companies for 2014 had still not been notified by the date on this report.

[36] Excl. contributions collected where there was no agreement with CEPS

[37] The main social security body which collects social security insurance contributions and distributes them to ACOSS, which in turn distributes the money to the various health insurance funds.

Those owed for 2013 were notified at the end of 2014 and collected by the URSSAF branches in December 2014 and January 2015. They amount to a total of EUR 9,657,767.

The table below shows the amounts invoiced to companies in 2014, pursuant to contractual clauses for sales made in 2013. It draws a distinction between the total amount corresponding to clauses specific to each company (individual clauses) and the total amount corresponding to clauses applicable to all companies concerned by a mechanism in the same category (pooled clauses).

Table 18: 2013 clawback payments made in 2014 per type of MD clause

	Amount owed for 2013 invoiced in 2014 in €	**Actual amount paid in €**
Individual clauses	**3,229,791**	**3,229,791**
Pooled clauses	**6,427,976**	**6,427,976**
Abdominal aortic endoprostheses	1,844,485	1,844,485
Mechanical circulatory support devices	696,357	696,357
Cochlear implants	7,000	7,000
Deep brain stimulation system	379,162	379,162
Intracranial stents	151,784	151,784
Spinal cord stimulators	3,349,188	3,349,188
All clauses	**9,657,767**	**9,657,767**

2.2. **Post-registration studies**

The principle of post-registration studies is currently stipulated in Articles R-163-18, for medicines, and R-165-11-7, for medical devices, of the French Social Security Code.

These studies may be requested by the French National Authority for Health/HAS (CT or CNEDiMTS) or CEPS.

In both the framework agreements signed by CEPS, with LEEM on the one hand and the professional organisations concerned by the medical device on the other, the arrangements for monitoring new healthcare products in current medical practice are specified, especially as regards post-registration studies.

As recalled by HAS in its guide dated 11 November 2011 on post-registration studies on health technologies "during assessment of a new technology by HAS, uncertainty often remains over the short or medium-term consequences of introducing this technology into the basket of reimbursable goods and services". This guide provides practical pointers regarding the methodological aspects of post-registration studies for the manufacturers concerned by the medicines or medical devices for which such trial requests have been made. The aim is to "collect pragmatic information that is essential for reducing the initial uncertainty and allowing relevant re-assessment of the technologies in question, both in clinical (benefits and risks for patients) and collective terms (economic, societal parameters, etc.)" and to "continue to avail of quality data under actual conditions of use, once the healthcare products have been made available on the French market".

2.2.1. ***The Real-World Study Surveillance Committee (medicines)***

2.2.1.1. ***Missions and running***

Article 11 of the CEPS-LEEM framework agreement dated 5 December 2012[38] provided for new arrangements for monitoring and assessing new medicines in actual medical practice. Pursuant to this Article, a real-world study surveillance committee (CSEVR) bringing together CEPS and HAS has been set up. The remit of this committee covers the studies that HAS and/or CEPS ask laboratories to carry out and which are covered by the agreement signed between CEPS and the laboratory. The committee is tasked with helping to implement and carry out studies in actual medical practice, particularly by:

- Clarifying and simplifying the whole process by holding periodic discussions with the laboratories to ensure the coordination and optimisation of requests. It asserts the commitment on behalf of HAS and CEPS to pool the requests of each institution so as to avoid repetition and help studies to be conducted under the best possible conditions.
- Keeping an eye on obstacles to study performance and feasibility within the deadlines set. The CSEVR examines any difficulties it will have noticed of its own accord as well as any of which it would have been informed by companies or LEEM. It decides on any measures that will enable the studies to be performed on time.
- Generally considering how post-registration studies might be improved and how such studies might impact the conclusions of the Transparency Commission and the decisions of CEPS.

In coordination with CEPS, HAS is in charge of assessing protocols and the feasibility of studies.

The CSEVR holds two-monthly meetings chaired by the CEPS Vice-Chairman and Chairman of the Transparency Commission.

Depending on the agenda, the CSEVR may invite other institutions or experts.

[38] Pursuant to Article 11 of the framework-agreement of 5 December 2012, a "*real-world study surveillance committee bringing together CEPS and HAS"* has been set up. *"The committee's purpose is to examine, at periodic intervals, the obstacles to study performance and to meeting the timeframes set in the protocol. It examines any difficulties it will have noticed of its own accord as well as any of which it would have been informed by companies or LEEM. Its observations and findings are discussed with each company concerned as well as LEEM when said observations and findings are general in scope."*

When the laboratory and HAS or CEPS are unable to reach a consensus during their discussions (study objective, means to be implemented, study performance timetable), the CSEVR may decide to organise a hearing with the laboratory in question. It may consult LEEM when these discussions are general in scope.

2.2.1.2. ***Members***

The following members take part in the CSEVR:

- Representatives of the French Healthcare Products Pricing Committee (CEPS), including:
  - CEPS Vice-Chairman and General Cabinet Office,
  - French National Health Insurance Fund for Employed Workers (CNAMTS),
  - Self-employed workers' health insurance plan (RSI) / Mutual health insurance fund for agricultural workers (MSA),
  - Directorate for Research, Studies, Evaluation and Statistics (DREES),
  - Directorate for Social Security (DSS),
  - Directorate-General for Health (DGS),
  - Directorate-General for Consumer Affairs, Competition and Fraud Control (DGCCRF),
  - Directorate-General for Care Provision (DGOS),
  - Directorate-General for Research and Innovation (DGRI),
  - Directorate-General for Enterprise (DGE),
  - National Union of Top-Up Health Insurance Bodies (UNOCAM),
- Representatives of the French National Authority for Health (HAS), including:
  - Transparency Commission,
  - Directorate for Public Health and Pricing Medical Evaluation,
  - Medicine Evaluation Department,
  - Public Health and Pricing Evaluation Department

2.2.1.3. ***What the committee does***

The committee met six times in 2014. During these meetings the committee:

- drew up its rules of procedure;
- made decisions about which post-registration studies need carrying out, continuing, postponing or calling off;
- identified any studies that have not got underway yet and/or which need to be sped up because the inclusion pace was such that the timeframes cannot be kept;
- took stock of all of the studies requested between 2011 and 2013 as well as in the fields of biotherapies for inflammatory diseases, hepatitis C, HPV vaccination and new anticoagulants, in order to outline the profiles, progress and corrective measures to take;
- discussed what the findings might be of studies planned in 2014.

The shared objective is to obtain validated findings of the assessments requested – whether medical or medico-economic – within compatible timeframes given the assessment timetables.

There were 128 post-registration studies in progress in 2014. Ten new requests have been decided on.

2.2.2. ***Medicine post-registration studies requested in 2014 by CEPS***

In 2014 CEPS attached special clauses to some post-registration studies in the belief that these studies should also form the basis for performance contracts between CEPS and the companies. Given the estimated costs for some proprietary products, the improvement in medical benefit as assessed by the Transparency Commission, the

prices of other reference products on the market, or the uncertainty of clinical findings in the case of conditional MAs for example, CEPS maintains special requirements in terms of real-world demonstration and may be obliged to revise prices accordingly. These clauses, which remain exceptional, have led to CEPS being ever more precise and particular in determining, with help from HAS, the criteria on which the real-world performances of medicines will be assessed.

Moreover, should an undertaking regarding a real-world study to which a company has committed not be fulfilled, the Committee may pronounce a fine stipulated in Paragraph 5 of Article L.162-17-4 of the French Social Security Code. The Committee did not have to deal with this type of situation in 2014.

2.2.2.1. ***CEPS study requests in 2014***

In 2014, CEPS re-addressed ten studies requested by the CT.

The purpose of the Committee's request was to:
- access the data of a register in two cases to take account of the risk/benefit in real-life;
- ask for additional data to the risk management plan in one case;
- check the conditions for responsible product use in three cases;
- monitor cohorts in two cases to check the impact on treatment consumption;
- provide real-world data for the product's re-assessment.

There were plans to set up scientific committees in four cases, in keeping with the provisions preventing conflicts of interest.

Real-world studies were requested:
- for seven registration applications;
- for one registration renewal;
- for two extended indications;
- for one orphan medicine.

2.2.2.2. ***Medicine post-registration studies mentioned in 2014 by the real-world study surveillance committee (CSEVR)***

The CSEVR examined 24 study case files in progress, of which:
- 16 were examined during one session;
- 2 were examined during two sessions;
- 3 were discussed during three sessions;
- 1 was mentioned at four sessions.

The CSEVR organised hearings with four laboratories.

The surveillance committee made the following decisions regarding these 24 case files:
- 6 decisions to call off the post-registration studies;
- 10 decisions to continue the post-registration studies;
- 6 stay-of-proceedings decisions particularly pending re-assessment;
- 2 decisions to inform the laboratory of the action taken given the inadequate answers received.

The surveillance committee also examined a request concerning surveillance of a register.

The findings of the post-registration studies in progress in 2014 will usually take between three and five years to be obtained.

2.2.3. ***Medical device post-registration studies requested by CNEDiMTS in 2014***

These only concern post-registration studies requested by CNEDiMTS, since the Committee only requested one pricing study in 2014.

Since 2015, they have been systematically re-addressed in the agreement signed between the company and CEPS with an obligation to reduce the tariff if no study is carried out.

With the agreement of the French National Authority for Health (HAS), the MD framework agreement, signed between the Committee and professional organisations, provided for consultation meetings when setting up post-registration studies (Article 10) requested by CNEDiMTS.

This is because the Committee and CNEDiMTS have often found that the studies requested at the registration stage for a product's behaviour to be assessed in practice were either poorly performed, or not at all. The idea for a three-party consultation meeting came about during discussions held between HAS and the Committee when drafting the framework agreement. This should be held within six weeks of the CNEDiMTS publication.
For a category of products, these meetings might concern a group of companies that have agreed to work on a common protocol, or companies on their own.

In 2014, 16 meetings were held, involving 27 different companies (22 individual products and one category of products in a group). For eight products, this was the second meeting.

CHAPTER II – CONTROLLING PROMOTIONAL ACTIVITY

1. Background and charter in force:

Article L162-17-8 of the French Social Security Code (CSS) introduced by the Act of 13 August 2004 provides that "a quality charter concerning the professional practice of people responsible for promoting proprietary pharmaceuticals via door-to-door or canvassing methods is signed between the French Healthcare Products Pricing Committee (CEPS) and one or more associations representing pharmaceutical companies".
The first Charter was signed by CEPS and LEEM on 22 December 2004.

On 21 July 2005, a rider to the Charter provided, on experimental grounds over the 2006-2008 period, for the Committee's definition of medicine groups for which a reduction in the number of visits and the setting of annual reduction rates were justified. Temporary or permanent price reductions could result if these rates were not complied with.

The first measures concerned four therapeutic groups (statins, antiasthmatic drugs, sartans and fluoroquinolones). The Committee had forwarded the list of medicines selected to the laboratories concerned, along with the new timetable of fewer medical visits.

However, following an appeal from two companies concerned by these reductions, the French Council of State, via two identical decisions dated October 2008, cancelled the provision of the Charter that had set up this measure, considering that the law had not "given jurisdiction to the signatories to the medical visit charter to authorise the committee to make a unilateral decision regarding the measures" in this area. The quantitative restriction measure was thus dropped and any decisions made on its basis cancelled.

On 21 July 2008, a second rider to the charter was signed to make it "applicable to the medical visit paid to healthcare establishments".

2. The new Charter and the main changes introduced

It became necessary to revise the outdated charter, particularly to take on board new legislation and regulations that had been introduced in terms of pharmaceutical advertising.

2.1. A new name and a more precise outline

The medical visit charter is now called: Charter concerning information via door-to-door or canvassing methods aimed at promoting medicines.

A more precise outline was adopted, divided into six chapters

- Responsibilities of people providing information via door-to-door or canvassing methods aimed at promotion
- Quality of the information provided
- Code of conduct
- Monitoring of the work of people providing information via door-to-door or canvassing methods aimed at promotion
- Joint monitoring of the charter
- Term and termination

2.2. An extension of the Charter scope:

The following changes have been introduced:
- the term "medical delegate" has been removed, as it is not defined in any legal text, and replaced with broader terms from the French Public Health and Social Security Codes: "*people responsible for promoting via door-to-door or canvassing methods"*;
- the Charter is now applied "*in any place" and "irrespective of the material format"* used for the door-to-door or promotional methods;
- the Charter now applies to physicians, pharmacists and more broadly to any healthcare professional approached through such methods, with the clarification "*any professional authorised to prescribe, dispense and use medicines"*;

- the Charter now applies in French overseas *départements* (the derogatory "transitional" provisions of the outdated version have been removed);

2.3. **Hospital visits:**

Without exceeding CEPS' remit, rules specific to hospital visits have been set out in the Charter, inspired by the work that HAS and the DGOS had conducted which could not be put into practice until now.

The practical organisation rules specific to each healthcare establishment must be referred to, under a charter applying to pharmaceutical companies and where these rules have not been harmonised at national level (this particularly concerns the collective nature or otherwise of such visits and the conditions for accessing internal departments).

Some recommendations have been made for all that: access to restricted areas is prohibited unless the managers concerned give their consent beforehand; meetings must be organised beforehand; managers must either give their consent beforehand or supervise in person any medicine or pharmacy interns carrying out door-to-door activities; no meetings with staff undergoing training, no specific data collection from prescribers or internal structures in hospitals, unless the data bears upon responsible product use.

2.4. **Documents presented during door-to-door or canvassing activities and training of medical delegates**

The following changes have been introduced:
- New rules concerning a priori monitoring by the ANSM of advertising media have been added, as have the more stringent ANSM recommendations since March 2013 (abstracts are no longer accepted as reference documents, etc.).
- The central role of the lead pharmacist in approving the documents used is confirmed.
- The list of documents to be presented as set out in the new Charter is longer than the one indicated in the legal texts (presentation of the ruling(s) entering products on the list for invoicing on top of hospital services and/or the outpatient medicines list, where applicable).
- A distinction is drawn between the initial training (attested by a degree, qualification or certificate, including by validation of learning through experience) and the *continuing professional development* of medical delegates, and the contents of this training is specified in detail (regulatory knowledge, scientific knowledge, etc.).
- The medical delegate's training as regards new products or new indications must be systematically appraised.
- The role that people responsible for promoting by door-to-door or canvassing methods play in a company's implementation of appropriate measures *to ensure the MA compliance* of its proprietary product is specified (L162-17-4-1, French Social Security Code): in practice, this new provision means that it is possible to ask the company to communicate positively to healthcare professionals to remind them of the MA prescription framework and, where applicable, to give out specific corrective messages.

2.5. **Code of conduct**

The regulations in force are recalled and a clearer distinction is drawn between the different advantages likely to be offered to people approached through such methods:
- for samples: the ban on handing out any samples is clearly underlined and the exception stipulated in the previous version regarding samples of medical devices associated with the proprietary product has been removed.
- for free gifts: the ban on offering or responding to any special requests is clearly underlined.
- for meals: the rules bearing on transparency of links are presented as before.

2.6. **Quantitative control and monitoring**

Article L162-17-8 of the French Social Security Code (CSS) has been rounded off by the 2012 Social Security Financing Act (LFSS) to bestow a legal basis, together with a sanctioning authority, upon CEPS for setting annual target figures concerning commercial and promotional practice trends which might undermine care quality.
The Charter therefore stipulates that CEPS may monitor promotional activities involving door-to-door or canvassing, particularly by setting quantified targets.

To determine these, CEPS may make use of:
- routine data from a *CEPS/LEEM promotional information observatory* set up to monitor promotional quality. All laboratories will be obliged to monitor the most heavily promoted medicine and report annually in this regard,

on the basis of a series of items (visit description, contents of the information provided, etc. See Appendix). CEPS will be able to ask companies to carry out the same monitoring for two other medicines.
- data communicated by HAS, ANSM or DGS for example.
- data from a *specific monitoring tool* for promotional practices (Promo Track) which CEPS obtained in 2013.

Where applicable, given the results of this monitoring – shared and documented within a joint monitoring committee (and bilaterally with the company (or companies) concerned) – CEPS may have to exercise the authority it has been given by the law in terms of quantitative control. As standard practice, pursuant to the texts in force, CEPS will negotiate a rider to the agreement bearing on quantitative control and may take unilateral action after two months if signing such a rider proves impossible.

CHAPTER III - TARIFF REDUCTIONS AND CHANGES TO THE REIMBURSEMENT CONDITIONS

1. Measures concerning the scope of the ONDAM community target

1.1. The ONDAM community target for medicines

In 2014, the price reductions concerning reimbursable medicines within the scope of the ONDAM community target led to EUR 833 million in savings[39].

Table 19: Savings in €M associated with 2008-2014 reductions in the prices of medicines

	Type of reduction	2010	2011	2012	2013	2014
A	Community medicines before marketing of generics	270	257	354	321	247
B	Community medicines when generics joined the market (1)	57	58	193	113	52
C	Community medicines on the substitution list	82	145	274	320	519
D	Medicines sold to outpatients in hospital pharmacies	39	10	54	30	15
	Total for community medicines	**448**	**470**	**875**	**784**	**833**
E	Medicines listed as able to be invoiced on top of "T2A" (DRG-based funding in hospitals)	7	45	76	60	80
	Total for all medicines	**455**	**515**	**951**	**844**	**913**

*(1)assuming that generics take up a 60% market share until 2013 then 80% from 2014**
The savings are calculated on the basis of the reduction in the retail price after tax in the community, the hospital tariff, the actual reimbursement percentage and the volumes as declared to GERS. Source: CEPS

The savings made by the price reductions that CEPS carried out can be broken down into several categories.

- Category A includes reductions in the prices of medicines issued in community pharmacies which are not on the substitution list. There can be various reasons behind such reductions, for example the price of a reference product falls, application of a clause, clawback payments are transformed into price reductions, alignment with a lower European price, an indication is extended, a reduction in the improvement in medical benefit or a group is reduced.

- Category B includes reductions in the prices of original medicines issued in community pharmacies when generics join the market. A downward trend concerning these savings can be noted since 2012 because of the fewer patent expiries and lesser significance of the products concerned.

- Category C includes reductions applied within the generic substitution list. These reductions are decided by CEPS after consultation with the generics surveillance committee, on which members of CEPS and the sector's associations sit (LEEM, GEMME, FSPF, USPO, UNPF and CSRP).
  During the latter committee's meetings, it lists the substitution rates within the different generic groups after 12, 18, 24 and 36 months of the first generic being on the market. At each of these intervals, the minimum substitution rate for generics has been defined: 60% at 12 months, 65% at 18 months, 70% at 24 months and 80% at 36 months. When the substitution rates observed are below this minimum rate, CEPS recommends fixed accountability tariff (TFR) or price reduction measures[40].

[39] So savings in categories A,B,C,D
[40] Note that once a generic has been on the market for 18 months, the ex-manufacturer price (PFHT) of the original product systematically falls by 12.5% and that of the generic by 7%

Price reductions associated with monitoring the substitution list can be rounded off by measures according to specific circumstances, the main ones being:

- Price convergence within a genericised group: the point of this is to even out the prices of generics on the one hand and original products on the other, by applying a target price to them – if necessary expressed in daily treatment cost (statins in October 2013, triptans in June 2014, ACE inhibitors/sartans in October 2014).
- European price referencing: this helps to reduce the differences with the prices of generics that are also sold on German, English, Italian or Spanish markets when the prices observed in these countries are lower.
- TFR trends: these may be reviewed to factor in the initial tariff level, which may be linked to a lower markdown level of generics than the level practised today. European prices are also compared.
- Lastly, on the basis of the legislation authorising it to do so, in 2015 CEPS set up a system for declaring the clawback payments manufacturers and distributors of generic medicines have granted to community pharmacists so as to ensure that the maximum authorised clawback threshold is complied with (40% of the ex-manufacturer price since 1 September 2014) and, where applicable, to base price reductions on this data.

- Category D includes reductions in the prices of medicines on the list for sale to outpatients.

In 2012 the amount of annual price or tariff reductions on medicines almost doubled compared with previous years, and has since stayed at this level. This has particularly been possible thanks to an increase in savings for categories B and C. On the one hand, the lapse in patents for medicines with high turnovers in 2012 enabled substantial savings to be made because of the fall in the original prices (totalling EUR 193 million in 2012 and EUR 113 million in 2013). On the other hand, the addition of new molecules to the generics substitution list increased the reductions made in category C, particularly for group convergence measures (protein pump inhibitors, Statins, ACE inhibitors/Sartan, etc.).

1.2. **The ONDAM community target for medical devices**

In 2014, savings made on medical devices and services totalled EUR 93.4 million (EUR 59.5 million in the community sector and EUR 33.9 million in the hospital sector). These were mainly the result of rising tariff reduction measures taken between 2011 and 2013 on products and services (EUR 82.1 million carried over from measures taken in 2013, and EUR 11.3 million in volume effect for measures taken from 2011 to 2013). The direct impact of part of the reductions applied in 2014 will mostly be felt in 2015, because of their application in the fourth quarter of 2014.

Table 20: 2014 savings associated with 2011-2014 reductions in the prices of medical devices within the scope of the ONDAM community target

Medical devices ([1])	2014 savings within the scope of the ONDAM community target (in €M)
Dressing items (2011)	-0.061
Breathing equipment (2011)	3.285
Insulin pump therapy (2012)	1.691
Insulin pump therapy (2013)	0.515
Self-treatment and self-testing equipment (2013)	6.523
Nutrition including brand names (2013)	8.021
Dressings (2013)	0.802
Viscoelastic (memory) foam cushions (2013)	2.797
Viscoelastic (memory) foam cushions (2014)	1.654
Incontinence (2013)	12.931
CPAP and remote monitoring (February 2013)	4.233
CPAP and remote monitoring (October 2013)	5.001[(2)]
Brand name dressings (April 2014)	0.122
Insulin pump therapy (2014)	3.459
Self-treatment and self-testing equipment (2014)	2.921
Brand name and technical dressings (2014)	3.788
CPAP and remote monitoring (2014)	1.778
Total	**59.460**

Source: CEPS

1. effective date of the reduction

2. factors in the EUR 12.001 million deduction corresponding to the cost incurred by the temporary rise in the CPAP tariff

2. **Measures within the scope of the ONDAM hospital target**

2.1. **The ONDAM hospital target for medicines**

All the savings measures concerned the scope of medicines that can be invoiced on top of hospital services, and they enabled EUR 80 million to be saved in 2014 (category E).

Most of these savings were made following the reductions in accountability tariffs for anticancer medicines (EUR 59.5 million).

The amount of savings thus made is a lot higher than in 2013 (EUR 60 million).

2.2. **The ONDAM hospital target for medical devices**

All of the reductions in the price/tariff of medical devices led to savings calculated on the basis of products and services list (LPP) tariffs of EUR 34 million on the ONDAM hospital target in 2014 (variation in the reimbursable tariff difference (ETI) not taken into account).

Two new reductions were decided in 2014: drug-eluting stents and non-active and bare-metal stents. This is a two-phase reduction, the first phase ending in 2014 and the second scheduled for 2016. A third reduction concerns the whole of the orthopaedics sector (including orthopaedic hip implants), with a second phase in 2015. The savings made in 2014 in this sector amount to EUR 5.9 million with the full effects expected in 2015.

These three reductions have enabled EUR 8.1 million to be saved since 2014, but the bulk of the savings will be measurable over the years to come because of carry-over effects. EUR 15.1 million come from the 2013 reduction concerning orthopaedic hip implants (EUR 15.0 million carried over and EUR 0.1 million in volume effect) and EUR 6.6 million from the reduction concerning conventional implantable cardiac stimulators (EUR 6.4 million carried over and EUR 0.2 million in volume effect).

Table 21: 2014 savings associated with 2011-2014 reductions in the prices/tariffs of medical devices within the scope of the ONDAM hospital target

Medical devices ([1])	2014 savings (in €M)
Drug-eluting stents (2011)	1.933
Meniscal repair systems (2012)	0.174
Drug-eluting stents (2012)	0
Orthopaedic hip implants (2013)	15.128
Abdominal aortic endoprostheses (2013)	1.935
Conventional implantable cardiac stimulators (2013)	6.623
Intracranial stents (2013)	0.018
Drug-eluting stents (October 2014)	1.771
Non-active and bare-metal stents (October 2014)	0.448
Orthopaedics including hip (October 2014)	5.856
Total	**33.886**

Source: CEPS
1. effective date of the reduction

PART THREE – STATISTICS CONCERNING THE COMMITTEE'S WORK IN 2014

CHAPTER I –CASE FILES PROCESSED

1. Applications submitted by companies and case files concerning changes in the prices of medicines

1.1. Case files concerning medicines dispensed in community pharmacies

The following statistics relate to applications submitted by companies and to price change files opened at the committee's instigation.

The case files are categorised in terms of a single type of application regarding a single product: first application for registration – either on the community medicines list only or on both the community medicines and public hospital medicines lists – but only for products available in community pharmacies, re-inclusion on the lists, price change, extended indications, or changed conditions of use.

Several different products relating to the same medicine may be grouped together in one file (for example different doses of the same product) and some of these may have several different formats (e.g. packed in boxes of 7 x 10mg tablets or 28 x 10mg tablets). Price change case files opened at the committee's instigation may cover several different products marketed by the same company.

***Text box 4**: The "Médimed" software application*

The purpose of the "Médimed" software application used by CEPS and brought into production in July 2006 is to track case files concerning medicines for which social security policyholders and local authorities can be reimbursed, as well as to produce rulings and notices for publication in the *Journal Officiel.*

This database contains all of the data in force characterising product formats with, especially for those which are reimbursable to social security policyholders, their prices and reimbursement percentages as well as the contractual clauses that are applicable to such proprietary products. The database also contains all of the decisions published or being made which concern them.

A record of the characteristics of proprietary products and product formats, saved in the database, can also be consulted by the user.

With the removal of the "vignette" price information sticker as of 1 July 2014, it became necessary to create a reference file of applicable prices that can be accessed by the diverse partners involved in the medicine chain.

This reference price file, updated almost daily, from the CEPS database, contains all of the data in force on medicines for which social security policyholders can be reimbursed as well as decisions concerning them up until their application date.

The Médimed application had to be adjusted in light of this project to guarantee the conformity of the data available for consultation and the traceability of the corrections made. The enforceability timeframes were integrated directly in the extraction "batch" of the reference file and great care was taken to ensure that this information is entirely in keeping with the decisions published in the *Journal Officiel*. This information can thus be used particularly by software publishers, and form the basis for pharmacies to invoice medicines and then for *l'Assurance Maladie* to settle reimbursements on the basis of validated, updated prices.

1.1.1. ***Case files opened in 2014***

In 2013, 1,332 case files concerning reimbursable medicines in the community sector were opened, corresponding to 9,078 product formats. In 2014, slightly fewer case files were opened (992) corresponding to 4,243 product formats. For three years now, the Committee has had a significant workload primarily involving price change files in response to the savings target set in the Social Security Financing Bill (PLFSS) for 2014. These price changes account for 52% of case files opened and 68% of product formats. The price reduction case files primarily concern generic medicines (70%). 67% of the first applications for registration concern generic medicines.

Table 22: Number and type of medicine case files opened in 2014, by application type

Type of application	Number of files	Number of product formats[1]	Number of files relating to generics	Percentage of files relating to generics
Extended indications	20	62	0	0%
Price reductions	403	2485	1730	70%
Price reduction following a TFR (change in margin)	52	188	188	100%
Price increases	20	140	2	1%
First listing	320	796	534	67%
Re-listing	177	572	2	0%
Total	**992**	**4243**	**2456**	**58%**

Source: CEPS - from Medimed software application, 01/06/2015

1. the same product or product format could be included in more than one application over the course of the year

1.1.2. ***Case files closed in 2014***

Fewer case files were processed and closed in 2014 than in 2013. A majority of these files concerned price reductions (50% of files processed).

Table 23: Number and type of medicine case files closed in 2014, by application type

Type of application	Number of files	Number of product formats[1]	Number of files relating to generics	Percentage of files relating to generics
Extended indications	22	54	0	0%
Price reductions	463	4459	3555	80%
Price reduction following a TFR (change in margin)	52	188	188	100%
Price increases	21	52	2	4%
First listing	288	734	465	63%
Re-listing	72	229	0	0%
Total	**918**	**5716**	**4,210**	**74%**

Source: CEPS - from Medimed software application, 01/06/2015

1. the same product or product format could be included in more than one application over the course of the year

In 95% of cases, the applications were closed on agreement between the company and the Committee.

Table 24: Numbers of products or product formats by type of application and decision for files closed in 2010

decision / Type of application	Accepted	Abandoned	Withdrawn	Rejected	Disagreement	Total
Extended indications	51	0	1	2	**NA**	**93**
Price reductions	4304	5	153	0	**NA**	**4459**
Price reduction following a TFR (change in margin)	188	0	0	0	**NA**	**188**
Price increases	12	1	3	34	**2**	**51**
First listing	686	13	17	18	**NA**	**734**
Re-listing	212	0	17	0	**NA**	**229**
Total	**5453**	**19**	**188**	**54**	**2**	**5716**

Source: CEPS - from Medimed software application, 01/06/2015

1.1.3. ***First applications for registration on the reimbursable medicines lists***

In 2014, 63% of the 734 first applications for registration concerned generics. In 99% of cases, first-listing applications for generics resulted in an agreement, compared with 83% for original products (with or without generic equivalents).

Table 25: Outcome of first listing applications handled in 2014 by numbers and type of product

decision / Type of product	accepted		abandoned		withdrawn		rejected		all
Generics	461	99%	4	1%	0	0%	0	0%	465
Original products	225	83%	9	3%	17	6%	18	7%	269
All	**686**	**93%**	**13**	**2%**	**17**	**2%**	**18**	**2%**	**734**

Source: CEPS - from Medimed software application, 01/06/2015

1.1.4. ***Case files still in progress at the end of 2014***

The end-of-year backlog of files is continuing to get smaller, falling from 646 on 31 December 2011 to 578 on 31 December 2012, to 565 on 31 December 2013 and to 547 on 31 December 2014.

Table 26: Number of medicine case files still in progress on 31 December 2014

Type of application	Total number of files in progress
Extended indications	47
Price reductions	69
Price increases	8
First listing	155
Re-listing	276
Total	**547**

Source: CEPS - from Medimed software application, 01/06/2015

1.2. Medicine case files in the hospital sector

The committee processed 33 registration applications in 2014. These were for new proprietary products or new product formats added to existing ranges of products already on either the outpatient medicines list or the list of medicines invoiced on top of GHS (DRG) funding. Each registration application comprises just under two tariff list entries on average (one entry per common dispensing unit).

Of these 33 new applications, 21 related to outpatient medicines and 12 to medicines invoiced on top of GHS funding.

Only 3 applications concerned generics; these were medicines for treating HIV.

6 applications concerned anticancer medicines and another 6, medicines derived from human blood. 3 medicines for treating hepatitis were processed, including one for hepatitis C (Sovaldi).

Table 27: New registrations on the hospital lists in 2014

Type of application / List	new applications	prices submitted	prices not submitted	no. of generics
T2A (DRG funding)	12	11	1	0
Hospital sales to outpatients	21	20	1	3
Total	**33**	**31**	**2**	**3**

Source: CEPS - from Medhop software application, 09/06/2015.

2. Medical device applications

2.1. Work on different case types

In 2014, the Committee processed 122 application files from companies. The number of applications still in progress at the end of 2014 was 145, whilst the committee received 205 new applications in 2014. This end-of-year backlog has increased because fewer applications were processed through the year, but above all because more applications were submitted.

Of the applications submitted in 2014, 43.9% were first applications for registration; 33.7% were applications for re-inclusion; 21% were requests for changes to the registration conditions and 1.5% applications for tariff increases.

In addition to the work involved in processing the applications, the committee also devotes a considerable amount of time to work on revising the categories for the lists, as described in point 3 below. This has enabled a certain number of notices of proposal to be published in the *Journal Officiel.*

2014 work was also marked by the negotiation and implementation of a certain number of price and tariff reductions, which lead to agreements and issuance letters being drawn up before a price notice is drafted. For any one subject it may be necessary for 12 agreements and letters to be drawn up in view of the diversity of stakeholders involved (including professional organisations). It is therefore understandable that, although not counted in the work tables, this increasing proportion of the Committee's workload is also taken on board to explain the fewer company applications processed. The price reductions that can be carried out when re-listing applications are being examined are no longer included in the re-listing timeframes since the actual processing of re-listing applications is done separately from price reduction negotiations. Twelve main product categories (brand or generic descriptions) were concerned in 2014, seven of which were subject to a preliminary notice of proposal.

The work presented in the tables does not take into account applications for change in distributor or for reference removal either. Such work, which also took time to process, resulted in the drafting and publication of 17 rulings in 2014.

Table 28: MD applications examined by the Committee in 2014

Type of application	Applications in process at the end of 2013*	Applications submitted in 2014	Applications closed in 2014	Applications in progress at the end of 2014
1st listing	70	90	67	93
Re-listing	48	69	25	92
Change	26	43	27	42
Tariff change	1	3	3	1
TOTAL	**145**	**205**	**122**	**228**

*Base adjusted as number of files in progress doubled
Source: CEPS

Of the 67 registration applications that were closed in 2014, 19 were rejected for registration by the committee, were abandoned or withdrawn by the company, or were closed by HAS. In 57% of these cases, the level of service was insufficient and was the reason for rejecting the application. Applications usually fail as a result of the committee rejecting the registration, although there are also instances when the company withdraws its application.

Table 29: MD applications processed by the Committee in 2014

Type of application	No. of applications processed	*Rejected, withdrawn or abandoned*	*Published in the JO*	average processing time for applications after submission (days)	average no. of examinations by the Committee
1st listing	67	*19*	*48*	328	1.3
Re-listing	25	*2*	*23*	345	1
Change	27	*5*	*22*	281	1
Tariff change	3	*1*	*2*	165	1.7
TOTAL	**122**	**28**	**96**	**316.8**	**1.2**

Source: CEPS

2.2. **Review of generic descriptions in 2014**

Four generic list categories were updated in 2014.

As in previous years, a summary on the progress of revision work carried out on generic list entries has been presented in table format on the basis of four statuses:

- in progress within the Committee (IP);
- notice of proposal published;
- new category published (ruling published in the *Journal Officiel*).

Table 30: Progress of revision work on generic list entries

Product type or name	Status	date received opinion from CNEDiMTS /CEPP	Committee	date notice of proposal published	date received new opinion from CNEDiMTS /CEPP	date published new category
Implantable pumps	revision LG	30/05/2008		06/03/2009	no opinion	28/05/2009
Self-treatment and self-testing	revision LG	15/02/2007		10/06/2009	06/10/2009	12/01/2010
Valve allografts	self-referral HAS	21/01/2010				Integration in the GHS 02/03/2010
DRESSINGS	revision LG	13/04/2010		30/07/2009	12/01/2010	07/08/2010
Vascular allografts	self-referral HAS	21/01/2010		15/09/2010	no opinion	23/06/2011
Dressing sets	self-referral HAS	22/03/2011		21/07/2011	no opinion	30/12/2011
Energy storing prosthetic feet	Referral DGS/DSS	28/04/2008		14/02/2012	12/06/2012	29/03/2013
Energy storing prosthetic feet	self-referral HAS	10/07/2013		15/10/2013	no opinion	04/02/2014
MD and associated services for oxygen therapy in cluster headache treatment	revision LG	23/04/2012		no opinion	no opinion	04/02/2014
Home-based parenteral nutrition	self-referral HAS + referral CEPS	24/07/2008 24/03/2012		19/03/2013	17/12/2013	18/06/2014
Bilirubin control and phototherapy devices for treating Crigler-Najjar syndrome type I	revision LG	30/07/2008		08/05/2013	08/10/2013	25/07/2014
Mobility equipment	self-referral HAS	04/07/2003		06/08/2010	13/09/2011	
External breast prosthetic devices	revision LG	29/05/2009		17/03/2011	31/05/2011	
Bone allografts	revision LG	21/01/2010		20/02/2013	28/05/2013	
Total hip replacement	revision LG	20/09/2007		21/03/2013	02/12/2014	
MD and associated services for oxygen therapy	revision LG	23/04/2012		29/10/2013	12/02/2014	
Home-based mechanical ventilation	revision LG	21/11/2012		04/12/2013		
Nebulisers for aerosol therapy	Referral DGS/DSS	12/01/2007	IP			
Stump socks	revision LG	06/02/2007 21/12/2007				
Stick and crutches	revision LG	07/11/2007				

Product type or name	Status	date received opinion from CNEDiMTS /CEPP	Committee	date notice of proposal published	date received new opinion from CNEDiMTS /CEPP	date published new category
Electronic devices for deafness correction	revision LG	15/05/2008				
TENS (transcutaneous electrical nerve stimulation)	revision LG	17/02/2009				
Breast implant	revision LG	29/05/2009	IP			
Cardiac stimulators Single, dual and triple-lumen implantables + ADAPTA DR	self-referral HAS	29/07/2009				
Pressure ulcer prevention medical aids	self-referral	23/12/2009 08/03/2011	IP			
Upper limb orthotic devices	revision LG	02/02/2010				
External upper limb prosthetic devices	revision LG	15/09/2010 22/12/2010				
Sit-to-stand lift, Walker, Patient lift	revision LG	10/11/2010				
Medical compression (elastic band contention)	revision LG	10/12/2010				
Artery embolisation implants	revision LG	08/07/2011	IP			
Posture aids for mobility equipment	Self-referral HAS	23/11/2011				
Home-based infusion equipment	revision LG	16/02/2012	IP			
Scooters	self-referral HAS	22/02/2012				
Orthopaedic elbow implants	revision LG	20/09/2012				
Compression/contention devices (elastic orthotic contention)	revision LG	10/10/2012				
Orthopaedic knee implants	revision LG	26/11/2012				
Face prosthetic devices	revision LG	19/12/2012				
Spinal implants	Referral DGS/DSS	04/04/2013	IP			
Made-to-measure pressure garments for severe burn victims	revision LG	25/09/2013				
Orthopaedic shoulder implants	revision LG	31/03/2014				
Contraceptive items	revision LG	07/05/2014	IP			
OSAHS/CPAP	revision LG	10/09/2014				
Medical beds with REVERSE TRENDELENBURG/TRENDELENBURG positions	Referral CEPS	08/10/2014	IP			
Fixed fee 7: fee for assisted ventilation using a mouth-piece as part of respiratory rehabilitation	revision LG	14/11/2014				

As part of its tariff revision work, the Committee has had to open up a case file concerning the revision of the dressing items category. This is still in progress.

CHAPTER II – APPLICATION PROCESSING TIMES

1. Processing times for medicine registration applications

1.1. Processing price applications

In 2014, one application was subject to registration via the fast-track price application procedure as stipulated in Article L.162-17-6 of the French Social Security Code.

The Committee accepted this application's registration 32 days after it was submitted.

1.2. Processing times for first applications for registration on the community reimbursable medicines list

1.2.1. ***Overall time***

The average processing time for applications in 2014 was 123 days. This is longer (89 to 123 days) for applications which were accepted as well as for applications which were not (319 to 336) days.

Acceptance is obtained within an average 73 days for generics and 226 days for non-generics.

Table 31: Processing times for medicine listing applications in 2014 by type (in number of days)

Type of product	Accepted	Abandoned, withdrawn or rejected	All
Generics	73	227	80
Non-generics	226	346	237
All	**123**	**336**	**137**

Source: CEPS - from Medimed software application June 2015

1.2.2. ***Interim processing times***

The overall time taken to process a first listing application has been broken down into the following five stages: from submission of the application up to delivery of the Transparency Commission (TC) opinion to CEPS; from delivery of this opinion up to CEPS' first session (examination), from the first to the last of CEPS' sessions devoted to the same case (negotiation), from the last session up to the signing of the rider (agreement) and from the signing of the rider by both parties up to publication of the registration ruling and price notice in the JO or to closure of the file in cases of withdrawn, rejected or abandoned applications.

Table 32: Interim processing times for medicine registration applications on the community list in 2014 (in number of days)

Type of product	TC	Examination	Negotiation	Agreement	JO or closure	TOTAL
generics	3	16	7	11	44	80
non-generics	77	39	33	27	62	237
All	**NS**	**24**	**16**	**16**	**51**	**137**

Source: CEPS - from Medimed software application June 2015

1.2.2.1. ***Stage one: Transparency Commission***

Applications must be lodged simultaneously with both CEPS and the Transparency Commission. During this first stage, the TC examines the application and notifies CEPS of its opinion. Only non-generic medicines, with some exceptions (change of pack format from that of the original medicine or non-reimbursable original medicine), go through this stage of the application.

For first-listing applications alone, concerning non-generics, there was an average of 77 days in 2014 between an application's submission and the delivery of the Transparency Commission's opinion to the Committee.

1.2.2.2. ***Stage two: Examination***

For non-generics, this stage runs from the date on which CEPS receives the TC's opinion to the first session during which CEPS examines the product or product format. This stage may include the appointment of a rapporteur after receipt of the TC's opinion, who examines the application in liaison with the pharmaceutical company and draws up a report which is given to CEPS, as well as the time taken to enter the relevant application on CEPS' agenda (at least one clear week after committee members have received the report).

The examination times for applications are 24 days on average in 2014, i.e. 2 days less on average than in 2013.

1.2.2.3. ***Stage three: Negotiation***

This third stage runs from the first to the last of the sessions during which CEPS examines the application. It corresponds to the time required by CEPS to draw up its proposal, if it is not finalised in a single session, plus the time needed for negotiations between CEPS and the pharmaceutical company. CEPS must examine the company's counter-proposals if the latter rejects CEPS' initial proposal following discussions with the rapporteur.

The average length of negotiations is 16 days in 2014, which is up by 2 days compared with 2013.

1.2.2.4. ***Stage four: Agreement***

This is the time between the last of CEPS' sessions devoted to an application and the signing of the corresponding contract rider. It corresponds to the time needed to draw up the terms of the rider, which may involve several exchanges of correspondence between CEPS and the company over sometimes complex clauses, and also the time required for the logistics involved in the two parties signing the rider. In practice, the fourth stage includes a final negotiating period which is difficult to separate from the time required for the practical arrangements.

The times for this stage are ten days shorter than in 2013, at 16 days on average.

1.2.2.5. ***Stage five: Signing of the decrees and publication in the* Journal Officiel**

This final stage includes CEPS' drawing up of the price rulings and notices of registration on the reimbursable medicines lists, which then need to be signed by the relevant departments at the Ministry of Health. This period also includes the time taken for UNCAM's Chief Executive to decide on the reimbursement rate and for these decisions to reach CEPS. Lastly, for all these texts to be published in the JO, they must first be sent to the Government's General Cabinet Office *(secrétariat général*).

This last stage took 51 days on average, i.e. 1 day longer than in 2013.

1.3. Processing of applications for registration on the hospital medicine lists

The processing times for applications for registration on the hospital medicine lists are worked out on the basis of medicines that were registered on the outpatient medicines list or the list of medicines invoiced on top of GHS funding for which a price was published in 2014.

The average interval between registration on one of the lists and publication of the price in the JO was 89 days (see Table 33). The average interval between registration on the outpatient medicines list and publication of the public prescription price was 99 days, whilst the interval before publication of tariffs for medicines registered on the list of medicines reimbursable on top of GHS funding was 73 days on average.

However, three applications for registration on the outpatient medicines list took a long time to be processed and this had a considerable effect on the average processing time. These applications excluded, the average interval between registration on the list of medicines reimbursable on top of GHS funding and publication of the accountability tariff in the JORF was 75 days, which is on par with the average processing time for medicines on the list for reimbursement on top of GHS funding.

For the latter list, the tariffs can be published at CEPS' initiative without going through any further procedures. On average the tariffs are published 10 days after the pharmaceutical company has been notified of CEPS' decision. For medicines on the outpatient list however, the price can only be published at the same time as that of the reimbursement rate after this has been registered with the public bodies, and this is 43 days on average after the pharmaceutical company has been notified of CEPS' decision.

Table 33: Interim processing times for applications for registration on the hospital lists in 2014 depending on the distribution channel

Times (no. days) / List	between registration and 1st session	between 1st session and 1st decision	between 1st decision and last decision	between the decision and publication	Total
Outpatients	32	7	17	43	99
On top of GHS funding	21	5	37	10	73
Total	**28**	**6**	**24**	**31**	**89**

Source: CEPS - from Medhop software application, 09/06/2015

In cases where the company submitted a price, in accordance with Article 8b of the framework agreement, the interval was 84 days. Where there was no price submission by the company, the interval was 109 days. In these cases, the published price or tariff is the price decided unilaterally by CEPS.

2. Application processing times for medical devices

On average, applications processed in 2014 were completed within 317 days after submission. This was slightly quicker (by 9 days) than in 2013. The outcome for 79% of these applications was publication in the *Journal Officiel*.

For first listing applications, the average time between submission of the application and completion of the process was 328 days, for all outcomes. CNEDiMTS delivered its opinion for these applications within an average of 121 days and it was sent to CEPS 8 days later. The first examination by CEPS took place on average 99 days after receipt of the CNEDiMTS opinion. One in six applications needed examining by the Committee several times, with an average interval between the first and last examination of 61 days. As a result, most of these applications only need examining once, or 1.3 times as the average figure. The decision was published within 80 days on average after the decision made during a committee session.

On average, re-listing applications were examined once by CEPS and took 345 days to process. Processing was done much more quickly in 2014, taking 80 days less, partly thanks to CNEDiMTS delivering its opinion much more quickly, and to the shorter average postponement.

Applications for changes to registration conditions were processed within an average of 281 days, which included 98 days between submission of the application and delivery of CNEDiMTS' opinion.

Of the three revaluation applications processed in 2014, one was subject to postponement, which explains why the actual time is longer than 90 days (legal time limit) and led to an average overall time of 165 days. Two resulted in revaluation and one in rejection on the Committee's part.

Table 34: Average processing times for MD applications in 2014 (number of days)

Type of application	interval between submission and CNEDiMTS opinion	interval before opinion sent to Committee	interval before 1st examination by Committee	interval between 1st and final examination*	interval between final examination and decision	Total time
1st listing	121	8	99	18	80	328
Re-listing	139	8	98	13	87	345
Change	98	7	89	5	82	281
Tariff change	23			100	42	165

Source: CEPS

**calculation on the basis of all applications depending on their type, but only concerns a handful of applications*

These times, which reflect the processing time from the submission date to publication in the *Journal Officiel* or to the application's closure for whatever reason, are to be weighted by the postponements which often arise during the application processing procedure. Indeed, 52% of registration applications processed in 2014 were postponed for an average 81 days and 33% of applications for changes were postponed for an average 57 days. If these postponements are taken on board, they cut the actual administrative processing time of an application, bringing it closer to the regulatory time of 180 days. For all that, during these postponements the company still

has to wait for its product to reach the market, or for its development. It is important to start by tracking an application's processing time that will have a real impact on a company.

The vast majority of these postponements are instigated by CNEDiMTS.

Lastly, 24% of re-listing applications processed in 2014 were also postponed, for an average of 92 days.

APPENDICES

APPENDIX 1: IMPLEMENTATION OF THE GUIDANCE LETTER FROM THE MINISTERS DATED 2 APRIL 2013

THE GUIDANCE LETTER FROM THE MINISTERS DATED 2 APRIL 2013	PRACTICAL ACTION
The Minister for the Economy and Finance The Minister for Social Affairs and Health, The Minister for Economic Regeneration, Paris, 2 April 2013 Dear Mr Chairman, The Government's pricing policy for healthcare products is organised around the following objectives: - guaranteeing universal access to quality healthcare - promoting responsible medicine use and efficient spending - utilising innovations as sources of therapeutic progress, - ensuring transparent pricing processes and coherent decision-making - meeting the annual health insurance expenditure growth targets (ONDAM). - in accordance with the National Compact for Competitiveness, Growth and Employment, supporting growth of the health industries – a priority sector for the future – and the development of jobs. You will ensure that prices are set and the agreement policy is carried out in line with these objectives.	
By participating in the ONDAM steering committee, you will help to set annual expenditure targets, to look for areas where savings might be made, to provide them with a multiannual framework and to meet them, where applicable by taking any corrective measures necessary through the year.	The CEPS Chairman now attends the ONDAM steering committee meetings
Your chairmanship of CEPS comes at a time when medicine expenditure is slowing down due to the control policies put into practice, especially by the Committee, and to structural factors specific to this sector: many products going off-patent and the fewer innovative products entering the market for more limited groups of patients.	The context described has changed particularly with the arrival of innovative medicines that have a major impact on the budget in 2014 and 2015.
For all that, better use and appropriate prescription of medicines – which will cut consumption that is expensive, unnecessary or without benefit for the patient – are still absolute priorities. Controlling the market composition effect on medicine sales, reducing the prescribed volumes in some therapeutic groups and	

developing prescription in the generics substitution list are key consequences in this regard. Whenever necessary, the Committee will suggest that the competent authorities set up systems for improving responsible use and economical prescription of medicines, or their optimum use within the context of smooth care pathways between the community and hospital sectors. It will play a part in this through contractual provisions, particularly when considering registration on the reimbursable medicine lists of a product that is likely to be used beyond medically justified need, and within the context of regulating medicine promotion.	The CEPS Chairman attended the steering committee for work being carried out under the Public Action Modernisation policy, in terms of developing the generics market. He signed the charter dated 24 March 2015
The marketing of new types of medicine (advanced therapy medicines) must be anticipated and encouraged. The Committee will endeavour to recommend suitable reimbursement procedures as required.	Clauses that provide a framework for sales volumes at the justified medicine level are concluded by CEPS at regular intervals. At the start of 2015 CEPS set up a foresight committee on medical innovation.
With the support of the Ministry for Economic Regeneration, the Committee will also keep an eye on the main economic trends in the healthcare products sector, irrespective of their status in reimbursement terms by *l'Assurance Maladie*.	
More generally, the Committee will come up with suggestions and ideas concerning medicine and medical device policy, particularly as regards the development of markets for so-called biosimilars and self-medication products.	
Given the growth in the medicine and medical device markets, and the situation regarding the *l'Assurance Maladie* accounts, we feel that it is necessary to specific the following guidelines for CEPS.	CEPS has played an active part in work on defining the economic conditions for the marketing of biosimilars. It has defined a pricing doctrine in this regard.
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The Government is strongly in favour of the principle of signing agreements with the healthcare products industry which, by increasing the clarity and effectiveness of the policies conducted, has demonstrated its efficacy.	
Whilst boosting territorial appeal for the health industries may not specifically form part of the Committee's remit, the clarity of the sector's pricing policy contributes to the Government's policy in terms of developing and establishing these industrial and research activities in France. With the same aim in mind, you will endeavour to increase the visibility for industry of the regulation measures that CEPS intends to put into practice: to this end, you will come up with the arrangements for bringing the outline of these measures to the attention of manufacturers one year before they are put into practice. You will also use your expertise to shore up the initiatives taken by the Government to develop this strategic industrial sector in the framework of the Health Industries Strategic Council (CSIS) and the Health Industries Sector Council.	CEPS is working on the clarity of regulation measures. Manufacturers are well versed in the way they work, their governing texts and their doctrine. The annual report plays a key role in conveying information. The CEPS Chairman communicates on the annual guidelines adopted at regular intervals and periodically informs companies of any regulation operations in the pipeline. The CEPS Chairman has been involved in some of the CSIS/CSF's work.
Regarding medicines, you will ensure that the new framework agreement is implemented transparently and openly, in liaison with the industrial partners. We are particularly bearing in mind certain new provisions of the agreement which may result in a subsequent rider where necessary.	Consultation meetings are organised at regular intervals between signatories to the framework agreement specific to the "medicines" sector.
Regarding medical devices, you will implement the provisions in	The guidelines of the 2011 framework

the new framework agreement on medical devices, dated 16 December 2011, especially the possibility of asking manufacturers or service providers for data or post-registration studies, the preference for registering by brand name and the rules for setting the maximum purchase price, revising tariffs and prices and price-volume clauses. Since knowledge of the medical device and service provision market is still too fragmented, you will put together databases of reimbursable products and services, possibly with contributions from elsewhere.	agreement on MDs are being implemented, particularly those concerning tariff revision or setting the maximum purchase price. Compilation of databases intended to improve knowledge of products, companies, markets and distribution margins is being hampered by methodological difficulties and a shortage of available resources. It has only been possible to set up sectoral surveys or observatories.
The work that CEPS accomplishes must play a greater part in ensuring responsible medicine use. You will ensure that the new tools CEPS is now equipped with under the law are put into use.	
In the event that a product is found to be used outside of its MA indications and the recommendations of the competent health authorities, and that a manufacturer fails to meet its contractual undertakings to ensure its responsible use, you will pronounce the corresponding financial sanctions.	CEPS keeps an eye out for this type of situation, but did not have to pronounce any sanctions in 2014.
When the turnover for a product or family of products clearly exceeds the target patient group of its MA and the recommendations of the competent health authorities, or when the amount reimbursed clearly exceeds the target patient group of its reimbursable indications, you will ensure that the manufacturers concerned make an active contribution to restoring responsible use of their product and you will introduce price reductions should they refuse or not do enough.	
Whenever necessary, you will suggest that the competent authorities set up schemes for raising prescribers' awareness about responsible use, and you will play a part in this through the agreement-based system, especially when the aforementioned cases arise.	
Improving manufacturers' promotional practices with healthcare professionals relies particularly on compliance with the medical visit charter. You will set about revising this charter so as that it henceforth includes the Committee's new possibility of setting annual growth target figures for the medical visit, and you will put this new regulation tool into practice.	The pharmaceutical promotion charter was renegotiated in 2013 and signed in 2014.
We would like CEPS to continue making an effective contribution to the control of medicine and medical device expenditure. Several strategic aims must underpin your action.	
As provided for by the law, tariff negotiations will take the findings of medico-economic assessments on board: the new framework agreement contains a number of provisions in this regard which you will ensure are closely complied with. In order to increase the actual extent to which the medico-economic assessment is factored into pricing mechanisms, you will set out the changes and procedures that you deem necessary by 30 September 2013 at the latest, after consulting with HAS and the manufacturers' representatives, and with account taken of the changes in progress in other European States. You will step up use of medico-economic assessment by submitting an opinion request to the HAS competent commission whenever you consider this necessary.	CEPS has been receiving opinions on the efficiency of so-called "innovative" products (improvement in medical benefit/ASMR rating of 1, 2 or 3) with a significant impact on *l'Assurance Maladie* since 1 October 2013. Implementation of the September 2012 decree (application on 1 October 2013) was prepared in close liaison with HAS

The Committee will endeavour to guarantee the efficiency of healthcare product reimbursement on the basis of real-world data gathered on these products. As such, the Committee will ensure that the post-registration studies are properly conducted and sanction any unjustified delay or shortcoming. The conditions for conducting and receiving these studies, for medicines and medical devices alike, will be defined by early dialogue between CEPS, HAS and the companies concerned and by setting up the post-registration study surveillance committee which must quickly become operational.	and manufacturers' representatives. Ms Polton is currently heading up discussions on medicine assessment, and CEPS has been closely involved in these.
Innovative product pricing (see below) is based on a research support policy aimed at ensuring that situation rent is not earned once a product goes off-patent. Major savings associated with the generics market involve both increasing prescription in the substitution list, maintaining high substitution rates and prices set as fairly as possible. You will endeavour to make proportional and schedule price reductions, beyond the 60% markdown applied to the original price, on the basis of sales volumes and methodologically adapted European price referencing.	The Medicine Real-World Study Surveillance Committee was set up in 2013 together with the Transparency Commission. It is up and running and meets at regular intervals. A joint CEPS-HAS committee has been monitoring post-registration studies on medical devices since 2011.
These efforts must also concern medicines which are soon to go off-patent but for which generic versions are still not possible, to ensure that this patent lapsing can lead to significant savings for *l'Assurance Maladie*.	
Furthermore, the Committee will continue to carry out additional price reductions applicable to proprietary pharmaceuticals belonging to generic groups that are not subject to a fixed accountability tariff (TFR), up to 12.5% for the original product and 7% for the generics, 18 months after the first generic version of the original product concerned has been marketed. These price reductions will particularly come in the form of a gradual reduction in the original product prices as soon as the first generic is marketed. Unless stated otherwise, the original product price will be brought down to the price of its generics five years after the first generic is marketed. In order to increase the generic market share more quickly before this price convergence, the "over time" TFR application policy will be continued on the basis of current substitution limits, adapting them where necessary. Regarding genericised original products, which are little substituted but whose conditions for transfer to a TFR tariff cannot be reunited (limited offer, narrow substitution window, etc.), you will ensure that additional price reductions are applied to them so as to obtain the savings that would have allowed successful substitution.	The reductions in generic prices planned in 2013 and 2014 were made on the basis of European price referencing. Reductions in the prices of medicines that are open to genericisation but which have not been genericised were planned in 2013 and 2014. Price reductions 18 months after genericisation were applied in 2013 and 2014. The convergence of prices of original products that have been genericised for five years began in 2013 and continued in 2014.
What's more, especially in highly genericised groups, you will carry out a convergence of prices within therapeutic groups whose products provide the same medical benefit, by aligning them at the lowest price.	Monitoring of the generic substitution list in 2013 and 2014 led to the fixed accountability tariff (TFR) being created. As an alternative, price reductions so as to obtain the same savings that a successful substitution would have brought about have been applied.
Innovations in the realm of healthcare products not only generate medical progress but also help to improve the way healthcare is organised. The Committee will endeavour to support these changes for the sake of efficiency, by shoring up its decisions with recommendations on controlling reimbursement of the products concerned and on healthcare organisation and/or by calling for	In 2013, a consistency measure was carried out on the proton pump inhibitor group. This measure was also negotiated for statins in 2013, for application in 2014. For ACE inhibitors and sartans, the negotiations held in 2014 resulted in

adapted medico-economic studies to be undertaken. CEPS will ensure that therapeutic progress brought about by products recognised as being innovative is fairly remunerated. This must enable patients to access medicines or medical devices that have demonstrated an improvement in medical benefit, as well as, where applicable, their associated biomarkers or procedures. Pursuant to the recently signed framework agreement, it must be possible to adjust, via agreements, reference to the European prices set for new innovative medicines, to set French prices, so as to factor in sales volume trends in France and the reference country, as well as new data specific to assessing the product or its actual reimbursement conditions. You will inform us of your analysis on the relevance of this external referencing with respect to the literature available, committee practice, and the arrangements for pricing and granting clawback payments in force in each reference country. Contact with your European counterparts would likely encourage information sharing and minimum coordination in the pricing policy for innovative products. The Committee will continue to limit the high price effects observed for some medicines by bestowing a fixed amount framework upon their turnover, so as to guarantee that *l'Assurance Maladie* does not bear too high a cost while ensuring that the patients concerned can access the products.	significant reductions in 2015. In terms of innovative products, the prices at face value of medicines with an ASMR rating of 1,2 or 3, registered in 2013 and 2014, lie at the maximum levels equivalent with those of the reference States. The European sales volumes and prices of innovative products are communicated to CEPS by the companies concerned. An information unit on international medicine pricing was set up by CEPS in 2013. In line with its doctrine, CEPS has applied turnover control frameworks, particularly for some orphan medicines.
Every time a set price results in a different improvement in medical benefit appraisal from the one presented in the HAS opinion, the reasons for this appraisal difference will be made publicly available.	This situation did not arise in 2013 or 2014.
The Committee will only be able to practise "financial risk sharing" on a reasonable and exceptional basis, by reserving this type of contract for medicines that present genuine prospects and meet uncovered therapeutic needs.	A few clauses of this type were concluded in 2013 and 2014 (see annual report)
Regarding medicines with no improvement in medical benefit, the Committee will endeavour to maximise the treatment cost savings on which their registration depends and, for each product concerned, present this source of savings in its annual report. For medicines with a minor improvement in medical benefit, it will recommend tariff conditions for registration on the reimbursable medicines list that will prevent any excess cost for *l'Assurance Maladie*.	A specific appendix reports on the pricing of new products with an improvement in medical benefit (ASMR) rating of 5, in each annual report.
You will also see to speeding up market access for medical devices.	
You will ensure that the prices are swiftly adjusted to the latest assessments available and change in the offer in each therapeutic group, particularly following a downward reappraisal of the improvement in medical benefit (ASMR) or improvement in expected service (ASA) by the Transparency Commission or National Medical Device and Health Technologies Assessment Committee.	The processing times for MD applications depend upon the resources available. Product reappraisals are put on the Committee's agenda at regular intervals, and any worthwhile subsequent action decided on accordingly.
The Committee will continue the "consistent pricing" policy by applying it to the groups which justify this, and in view both of the marketing of generics and any tariff changes affecting them. It will also set up "consistent pricing" within homogeneous groups for which less expensive proprietary products are marketed –	Consistency reductions are applied at regular intervals.

particularly "biosimilars". For medical devices, revision of generic list entries must also be an opportunity to review the corresponding tariffs and prices. It is particularly important for the committee to finalise in 2013 its revision work of the generic list entry tariffs and category concerning total hip replacements, for which the National Authority for Health (HAS) delivered an opinion in September 2007, and to continue its revision work of the categories for the other generic list entries revised by HAS. In order to limit patients' out-of-pocket expenses, the pricing committee must give precedence to setting maximum purchase prices both when revising generic list entries and when registering new products and services.	Measures to revise generic list entries were initiated in 2013 and 2014.
Specifically with regard to products used in hospitals, especially those invoiced on top of tariffs for 'standard hospital stay groups' (similar to diagnosis-related groups) (GHS), the Committee will help to control such expenditure and to monitor its growth by making use of the legal and agreement-based tools it has at its disposal, such as setting accountability tariffs and defining turnover budgets. The Committee will also observe at regular intervals the new data available and the actual prices at which hospital medical devices and medicines are purchased so as to adjust the accountability tariffs and thus take advantage of buoyant purchasing policies in establishments or of the arrival of a generic or "biosimilar" competitive offer.	The Committee examines the actual prices at which hospital medical devices and medicines are purchased on a regular basis and adjusts the accountability tariffs accordingly.
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We set great store by the fact that the committee you chair – which brings together the main competent institutions and government bodies in the field – plays its role to the full in terms of boosting and coordinating the pricing policy for medicines and medical devices, under our authority. As such, for work involving the anticipation, expertise and monitoring of measures considered or adopted and, more generally, the medicine and medical device market and the companies that produce them, you will be supported whenever necessary by the government bodies, establishments and institutions that sit on the committee, the ATIH, DREES and INSEE.	The ATIH now supplies data on the tariffs of products on the additional invoicing list practised in the public and private sectors alike.
In liaison with the Chairpeople of HAS, CT, CNEDIMTS and CEESP, you will also ensure that your work ties in as effectively as possible, in keeping with each body's remit.	The price indicator for medicines is presented in the CEPS annual report.
Lastly, we ask that you would ensure the Committee's active participation in preparing and implementing the measures decided within the CSIS and the health industries sector committee, particularly in terms of boosting France's appeal for the health industries, which is of the utmost importance for developing research, economic growth and achieving trade balance equilibrium.	Regular work discussions in keeping with each body's remit have been set up with the Transparency Commission, Medical Device Evaluation Commission and Public Health and Economic Evaluation Commission of the National Authority for Health.
Yours sincerely, The Minister for the Economy and Finance	The CEPS Chairman has been involved in some of the CSIS/CSF's work.

Pierre Moscovici The Minister for Social Affairs and Health Marisol Touraine The Minister for Economic Regeneration Arnaud Montebourg	

APPENDIX 2: FRAMEWORK AGREEMENT OF 5 DECEMBER 2012 BETWEEN THE HEALTHCARE PRODUCTS PRICING COMMITTEE AND THE PHARMACEUTICAL COMPANIES

Having regard to European Union Law, the French Social Security Code and national ministerial policy;

Whereas Article L. 162-17-4 of the Social Security Code provides that an agreement may be drawn up setting forth the contractual framework for relations between the Healthcare Products Pricing Committee (CEPS) and each of the companies producing the medicines described in Article L. 162-16-4;

Whereas, subject to the provisions of the French Public Procurement Code, Article L. 162-16-5 of the Social Security Code provides that, with regard to proprietary pharmaceuticals which have been granted marketing authorisation and are registered on the list provided in Article L. 5126-4 of the French Public Health Code, an agreement should be made setting forth the procedure and conditions governing manufacturers' price submissions, the criteria for opposition by CEPS, the conditions under which the declared retail prices may be reviewed and the undertakings to be made by the company;

Whereas Article L. 162-16-6 of the Social Security Code provides that, with regard to the proprietary pharmaceuticals mentioned in Article L. 162-22-7 of the same code, an agreement should be made setting forth the procedure and conditions governing manufacturers' price submissions, the criteria for opposition by CEPS, the conditions under which the declared retail prices may be revised and the undertakings to be made by the company;

Whereas it is fitting that medicines should be given their rightful place in prevention and healthcare and that this requires both rapid access for patients to innovative medicines, improved efficiency and rationalisation of expenditure on medicines and sustained efforts to avoid excessive consumption and promote responsible usage;

Whereas medicines can be both a source of improvement in quality of care and a source of economies for the public purse when used solely for proven medical purposes, within a competitive market in which generic medicines, biosimilar medicines and self-medication are free to play their part;

Whereas advances in treatments, the demographic situation, epidemiological data and the government's public health plans must be taken into account when appraising growth in the consumption of medicines;

Having regard to the benefits of maintaining and developing a strong, competitive pharmaceutical industry and of protecting intellectual property, trademarks and registration data within European Union territory;

Whereas the majority of spending on medicines is financed out of the public purse, whose resources are finite by nature, and whereas it is therefore fitting that there should be regulation in place which is proportionate to the contribution made by medicines, in accordance with the law and ministerial policy and under fair, transparent conditions;

Whereas the most desirable means of achieving the goals set forth hereabove is through strengthened cooperation between the public bodies and the pharmaceutical companies;

Whereas the greater need for transparency in public action and agreement policy particularly leads to signatories deciding to present more fully the contents of clauses on complying with posologies and the target patient groups.

Whereas the most desirable means of achieving the goals set forth hereabove is through strengthened cooperation between the public bodies and the pharmaceutical companies without its arrangements affecting the confidentiality of business;

The Healthcare Products Pricing Committee (hereinafter "CEPS") and the pharmaceutical companies now agree to amend their framework agreement as follows.

CHAPTER I: EXCHANGING INFORMATION AND MONITORING SPENDING COVERED BY NATIONAL HEALTH INSURANCE

Article 1: Exchanging information

For the sake of transparency, the parties agree on the necessity to improve and share the information they each hold regarding consumption and prescription of reimbursable medicines and the actual reimbursements paid out for medicines.

The representatives of LEEM will facilitate access by members of CEPS, via electronic means in particular, to the commercial information which the companies have available.

They will continue to send CEPS, both in hard copy and electronic format, commercial data, of which the companies shall retain ownership, including but not restricted to the statistics produced by the industry's statistics gathering association (GERS) regarding sales to both community pharmacies and healthcare establishments. Furthermore, to enable CEPS to make the necessary forecasts, at the end of each quarter CEPS shall be sent information on the quarterly declarations of sales by volume (number of common dispensing units) and by value (turnover before tax per common dispensing unit) to healthcare establishments which the companies governed by this agreement undertake to make to GERS, in accordance with the agreement signed between GERS and CEPS. The quarterly sales declarations shall be made with regard to both medicines covered by temporary authorisations for use (ATUs) and medicines that have marketing authorisation (MA), including orphan medicines, and shall cover all companies whether or not they are members of GERS.

The companies undertake to send to CEPS upon request the information available to them regarding real-life use of the products for the various indications stated in their MAs. For medicines that have been granted an ATU (whether in the context of a cohort programme or a named patient programme), before the file is examined the companies shall send a summary and analysis of the data from the information gathering and therapeutic use protocol to both the Transparency Commission and CEPS, to provide them with a body of information, in particular on how the product should be used and the nature of the patient group receiving the treatment.

The companies also undertake to allow CEPS access to information regarding current prices in force in other EU countries and the reimbursement situation and sales volumes in these countries.

CEPS and national health insurance (*l'Assurance Maladie*) shall make available to LEEM detailed information regarding the reimbursements paid out by national health insurance and reports of studies conducted into the prescription and consumption of medicines, under the same conditions in which they are made available to the professional healthcare associations, in particular studies regarding statistics derived from the coding of medicines claimed back from national health insurance by the healthcare establishments, as soon as these statistics are available.

CEPS shall inform LEEM every year of its forecasts regarding growth in sales of reimbursable medicines and its forecasts regarding implementation of the end-of-year adjustments under the terms of Articles 17 and 18 herebelow.

CEPS and LEEM agree to set up a joint monitoring group which will be responsible for overseeing the implementation of this framework agreement.

A Generics Monitoring Group shall also be formed, which shall be made up of members of CEPS and representatives of companies operating in the generics market: pharmaceutical companies, wholesaler-distributors and community pharmacists. LEEM shall ensure that companies selling generic medicines are specifically represented among the pharmaceutical industry representatives. The group shall meet to discuss the matters set out in Article 13 herebelow among others.

Article 2: Monitoring spending covered by national health insurance

The parties agree to monitor spending on medicines every three months in consultation with each other, in particular regarding the information mentioned in Article L.162-17-3, Paragraph II of the Social Security Code. This consultation shall be organised within the framework of the above-mentioned joint monitoring group set up under Article 1 hereabove. The parties shall consult on all medicines covered by compulsory national health insurance, both those distributed to community pharmacies and those included on the lists set out under Articles L. 162-16-5 and L. 162-16-6 of the Social Security Code.

Article 3: Intellectual property.

Companies selling pharmaceutical products to which they hold one or more patents or supplementary protection certificates (SCP) may declare these to CEPS along with the respective expiry dates. The committee shall make such declarations accessible to any pharmaceutical company that requests access to them.

Details of the registration of any generic pharmaceutical product on the national health insurance reimbursable medicines lists and where applicable the public hospital approved medicines list shall not be published more than six months before the declared expiry date of the intellectual property rights concerned, where CEPS has been notified of such date.

However, any pharmaceutical company which believes that it is able to sell the generic products in question without infringing the declared rights may apply for their product to be registered on the appropriate lists. In this event, the pharmaceutical company must inform CEPS, which in turn shall promptly inform the company selling the original medicine as mentioned in the first paragraph hereabove and shall then begin the registration procedure.

Article 3a: Early transfer of rights

The owner of the intellectual property rights to a reference proprietary product may, subject to the provisions of the French Intellectual Property Code, assign the following rights before they have expired to a duly authorised pharmaceutical establishment acting in the capacity of sub-contractor under the terms of Chapter 7 of the Good Manufacturing Practices stipulated in Article L.5121-5 of the Public Health Code:

- the right to purchase sufficient quantities of raw materials and generally speaking to carry out any activities that are necessary and essential for the manufacturing process described in the following paragraph;

- the right to manufacture a generic version, as defined in Article L.5121-1, Paragraph 5 of the Public Health Code, of the proprietary product in question, on behalf of a pharmaceutical establishment authorised to use the marketing authorisation for the corresponding generic product;

- the right to release batches of the generic product thus manufactured 48 hours before the expiry of the intellectual property rights of the original proprietary product rights' owner, for the sole purpose of preparing stocks of the product and to the exclusion of any other act, carried out alone or jointly with the pharmaceutical establishment marketing the generic product, which might lead to the sale or delivery of the generic medicine. These batches released at this time may not be delivered until after the expiry of the intellectual property rights pertaining to the original proprietary product. The sub-contractor shall guarantee to the original proprietary product rights' owner that the pharmaceutical establishment marketing the generic product will refrain from any actions pertaining to sale or delivery as stipulated above.

The authorisations granted by the intellectual property right owners pursuant to this Article shall give rise to clawback credits, the sum of which shall be set, depending on the scope of the authorisations, by mutual agreement between the company and CEPS.

CHAPTER II: MEDICINES SOLD IN COMMUNITY PHARMACIES. AGREEMENTS

Article 4: The contractual framework

Any company which sells medicines covered by compulsory national health insurance, provided the company is certified pursuant to Article L. 162-17-4 of the Social Security Code, shall be offered the opportunity to enter into a multiannual agreement with the Healthcare Products Pricing Committee (CEPS).

The agreements shall be drawn up with a view to ensuring that this framework agreement is implemented, whilst taking into account each company's individual situation and future development prospects and working within the rules set forth in the Social Security Code and the policy guidelines passed on to CEPS each year by the relevant ministers.

Within this framework and save for any exceptions warranted by any specific aspect of the French market, the agreements guarantee for medicines having, on the one hand, applied for and obtained an ASMR rating of I to III and, on the other hand, received a medico-economic opinion from the CEESP within the statutory timeframes enabling CEPS to determine the conditions for their efficiency, that the price set will be no lower than the lowest price in force in the 4 main comparable EU markets mentioned in Article 7 herebelow, for a period of five years starting from the date the medicines become available to patients by virtue of their registration on the community or hospital reimbursable medicines list. This guarantee also applies to medicines which have been given an ASMR rating of IV in relation to medicines recently rated at ASMR levels I to III, where the Transparency Commission's opinion indicates that this rating is more beneficial to them than a rating which would have placed them at the same ASMR level as these reference products. An extra year shall be added to this guarantee for the paediatric medicines listed in Article 10 herebelow for which studies have been conducted in implementation of the paediatric investigation plan arranged with the ANSM Board. In the event that the Great British Pound should fall strongly against the Euro within a short space of time, this shall not be allowed to have any short- or medium-term impact on the French equivalent of the new sale price in Euros of medicines sold in the United Kingdom, in respect of medicines whose prices were set prior to this depreciation. For medicines with a cohort temporary authorisation (ATU), CEPS can ask via agreement either for a reduction in the price guarantee timeframe by taking into account the ATU timeframe and the number of patients treated under a temporary authorisation (ATU), or for all or part of the expenditure incurred under the ATU to be reimbursed.

In order to ensure that CEPS can examine the price application in the best possible conditions, the company forwards figures concerning forecasted or observed sales volumes for the product concerned to it for each of the comparable European markets mentioned in Article 7 herebelow. It also forwards to CEPS the electronic, configurable version of the medico-economic model it has drawn up.

Every year, the company communicates to CEPS the prices, sales volumes and reimbursement arrangements on the comparable European markets during the price guarantee period.

Reviewing prices and clauses

Prices and affiliated clauses may be reviewed either at the company's or CEPS' request, in particular when a change occurs to any of the factors on which the existing price and the parties' undertakings were based; or when new information emerges in France or the European Union, especially regarding the product's assessment, the medico-economic analysis or current prices, or when the essential products mentioned in Article 12 herebelow undergo a significant variation in their product costs, particularly due to product safety requirements.

The initial rider can provide that the conditions for selling the product can be revised via agreement in terms of the sales volumes observed, both in France and on the comparable European markets, considered as a whole. In its analysis, CEPS will particularly assess the respective conditions for use and marketing.

Reviewing the guarantee timeframe

When a product covered by a European level price guarantee is approved for extended indications which are rated at ASMR IV or V and concern a significantly larger patient group than the group covered by the ASMR rating which initially warranted the guarantee, the initial period of the European level price guarantee may be shortened.

When a product covered by a European price level guarantee is approved for extended indications rated at ASMR I to III, the initial period of the guarantee may be extended for up to one year, provided that the new indication(s) concern a sufficiently large patient group in relation to the group covered by the existing indications.

For medicines which have been under temporary authorisation (ATU), the companies undertake to take the necessary steps to adhere to the deadlines set by ANSM for bringing the medicines into line with the terms of their marketing authorisations and to submit their applications for registration under their new marketing authorisations on the public hospital approved medicines list and/or the national health insurance reimbursable medicines list, no later than 30 days after receiving notification of the MA decision or specific national conditions. Failure to do so shall lead to the period of their European level price guarantee being reduced by a period equivalent to the length of the delay.

Reviewing the rider

When a "volume clause" is inserted at the time the price, tariff or outpatient prescription fee is set, relating to the medicine's target patient group or to the indication for which the medicine was given an ASMR rating, including medicines mentioned in Article 10 a), the clause may be revised in the light of new information emerging from the post-marketing studies required by the health regulatory bodies, including relevant epidemiological data and other data that could lead to revising the target patient group, after the Transparency Commission has been consulted on the matter and a case file including a summary of the updated pharmacovigilance data has been studied.

Article 5: Format and content of the multiannual agreements.

The agreements must adhere to the pro-forma agreement appended. They are made up of three parts:

Part One summarises the prices of medicines which the company sells and which are registered on the national health insurance reimbursable medicines list and the special conditions attached to them where applicable, in the form of a price table and a schedule of clauses. It also includes for information purposes a list of the company's proprietary products that are registered on one or other of the lists provided in Articles L. 162-16-5 and L. 162-16-6 of the Social Security Code, together with their published outpatient prescription prices or tariffs and decisions made by CEPS under Article L. 162-22-7-1 of the Social Security Code where applicable or any undertakings made, especially those made under Article 8 c) herebelow.

Part Two contains, pursuant to Article L. 162-17-4 of the Social Security Code, the company's undertakings with regard to controlling its marketing policy and ensuring responsible use of the medicine, and any conditions setting forth the company's contribution to achieving the objectives described in Chapter IV herebelow and to implementing government policy.

Part Three establishes the company's acceptance of the provisions of this framework agreement, in particular those stipulated in Articles 17 and 18 herebelow where applicable, under the conditions provided in said Articles.

Companies which decide not to take advantage of the financial regulation mechanism described in Articles 17 and 18 herebelow, or for whom the mechanism is cancelled either by the company itself or by CEPS, may nonetheless enter into or maintain an agreement with CEPS under the terms of Article L. 162-17-4; however, the agreement will not exempt the company from the contributions stipulated in Article L.138-10.

The agreements may be supplemented by riders. Parts One and Two shall be renewed each year during the first six months of the calendar year. Part Three shall be renewed before 31 December each year.

Article 6: General measures to promote new medicines

a) **Pre-application procedure for medicines with centralised marketing authorisations**

Subject to any subsequent decision by the European Commission, any pharmaceutical company whose product marketing authorisation application has received a favourable opinion from the human medicines committee of the European Medicines Agency may immediately submit a pre-application to CEPS, the Transparency Commission and the ministers responsible for registration, to allow them to examine in advance the issues involved in registering the new product as a reimbursable medicine and to shorten the registration process. This procedure does not exempt the company from the official procedure governing the submission of applications for registration of a product on the reimbursable medicines list and price setting, in accordance with the procedures outlined in Article R. 163-8 of the Social Security Code. Once the official application has been submitted, CEPS shall appoint a rapporteur to begin processing any elements of the application which do not require the Transparency Commission's opinion.

b) **Special processing times for medicines which have been given an ASMR rating**

The parties agree upon the benefit of shortening the usual statutory 180-day listing procedure in the case of medicines which represent an advance in treatment.

For all medicines with an ASMR rating of at least IV but which nonetheless would not fall within the scope of Article 7 herebelow, CEPS undertakes to write to the company within 75 days after the date on which the Transparency Commission delivers its final opinion, proposing a draft agreement or, failing this, to set out the reasons why it has not yet been able to formulate a proposal.

This same procedure shall be implemented for paediatric medicines which address the list of paediatric needs sent to LEEM by CEPS.

c) **Statutory processing times**

For all proprietary products, CEPS shall ensure that the statutory processing time of 180 days is adhered to, among other ways by keeping track of the intervals before publication of the undertakings which CEPS signs.

d) **Evaluation**

The procedure and the undertaking stated in the above paragraphs shall be subject to a joint annual assessment by LEEM and CEPS.

Article 7: Fast-track registration for innovative medicines: price submission

The fast-track registration procedure provided in Article L.162-17-6 of the Social Security Code for certain medicines which have been recognised as making an innovative contribution shall be applied under the following terms and conditions:

a) **Description of the procedure.**

No earlier than the day after and no later than one month after it has received the Transparency Commission's final opinion, a company which meets the conditions mentioned in paragraph b) herebelow may apply for a fast-track price-listing procedure for proprietary products which meet the conditions mentioned in paragraph c) herebelow. This application must contain the undertakings stipulated in paragraph d) herebelow.

CEPS may accept the application, oppose it or organise a hearing with the company before making its decision.

In the event that neither the company nor CEPS request a hearing and that CEPS has not informed the company of its opposition to the application under the terms set forth in paragraph e) herebelow after two clear weeks following the week in which CEPS received the company's application, the application shall be deemed to have been accepted. The agreement shall then be signed within 48 hours and the registration ruling and price notice shall be published in the *Journal Officiel* (the official gazette of the French government) at the earliest possible opportunity.

In the event of opposition by CEPS, the price shall be set according to due process.

If a hearing is requested, this must be made known within one week of the application's submission. The company may amend its application after the hearing. If a hearing does take place, the processing time is extended to three clear weeks following the week in which CEPS received the application. The agreement is signed, CEPS signals its opposition and the pricing process is resumed under the same conditions as if a hearing had not taken place.

The first two working weeks of August and the last week of the year shall not be taken into account when calculating processing times. Furthermore, no price submissions may be made during these periods.

b) Companies concerned

This procedure is open to any company which has a multiannual agreement with CEPS, pursuant to the terms of Article L. 162-17-4.

c) Medicines concerned

Proprietary products which the Transparency Commission has rated at ASMR level I to III, provided that these ASMR levels are applicable to the main indications specified in the products' marketing authorisations.

Proprietary products which the Transparency Commission has rated at ASMR level IV, subject to the following additional conditions:

1°) There must be a reference medicine and the daily treatment cost of the new medicine, based on the submitted price, must be equal to or lower than that of the reference medicine. CEPS reserves the right however to accept price submissions for products where the daily treatment cost would be higher than that of the reference medicine if the applications can demonstrate that the additional cost is outweighed or exceeded by savings on other items of national health insurance expenditure.

2°) The medicine must not be intended to replace a medicine which has been genericised or is soon to be open to genericisation.

Each proprietary product concerned by the categories above must have received a medico-economic opinion from the CEESP, issued within the timeframes specific to the fast-track price submission procedure and enabling CEPS to determine the conditions of its efficiency.

d) Undertakings to be made by the companies

-Regarding prices: the company undertakes to submit a price which is consistent with the approved prices in the following countries: Germany, Spain, Italy, and United Kingdom.

- Regarding sales volumes: in the event that its sales volumes exceed the volumes in the mandatory forecast for the first four years as stated in the price submission application, the company undertakes to compensate by means of contractual clawback payments for any additional costs to national health insurance which are not justified by public health decisions made later by public bodies.

- The company undertakes, every year, to communicate the prices practised, sales volumes observed and arrangements for reimbursement in each of the aforementioned countries. Should the product assessment or medico-economic analysis change, or if it later emerges that the prices practised in one or more of these countries compromise consistency between the French market and comparable European markets considered as a whole, the company also undertakes to restore this by accepting a contractual change to the price submitted.

The initial rider can provide that the conditions for selling the product may be revised via agreement in terms of the sales volumes observed, both in France and on the comparable European markets, considered as a whole. In its analysis, CEPS will particularly assess the respective conditions for use and marketing.

- The company undertakes studies which it may be requested to carry out in application of Article 11 herebelow.

- The company lastly undertakes, subject to general or specific obligations of information governing pharmaceutical companies, to inform both CEPS and the Transparency Commission of any new scientific information which comes to light and which may negatively affect the benefit-risk ratio as evaluated during the Transparency Commission's assessment. Where the company is aware of any such information prior to the deadline for receipt of CEPS' opposition, it shall waive the right to the fast-track procedure.

In addition to the above-stated mandatory undertakings, the company may make other undertakings (regarding posology, daily treatment cost, consultations, etc.) which, in the light of the characteristics of the product in question, it feels will make its application more favourable to CEPS.

The company shall have the opportunity to present all useful observations to CEPS prior to entering into the contractual obligations.

e) **Conditions governing CEPS' right to opposition**

The committee must present its opposition in writing, providing valid grounds for the opposition. It may oppose an application on the following grounds:

- Due to explicit public health considerations.

- If the level of the proposed product price is excessive in relation to the prices in force in the four EU Member States mentioned in d) above or in relation to the medico-economic opinion delivered by the CEESP which enables CEPS to determine the conditions for its efficiency.

- If the sales forecasts are inconsistent with the size of the patient group identified by the Transparency Commission.

- Due to obvious inadequacy of the undertakings made by the company.

- If the company has breached any of its undertakings made during a previous application.

- With regard to ASMR IV-rated medicines, where the special conditions regarding these medicines are not met or simply where the product represents additional costs in relation to the reference product.

CHAPTER III: MEDICINES PURCHASED BY HOSPITALS

Article 8: Implementation of Articles L 162-16-5 and L 162-16-6 of the Social Security Code

a) **Common procedure.**

For the purposes of Articles L. 162-16-5 and L. 162-16-6 of the Social Security Code, outpatient prescription fees for the products included on the list provided in Article L.5126-4 of the Public Health Code and "accountability tariffs" (*tarifs de responsabilité*) for products included on the list provided in Article L. 162-22-7 of the Social Security Code shall be determined on the basis of the common procedure outlined in paragraphs b) to e) herebelow, subject to any specific conditions detailed in these Articles where applicable.

b) **Conducting the procedure.**

Price submissions formulated according to the terms of paragraph c) herebelow should be handed to CEPS in return for proof of receipt or sent by registered post within one week after details of the product's inclusion on one of the lists mentioned in paragraph a) hereabove have been published in the *Journal Officiel*, or in the case of products registered on the list provided in Article L. 5126-4 of the Public Health Code before receiving marketing authorisation, within ten days following receipt of the marketing authorisation decision.

CEPS may find the submission inadmissible or may oppose the submitted price under the terms stipulated in paragraph d) herebelow, within two weeks following receipt of the submission. In the event of inadmissibility or opposition, the company shall be given two weeks starting from the date of receipt of CEPS' decision within which to draw up a new submission or to amend its initial submission. CEPS shall then have ten days within which to find the submission still inadmissible or to oppose the price submitted. In this instance, CEPS' decision regarding inadmissibility or opposition shall be final, pursuant to the above-mentioned Articles of the Social Security Code. If, after CEPS presents its initial opposition, the company does not draw up a new declaration or amend its initial declaration within the above-mentioned two-week time limit, CEPS' opposition shall be final.

If CEPS does not find the submission inadmissible or oppose the submission within the time limits mentioned in the previous paragraph, it shall publish the prescription fee or "accountability tariff" in accordance with the price submitted at the earliest possible opportunity.

In the event that the company does not adhere to the time limit for submission stipulated in the first paragraph hereabove, CEPS may announce its opposition to the price at its own convenience, provided that it adheres to the overall seventy-five day statutory time limit for the procedure. If CEPS does oppose the price, the time which the company shall have to draw up a new submission or amend its initial submission shall be reduced by a length of time equivalent to the initial delay. If this delay is more than ten days, any opposition by CEPS shall be final.

In the event of final opposition, or if the company has not drawn up an admissible submission within thirty days after the start of the time limits stipulated in the first paragraph hereabove, CEPS shall set the prescription fee or accountability tariff unilaterally.

c) **Content of company price submissions.**

For each product included in the price submission, the company's submission must contain the following, failing which the submission shall be inadmissible:

- The proposed retail price to healthcare establishments per pack type.

-The current prices in force and the forecasted sales volumes in the main EU Member States and the product's reimbursement status in these States, plus, for products which have been on sale for more than one year, the annual sales volumes recorded in these States.

- Where applicable, up to three years' worth of data on the prices at which the products have been sold to French healthcare establishments.

- The Transparency Commission's opinion or opinions, where such opinions have already been delivered.

- An estimated sales forecast for the next three years.

- An undertaking to inform CEPS each year of the prices in force, forecasted sales volumes for products which have been on sale for less than a year and volumes sold, in the main EU Member States, as well as any alterations to the product's official reimbursement status.

Depending on the particular nature of the products in question, price submissions may also contain undertakings by the company, in particular regarding implementation of Article L. 162-18 of the Social Security Code or the conduct of follow-up studies on the products.

d) **Criteria for opposition by CEPS**

CEPS must provide explicit, clear grounds for its opposition.

It may oppose the proposed price on the grounds of the medico-economic assessment which CEPS will have carried out particularly in light of the CEESP's opinion delivered within the statutory timeframes.

It may also oppose this price on the grounds that it is exceptionally high in relation to the prices in force in the comparable EU Member States, with account taken of the expected and then observed level and growth in sales volume in France and on each of these markets.

Finally, it may oppose the price due to the inadequacy of any undertakings made by the company, in particular, in cases where the proposed price is only justified for some of the indications included in the marketing authorisation, if there is a clear risk that the quantities sold will incur exceptionally high national health insurance spending or if, given the current market, the product's inclusion on one of the lists could lead to sales volumes giving rise to volume rebates on the company's proposed price.

e) **Reviewing tariffs and prices.**

Prices and tariffs may be reviewed either at the company's or CEPS' request, in particular when a change occurs to any of the factors on which the existing price or tariff and the parties' undertakings were based; or when new information emerges in France or the European Union, especially regarding the product's assessment, the medico-economic analysis or current prices, or when the essential products mentioned in Article 12 herebelow undergo a significant variation in their product costs, particularly due to product safety requirements.

The initial rider can provide that the conditions for selling the product can be revised via agreement in terms of the sales volumes observed, both in France and on the comparable European markets, considered as a whole. In its analysis, CEPS will particularly assess the respective conditions for use and marketing.

Article 9: volume clauses

When CEPS intends to apply the terms of Article L. 162-22-7-1 of the Social Security Code to a medicine included on the list provided under Article L 162-16-6 or it is considering inserting a "volume clause" for a medicine included on the list provided under Article 162-16-5, which would include provisions on clawback payments or price reductions, CEPS shall inform the company selling the medicine of its intention; however, the publication of the tariff or the outpatient prescription price shall not be delayed until this process has been completed.

CEPS shall make every effort to reach an understanding with the company and to formally set out this understanding in a rider to its agreement with the company.

If no agreement is reached, once the company has been given the opportunity to present its comments, CEPS shall notify the company of its decision under Article L. 162-22-7-1 or if applicable of the conditions under which it will announce that it is requesting a price reduction in the light of the quantities that have been sold.

Article 9a: implementation of Article L. 162-16-5-1 of the Social Security Code

Declarations regarding the maximum fees chargeable to healthcare establishments, which the companies are obliged to make under the terms of Article L. 162-16-5-1 of the Social Security Code, must be sent to CEPS within one month after the medicine has been given temporary authorisation (ATU) by the ANSM Chief Executive.

These fees shall be published on the CEPS website.

If any clawback payment is owed by virtue of the price or tariff published after the medicine has obtained marketing authorisation, this payment shall be determined at the time the price or tariff is set. The payment shall take into account the sums actually charged to the healthcare establishments and any quantities which were supplied free of charge.

Article 9b:

If a company considers that its medicine could be put registered on the list mentioned in Article L162-22-7 of the Social Security Code and has approached the secretariat of the hospitalisation board in this regard, it may anticipate the price or tariff submission to CEPS without this changing the provisions in paragraph b) of Article 8 hereabove. If there is no registration, the price or tariff submission procedure is halted.

CHAPTER IV: ACCESSING INNOVATION AND IMPROVING THE COST-EFFECTIVENESS OF SPENDING ON MEDICINES

Section I: Innovative medicines, orphan medicines and paediatric medicines

Article 10: Special advantages for innovative medicines, orphan medicines and paediatric medicines

In the context of agreements with CEPS, innovative medicines, orphan medicines and paediatric medicines shall benefit from the provisions of Article 18 herebelow, in particular concerning provisional, full or partial exemption from clawback payments per pharmacotherapeutic class grouping.

The parties wish to promote the orphan medicines market in connection with the EU's incentive policy as expressed in Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999.

The parties also wish to promote steps to bring paediatric medicines onto the market, in line with the EU regulation.

CEPS shall forward to LEEM the list of paediatric needs drawn up by ANSM: new paediatric product formats or approval of paediatric indications for existing product formats.

If a medicine is included on the list produced by the European Medicines Agency's paediatric committee or appears on the list of paediatric needs drawn up by ANSM, its ex-manufacturer price shall be set so as to guarantee a daily treatment cost which is equal to the product's daily treatment cost for adults. These provisions shall only apply to products which are defined as orphan medicines pursuant to Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999.

Article 10a: Access to orphan medicines

To ensure that the patients concerned continue to have access generally to orphan medicines under conditions that are acceptable to the pharmaceutical companies and *l'Assurance Maladie* alike, and subject to the provisions of Article 4 hereabove, CEPS may request a company selling an orphan medicine costing more than €50K per patient per year, under the terms of its agreement with the company, to undertake to supply the product to all patients eligible for the treatment without restriction in return for setting a price in keeping with standard international prices, up to a set turnover threshold.

Article 10b:

As an exception to the common law pricing arrangements under which it would not be possible to reach an agreement, when the potential improvement of a medicine – particularly in public health terms – cannot be fully demonstrated during the pre-MA clinical trials and when said demonstration may be achieved through "real world" studies, CEPS may suggest a conditional price for this medicine to the laboratory.

The expected improvement – particularly in public health terms – will have to be demonstrated and qualified by an appropriate study, backed up by specific findings associated with indicators that are set by agreement with the laboratory concerned.

At the end of the study and once HAS has validated its findings and the extent to which the expected findings have been obtained, the price may then be increased or reduced depending on the findings recorded.

Article 10c:

Based on the importance of a medicine's medically justified responsible use and in liaison with the applicant company, CEPS shall report to the competent authorities the need or merits of registering the procedure and/or biomarkers associated with an innovative medicine in the list category.

Article 11: Real-world monitoring of new medicines in clinical practice

The parties are agreed on the benefits of gathering data on use of new medicines in real-life situations. With the expected growth in the number of real-world studies, the parties are finding that they are having to step up the efficiency of the procedures for defining, implementing and assessing the findings of such studies.

To this end, they will endeavour to clearly define the study priorities, to control the number of studies and the objectives set for each of them and to set realistic deadlines for designing and then implementing the studies.

This Article relates to studies which are governed by a contractual clause between CEPS and the company concerned. The studies may be initiated at the instigation of either CEPS or HAS, hereafter referred to as the Transparency Commission or CEEPS.

CEPS will endeavour to promote ongoing coordination with HAS to ensure that only one request for studies is sent to the company (no matter which body sends it).

The recommendations of ADELF (French-speaking epidemiologists' association) and good epidemiological practice shall apply to the manner in which the data is gathered and the studies are audited. The relevant public bodies may exercise their right to monitor compliance with these rules.

The aim of these contractual studies, the obligation to set up a scientific committee where applicable and the timescale within which the studies must be conducted and their findings obtained shall be set forth in a rider to the agreement, which may also make provision regarding the consequences of non-compliance with the timescales.

If the company can demonstrate that the findings of the study it has been requested to carry out would fully or partly duplicate the findings which the studies required as part of the marketing authorisation application process and included in the approved risk management plan would produce within the same length of time, the contractual study shall be modified accordingly. In such cases, CEPS and HAS must be given copies of the findings of the studies included in the risk management plan.

Where a scientific committee is formed, information on the committee's members and their declarations of interest must be sent to the Transparency Commission and the DGS (Directorate-General of Health), who may raise objections on the grounds of the extent of independence or competence of the members approached. The scientific committee shall be responsible for deciding which type of study is best suited to address the issues raised and/or for approving the study protocol; the committee shall also give an independent expert opinion on the team appointed to carry out the study. The contract rider stipulates that the studies must be published, notwithstanding any intellectual property rights associated with them.

Before the study protocol is drafted, HAS and CEPS must agree on the study's objectives and the list of questions to be addressed as a result.

This protocol must be submitted to HAS, which will give an opinion as to whether the study design is fit to address such questions. This procedure involving HAS shall not entitle the company to any extension of the agreed schedule for starting the study and producing the findings.

The findings of the studies shall be submitted to CEPS and HAS. HAS shall assess the findings and determine with CEPS the extent to which the study's objectives have been met. The parties to the agreement shall discuss what action to take on the basis of the findings

In view of the draft budget estimated for the study, which is submitted to the Committee, the latter shall oversee regulation of the costs involved in the studies, which must be reasonable in relation to standard industry practice (regarding number of cases, complexity, etc.) and shall ensure that the overall, proven costs to the company of carrying out the study are proportionate to the anticipated pre-tax turnover from sales of the medicine. In the event that the costs are disproportionate in this respect or that the scope of the study is extended for public health purposes to include elements other than the use of the product in question, the company may be compensated for the additional costs incurred via a reduction of its contractual clawback payments.

CEPS and HAS may request the companies to draw up protocols which could allow the findings to be extended to other products with related therapeutic targets.

These provisions do not rule out the possibility that other studies presented at the company's own initiative may be taken into account.

Penalty payments payable in the event of failure to carry out the studies within the agreed timescale, under the terms of Paragraph 5, Article L. 162-17-4 of the Social Security Code, shall be set according to the procedure provided in Article 15 b) herebelow.

A Real-World Study Surveillance Committee is set up, bringing together CEPS and HAS. The committee's purpose is to examine, at periodic intervals, the obstacles to study performance and to meeting the timeframes set in the protocol. It examines any difficulties it will have noticed of its own accord as well as any of which it would have been informed by companies or LEEM. Its observations and findings are discussed with each company concerned as well as LEEM when said observations and findings are general in scope.

Article 12: essential medicines

If a company plans to halt production or sale of one of its proprietary products which satisfies a particular medical need that would no longer be fulfilled if the product were removed from the market, the company undertakes to enter into discussions with CEPS regarding the financial situation involved in keeping the product on the market, failing which the company's status as an approved supplier may be removed.

Moreover, if a company requests a price increase for one of its proprietary products that satisfies a medical need not catered for by any other less expensive medicine and the price increase is justified in view of the financial circumstances surrounding the production of the medicine, when evaluating the request account shall be taken of obligations arising from tests on traces of the medicine in water and of the specific cost of the collection and disposal of sharps waste from patients self-medicating with the product.

Section II: Sources of savings

Article 13: Development of generics and fixed accountability tariffs (TFRs)

The parties to this agreement agree that the development of the generics market represents a valuable contribution to the funding of medical advances.

The generics monitoring group shall study the development of the generics market and carry out a critical analysis of how the market is functioning and the prevailing economic conditions for companies affected by the development of this market.

The group shall be consulted about all plans to set or to change a “fixed accountability tariff”, as shall the manufacturers of the proprietary products concerned.

The group shall also be consulted about all public plans to lower generics prices and about changes that CEPS is considering introducing to its overall price setting procedure for the substitution list: allowance entitlements, price increase rules for proprietary and generic products alike, etc.

CEPS shall take into consideration the logistical pressures which the pharmaceutical companies will be put under by any changes to the fixed tariff levels.

Article 13a: Price consistency

In the event that a significant number of less expensive medicines, in particular generics, emerge within a pharmacotherapeutic group in which this is justified in view of the degree to which the medicines that constitute the group are sufficiently interchangeable from an economic point of view in terms of the nature and degree of the medical benefit they provide, the prices of the more expensive medicines, in particular of those still protected by patents, may be gradually brought into line so that, in the long term, there will be no significant gap between the prices of these medicines and those of the less costly ones. The desired price reductions may not be introduced until at least one year after these less expensive medicines have come onto the market and shall only apply to medicines that represent little or no medical progress in the majority of their indications.

Article 13b: Transforming clawback payments into price reductions

For all products that do not have a price guarantee period, three years after their registration CEPS will ask, where necessary, that the contractual clawback payment be transformed into a price reduction.

At the end of the price guarantee period mentioned in Article 4 hereabove, CEPS, with account taken of the international impact for the company, shall ask the latter to convert by agreement all or part of the clawback volume previously recorded into a price reduction.

Article 13c: biosimilar medicines

The parties to this agreement agree that the development of the biosimilar medicines market represents a valuable contribution to the funding of medical advances.

Article 14: Development of self-medication not covered by national health insurance

The parties agree that responsible self-medication should be allowed to develop in France, as it will contribute to the responsible use of medicines without affecting the levels of payments made by national health insurance.

In keeping with the policy guidelines of the ministers concerned, particularly those presented in the Health Industries Strategic Council (CSIS), CEPS makes an active contribution to the emergence of a self-medication market in France.

Article 15: Information for prescribers, promotion and advertising

a) **Information for prescribers and promotion of medicines**

The parties undertake to help bring the legislation concerning medicine promotion swiftly into practice, via agreements if needs be.

They therefore undertake to update the medical visit charter in 2013.

b) **Advertising bans**

For the purposes of Article L. 162-17-4 of the Social Security Code, in particular in relation to advertising bans issued by ANSM and the financial penalties which may arise therefrom, the parties agree that CEPS shall follow the procedure below when making its decisions.

For advertising bans which CEPS considers may give rise to financial penalties:

- the committee shall designate a rapporteur who will examine the case and present it at a committee session;
- CEPS shall draw up a draft decision giving its grounds for the decision;
- CEPS shall send the company the draft decision, asking the company to present any comments in writing;
- the company may request a hearing by CEPS; it may also enlist the help of experts or legal advisers;
- CEPS shall then hold fresh discussions and shall notify the company of its decision.

c) **Unjustified prescription outside of the MA framework**

Companies contribute to responsible medicine use, particularly by ensuring that their proprietary products are prescribed in keeping with their marketing authorisations (MAs) and, where applicable, with the temporary recommendations for use.

They undertake to take measures for preventing and limiting demonstrated use of medicines outside of their MA indications when such a use does not correspond to the recommendations of the competent health authorities.

The agreements signed with companies can set targets for reducing prescriptions outside of the MA framework, particularly for public health reasons.

They specify what action is being taken, especially as regards prescribers, to limit such prescription practices as far as possible. They define tools for measuring the impact of such action and communicate their outcome to CEPS.

CEPS can agree on priority action with companies on the basis of current knowledge or changes made to health agencies' recommendations.

In the event these undertakings are not fulfilled, once the company has been given the opportunity to present its comments CEPS shall pronounce a financial penalty against said company.

Article 16: Cooperative action to promote responsible use of medicines

The pharmaceutical companies undertake to actively pursue action undertaken with regard to the responsible use of medicines, in liaison with the appropriate social security bodies.

When HAS, UNCAM, INCA or ANSM are planning actions of a public or general nature which may affect the economic balance of the medicines sector, LEEM may request CEPS to arrange suitable consultations, after having applied to the ministers concerned if necessary.

CHAPTER V: ANNUAL FINANCIAL ADJUSTMENTS

Article 17: Annual financial adjustments: principles

Any company wishing to be exempted from the contributions required under the terms of Article L. 138-10 of the Social Security Code must undertake in the form of a contractual clause, to pay clawback payments, known as end-of-year quantity clawbacks, to the relevant URSSAFs.

However, regardless of whether or not the company has signed an agreement, no end-of-year quantity clawbacks shall be payable if the cumulative growth of sales of reimbursable medicines to community pharmacies and sales to healthcare establishments of medicines included on the list provided in Article L. 5126-4 of the Public Health Code or on the list provided in Article L. 162-22-7 of the Social Security Code, for all the companies put together, does not exceed the sales-weighted mean value of the 'K' growth rates set each year by the Social Security Financing Act (LFSS) pursuant to Article L. 138-10. Furthermore, CEPS undertakes to ensure that the total amount of all the end-of-year quantity clawbacks paid by all the companies put together is less than the sum of the contributions which those companies would have had to pay if none of them had entered into the agreement.

At the end of each year, and by 31 January of the following year at the latest, companies which sell products included on the list provided in Article L. 5126-4 of the Public Health Code or on the list provided in Article L. 162-22-7 of the Social Security Code must send a declaration to CEPS, in the format of the pro-forma declaration appended, giving details, for each product and product format, of the volume and actual turnover of its sales to healthcare establishments over the year and identifying among these figures all sales of products which were on one of the lists on 31 December in the year for which the payments are owed and had been on the list since at least 1 January of the previous year.

The contractual clawback payments shall be paid to the appropriate URSSAF by 30 April the following year, on the basis of an assessment drawn up by CEPS following discussions during which the company may present arguments for a review of the amount of clawback payments calculated.

The end-of-year quantitative clawbacks are made up of payments per pharmacotherapeutic class grouping and payments based on turnover.

a) **Clawback payments per pharmacotherapeutic class grouping**

Each year, CEPS shall draw up a table dividing the medicines concerned into groups for the whole of the sector concerned. These groups are made up of sets of pharmacotherapeutic groups defined using the EPHMRA codes. CEPS shall set a growth rate for each group, in such a way that the weighted mean value of the rates is equal to the weighted mean of the 'K' growth rates established for the year in question by the Social Security Financing Act.

LEEM shall be consulted before the table is finalised.

The gross clawback payments owed by the companies, before deducting any exemptions as provided in Article 18 herebelow, shall be calculated as follows:

For each of the medicine groups in which the annual growth rate is higher than the rate set by CEPS, the total amount owed by all the companies who have agreements with CEPS and sell medicines belonging to that group shall be equal to the difference between the two rates multiplied by a given coefficient, which shall be the same for all groups and shall be set by CEPS in the light of the forecast sales growth for all the medicines concerned. For medicines sold to healthcare establishments, the sales taken into account shall be those corresponding to products included on one of the lists as at 31 December in the year for which the payments are owed which had been on the list since at least 1 January of the previous year.

The total clawback payment owed for each group shall be split into two portions, and the relative sizes of these portions, which shall be identical for all groups, shall be determined after consultation with LEEM. The first portion shall be split proportionally between all the companies with agreements who are selling medicines belonging to that group, on the basis of their respective sales figures. The second portion shall be split proportionally between those companies whose annual growth rate is higher than the rate set by CEPS, on the basis of their respective excess turnover amounts.

Sales to healthcare establishments shall be calculated by multiplying the number of units sold by their prescription price or their accountability tariff.

b) **Clawbacks based on capped turnover rates**

The companies shall also be liable where applicable for a clawback payment based on the difference between their turnover and a fixed threshold stipulated each year in a contract rider. The rate for this clawback is set, unless otherwise stipulated in the contract, at 10%.

For sales to healthcare establishments, the turnover figure used shall be the actual turnover.

When the sum of the safeguard contribution which the company would have had to pay if it had not signed the agreement is used as a basis for working out the threshold mentioned in the paragraph above, this sum is adjusted to cancel out, where applicable, sales of generics and products on fixed accountability tariffs and sales of medicines which were not claimed back from national health insurance.

Article 18: Annual financial adjustments: special implementation conditions

a) Exemptions from clawback payments per pharmacotherapeutic class grouping

1) Medicines which were given an ASMR rating when they were registered on the reimbursable medicines lists.

- ASMR I & II: full exemption for 36 months and 24 months respectively.

- ASMR III: 50% exemption for 24 months.

- ASMR IV: 25% exemption for 24 months.

For medicines sold to community pharmacies, these exemptions shall be effective as of the date they are sold, and for medicines on the list provided in Article L. 5126-4 of the Public Health Code or on the list described in Article L. 162-22-7 of the Social Security Code, from the date on which the relevant sales are included in calculations for the clawback payments per pharmacotherapeutic class grouping.

Companies may opt for a fixed, non-extendable exemption period which is longer than the periods provided above, up to a period of five years. In such cases, the exemption rate shall be reduced to ensure that the length of the exemption multiplied by the rate remains constant.

Where the ASMR rating only relates to some of the medicine's indications or where different indications have different ASMR ratings, the exemptions shall be worked out in proportion to the sizes of the patient groups concerned.

When a medicine has been covered by a temporary authorisation (ATU) or by a temporary treatment protocol for one of its indications which is not included in the marketing authorisation, the agreement may stipulate clawback exemptions on a case-by-case basis, based on a similar method to the one described above. These exemptions shall be deducted from those arising from any ASMR rating given to the indication in question once marketing authorisation has been obtained.

2) Extended indications with an ASMR rating.

The sum of the clawback payments shall be reduced according to the same rates and for the same periods as stipulated in paragraph 1) above, in proportion to the amount of turnover made by virtue of the new indication, starting from the date of the Transparency Commission's final opinion. Likewise, if a medicine which has been exempted on the basis of its ASMR rating has one of its non-ASMR rated indications extended, the exemption shall be proportionally reduced, starting from the date of the Transparency Commission's opinion on the extended indication, according to the size of the patient group concerned. The pro-rata rates shall be established in the individual agreements.

3) Orphan medicines and paediatric medicines

Orphan medicines as defined in the legislation, whose annual turnover before tax does not exceed EUR 30 million, shall be exempted from clawback payments, unless otherwise stipulated in the agreements. For the purposes of the agreements, orphan medicines may be taken to include both legally defined orphan medicines and de facto orphan medicines which were marketed before the relevant legislation came into force.

Paediatric medicines included on the list announced by CEPS shall be exempt from clawback payments, under the same conditions as those stated in paragraph 1) above except that their ASMR ratings shall be set one level higher for these purposes than the level set by the Transparency Commission.

4) Low-cost medicines

Generic medicines, medicines on generic prices and medicines on fixed accountability tariffs (TFR) whose price is equal to or lower than that of the tariff, shall be exempt from clawback payments.

5) Medicines for which a significant percentage of sales are not presented for reimbursement.

The clawback payments owed shall be reduced proportionally in relation to the value of sales which were not presented for reimbursement, calculated from national health insurance reimbursements data.

b) Rules governing double clawbacks per pharmacotherapeutic class grouping and for products under special contractual conditions.

Where clawback payments are owed under the terms of an individual agreement relating to a specific medicine (e.g. daily treatment cost refunds, volume rebates, etc.), any clawback payment per pharmacotherapeutic class grouping which the company owes for this medicine shall be recalculated to take the sales of this medicine and any excess turnover made on it as the net sales actually earned by the company (GERS turnover data-specific clawback payments).

c) Clawback credits.

Clawback credits apply to all clawback categories agreed between companies and CEPS.

1) ***Clawback credits for price reductions or reimbursement reclassifications***

Price reductions proposed by the companies, with the exception of reductions proposed following the creation of generic groups or in groups on fixed accountability tariffs, shall give rise to a clawback credit equivalent, unless otherwise stipulated in the agreements, to the amount of the reduction of the ex-manufacturer price multiplied by the number of units sold during the twelve months preceding the reduction.

Price reductions proposed by CEPS under the terms of Article L. 162-17-4 of the Social Security Code and put into practice through the company's agreement with CEPS may give rise, under the terms stipulated in the agreement, to clawback credits.

The above two paragraphs shall be applicable to reductions in the outpatient prescription fees or the tariffs for medicines included on one or other of the lists under Articles L. 162-16-5 and L. 162-16-6 of the Social Security Code, provided that these reductions also relate to the sale prices used in practice and on condition that the reductions are not being introduced for the purpose of bringing the prices back into line with current prices in the main European Union Member States.

Reimbursement reclassifications may give rise, under the terms stipulated in the agreements envisaged in Articles 4 and 5 hereabove, to partial compensation in the form of clawback credits.

1a) other clawback credits.

Pharmaco-epidemiological studies, pursuant to Article 11 hereabove, the maintenance or development of research or production capacities and compliance with societal or environmental standards may give rise to clawback credits whose amount is determined by agreement.

2) ***Clawback credits for Braille***

Contributions which companies make to funding the production of patient information leaflets in Braille shall be recognised in the form of clawback credits.

3) ***Carrying over credits***

The companies shall be entitled to carry any clawback credits they receive over into subsequent years.

CHAPTER VI: SCOPE OF THE AGREEMENT

Article 19: Scope and term of the framework agreement

This agreement, which replaces the “community” framework agreement of 13 June 2003 as amended and the "hospital" framework agreement of 23 March 2004 as amended, shall be effective until 31 December 2015.

It constitutes a framework agreement under the terms of Article L. 162-17-4 of the French Social Security Code.

Subject to legislation and regulations relating to the pharmaceutical sector and in particular to the taxes applicable to the sale and marketing of medicines, this agreement sets out the conditions regarding financial regulation of medicines as they apply to companies which enter into an agreement with CEPS pursuant to Article L 162-17-4 of the French Social Security Code.

The agreement may be supplemented by riders.

In the event that one of the parties should withdraw from the agreement before it expires, the terms of the agreement shall be extended for a maximum period of one year until such time as a new agreement is signed or, for the purposes of Article 8 hereabove, until publication of the decrees provided in Articles L. 162-16-5 and L. 162-16-6 of the French Social Security Code.

In the event that the overall balance of this agreement should be altered, in particular following amendments to the applicable statutory or legislative provisions, a major change in government policy or consequences of the enlargement of the European Union, in such a way as to increase the burden of the pharmaceutical companies' obligations, the agreement shall be renegotiated in order to re-establish a balance between the parties. If such negotiations are unsuccessful, the agreement may be terminated by either party.

Signed in Paris on 5 December 2012

The Chairman of the pharmaceutical companies' trade association (LEEM) Christian Lajoux	The Chairman of the Healthcare Products Pricing Committee (CEPS) Dominique Giorgi

APPENDIX 3: FRAMEWORK AGREEMENT OF 16 DECEMBER 2011 BETWEEN THE HEALTHCARE PRODUCTS PRICING COMMITTEE (CEPS) AND THE SIGNATORY PROFESSIONAL ORGANISATIONS CONCERNED BY THE PRODUCTS AND SERVICES ON THE LIST PROVIDED FOR IN ARTICLE L 165-1 OF THE SOCIAL SECURITY CODE

Having regard to European Union Law, the Social Security Code, the Public Health Code and national ministerial policy;

Whereas Point II of Article L 165-3 of the Social Security Code provides that the Healthcare Products Pricing Committee (hereinafter referred to as "CEPS") can sign an agreement with one or more representative associations or organisations bringing together manufacturers or distributors of the products and services mentioned in Article L 165-1 of the Social Security Code (hereinafter referred to as the signatory organisations);

Whereas, subject to the provisions of the Public Procurement Code, Point I of Article L 165-3 of the Social Security Code provides that, for the products and services mentioned in Article L 165-1 of the Social Security Code, CEPS can sign agreements with one or more manufacturers or distributors of a product or service (hereinafter the companies) or, where applicable, with their representative professional organisations;

Whereas it is fitting that the products and services mentioned in Article L 165-1 of the Social Security Code should be given their rightful place in prevention and healthcare and that this requires both rapid access for patients to these products and services when these are innovative, improved efficiency and rationalisation of expenditure on such products and services and sustained efforts to avoid excessive consumption and promote responsible usage;

Whereas advances in treatments, the demographic situation, epidemiological data, the government's public health plans and current best practice must be taken into account when appraising growth in the consumption of the products and services mentioned in Article L 165-1 of the Social Security Code;

Whereas the majority of spending on products and services mentioned in Article L 165-1 of the Social Security Code is financed out of the public purse, whose resources are finite by nature, and whereas it is therefore fitting that there should be regulation in place which is proportionate to the contribution made by such products and services, in accordance with the law and ministerial policy and under fair, transparent conditions;

Whereas the most desirable means of achieving the goals set forth hereabove is through strengthened cooperation between the public bodies and, on the one hand, the signatory organisations and, on the other, the companies concerned by the products and services mentioned in Article L 165-1 of the Social Security Code;

Whereas this agreement serves as a reference for relations between, on the one hand, CEPS and the signatory organisations and, on the other, CEPS and the companies of the sectors they represent;

CEPS, represented by its Chairman, Mr Gilles Johanet, and:

- *Association des Fabricants Importateurs Distributeurs Européens d'implants Orthopédiques et traumatologiques* (AFIDEO), represented by its Chairman, Mr Jean-Luc Moyat,

- *Association des Optométristes de France* (AOF), represented by its Chairman, Mr Philippe Verplaetse,

- *Syndicat de l'industrie des Dispositifs de Soins Médicaux* (APPAMED), represented by its Chairman, Mr Damien Peras,

- *Chambre Syndicale Nationale des Orthésistes* (CSNO), represented by its Chairwoman, Ms Patricia Pisanu,

- *Chambre Syndicale Nationale des Podo-Orthésistes* (CSNPO), represented by its Chairman, Mr Raymond Massaro,

- *Chambre Syndicale de la Répartition Pharmaceutique* (CSRP), represented by its Chairman, Mr Claude Castells,

- *Établissement Français du Sang* (EFS), represented by its Chairman, Professor Jean Tobelem,

- *Fédération Nationale des Podologues* (FNP), represented by its Chairman, Mr Louis Olié,

- *Fédération des Syndicats Pharmaceutiques de France* (FSPF), represented by its Chairman, Mr Philippe Gaertner,

- *Syndicat Français de la Nutrition Spécialisée* (SFNS), represented by its Vice-Chairman, Mr Hervé Le Henand,

- *Syndicat de l'Industrie du Diagnostic In Vitro* (SFRL), represented by its Managing Director, Ms Élisabeth Campagne,

- *Syndicat National des Associations d'Assistance à Domicile* (SNADOM), represented by its Chairman, Professor Bernard Paramelle,

- *Syndicat National des Fabricants et Distributeurs en Ophtalmologie* (SNFDO), represented by its Chairman, Mr Pascal Rétif,

- *Syndicat National de l'Industrie des Technologies Médicales* (SNITEM), represented by its Chairman, Mr Christian Seux,

- *Syndicat National des Orthopédistes, Orthésistes et Podologistes* (SNOF), represented by its Managing Director, Mr Guy Capron,

- *Syndicat National des Prestataires de Santé à Domicile* (SYNALAM), represented by its Chairman, Mr Olivier Lebouché,

- *Syndicat National des Centres d'Audition Mutualistes* (SYNAM), represented by its Chairman, Mr Marc Gréco,

- *Syndicat National des Centres d'Optique Mutualistes* (SYNOM), represented by its Chairman, Mr Christian Py,

- *Union Des Opticiens* (UDO), represented by its Chairman, Mr Henry Saulnier,

- *Union Nationale des Ocularistes Français* (UDOF), represented by its Chairman, Mr Michel Durand,

- *Union des Fabricants d'Aides Techniques* (UFAT), represented by its Chairman, Mr Pierrick Haan,

- *Union Française des Orthoprothésistes* (UFOP), represented by its Chairman, Mr Cyril Lecante,

- *Union Nationale des Prestataires de Dispositifs Médicaux* (UNPDM), represented by its Chairman, Mr Pierre Auphelle,

- *Union Nationale des Pharmacies de France* (UNPF), represented by its Chairman, Mr Michel Caillaud,

- *Union des Podo-Orthésistes de France* (UPODEF), represented by its Chairwoman, Ms Marie-Line Boucharenc,

- *Union des Syndicats de Pharmaciens d'Officine* (USPO), represented by its Chairman, Mr Gilles Bonnefond,

now agree to amend their framework agreement as follows.

CHAPTER 1: EXCHANGING INFORMATION

Article 1: The general context for exchanging information

For the sake of transparency, the signatory parties agree on the necessity to improve and share the information they each hold, as a priority on the national market, for better knowledge of the markets concerning the products and services mentioned in Article L 165-1 of the Social Security Code.

Article 2: Statistics

The medical devices sector does not have a panel covering all of the products and services mentioned in Article L 165-1 of the Social Security Code in an exhaustive manner.

The signatory parties undertake to do what they can to ensure that statistics on the markets concerning the products and services mentioned in Article L 165-1 of the Social Security Code improve. They shall also help to develop new databases. To this end, the parties task a commission, on which representatives of each of them sit, with analysing all of the possibilities in this sector within the year following the signature of this framework agreement.

If the signatory organisations or companies obtain information from external bodies, they shall bring this to CEPS' attention to back up the applications presented.

Article 3: Data gathered at CEPS' request

In order to obtain knowledge of a market concerning products and services mentioned in Article L 165-1 of the Social Security Code, or of products associated with a service, CEPS asks a signatory organisation to gather data from its members. Such data must shed light on market realities so as to contribute to knowledge of costs.

In this respect, the signatory organisations shall, as far as possible, equip themselves with a means of collecting commercial data anonymously, in accordance with the competition regulations.

Article 4: Data concerning a product or service registered by brand or commercial name

The agreement covering registration of a product or service by brand or commercial name may contain a clause providing that the company undertake to communicate to CEPS, at the latter's request and within the timeframes considered necessary, the sales in terms of quantity and value of the product or service concerned as well as, if possible, other data relating to the special characteristics of said product or service, such as the conditions for use or performance in each of the reimbursable indications.

Where applicable, the agreement provides for communication drawing a distinction between sales made in France to private establishments and public establishments or between the community sector and healthcare establishments.

Article 5: Studies of a medical nature or on treatment adherence

Companies undertake to systematically communicate any changes in data on which the registration is based to CEPS and the CNEDiMTS. Failure to communicate such information provides grounds for taking a product or service off the list as provided for in Article R 165-5 of the Social Security Code. They also communicate any information they have on the prescription and actual conditions for use concerning products and services mentioned in Article L 165-1 of the Social Security Code in their different indications.

Article 6: Market research conducted by CEPS

When CEPS carries out, or has carried out, market research on a product or service mentioned in Article L 165-1 of the Social Security Code, it shall bring this to the attention of the signatory organisation(s) concerned or, where applicable, of the company(ies) concerned.

Article 7: Market research conducted by the signatory organisations

If a signatory organisation carries out, or has carried out, market research on a product or service mentioned in Article L 165-1 of the Social Security Code, it shall bring this to CEPS' attention.

Article 8: Market data collection by the signatory organisations

When this framework agreement is signed, the following signatory organisations: SFNS, SFRL, SNITEM, SYNALAM, UFAT and UFOP shall gather data on the markets of some products on an annual basis from their members. An agreement protocol is signed by CEPS with each of these signatory organisations so as to get hold of such data.

If other signatory organisations set up similar data collection systems, a special agreement will also be signed with them.

Article 9: Information on foreign markets

Information on foreign markets, particularly on those of the European Member States, which is gathered by the signatory organisations by the companies or external bodies, shall be brought to CEPS' attention. Such data or information shall concern current prices, reimbursement conditions or sales volumes recorded on such markets.

CHAPTER 2: POST-REGISTRATION STUDIES AND OTHER STUDIES

Article 10: Implementation of studies for products registered by brand or commercial name

The parties are agreed on the benefits of gathering additional data on new products for which this proves necessary. In such an event, a study request shall be submitted at the same time as a new product is registered by brand or commercial name, at the instigation of the Medical Device and Technology Assessment Committee (CNEDIMTS), or CEPS.

When the study request is made by CNEDiMTS, a meeting is organised by CEPS within six weeks of the opinion requesting the study on the product being published, with the National Authority for Health (HAS) and the company. Through this meeting it must be possible to weigh up the study request and the constraints, by calling on the involvement, where necessary, of the associations of pharmacists and service providers under Article L 5232-3 of the Public Health Code.

The minutes of this meeting must be drawn up afterwards, under CEPS' auspices, and approved by the parties. Should the cost of the study prove to be unreasonably disproportionate to the product's expected turnover, this shall be stated in the minutes and the reason given. CEPS takes this difficulty on board when negotiating with the company.

In the context of observational studies, the recommendations of ADELF (French-speaking epidemiologists' association) and good epidemiological practice shall apply to the manner in which the data is gathered and the studies are audited.

In the context of medico-economic studies, the HAS recommendations on the principles and methods of economic assessment shall apply for conducting the studies requested.

The aim of these contractual studies, the obligation to set up a scientific committee and the timescale within which the studies must be conducted and their findings obtained shall be defined by the product registration agreement, which may also make provision regarding the consequences of non-compliance with the timescales. Failure to comply with these contractual clauses may give rise to the penalties provided for in Paragraph 3, II, of Article L 165-3 of the Social Security Code pursuant to the procedure in Article 18 in accordance with Article R 165-35 of the Social Security Code.

The relevant public bodies may exercise their right to monitor compliance with these good practice recommendations for conducting studies.

When a scientific committee is formed, information on the committee's members and their declarations of interest must be sent to CNEDiMTS and CEPS. The scientific committee shall be responsible for deciding which type of study is best suited to address the issues raised and for proposing and/or approving the study protocol. The agreement stipulates that the studies must be published, notwithstanding any intellectual property rights associated with them.

Whether or not CNEDiMTS has instigated the study, it must be sent the study protocol so that it can give an opinion as to whether the study design is fit to address such questions. This procedure involving CNEDiMTS shall not entitle the company to any extension of the agreed schedule for starting the study and producing the findings.

A clause is drawn up on the study request in the product registration agreement signed between CEPS and the company concerned. This clause particularly stipulates the study purpose and the implementation timeframes. If a meeting was organised with CNEDiMTS, the clause is written on the basis of the approved minutes from this meeting.

Article 11: Implementation of studies for products subject to a renewed registration application by brand or commercial name

When submitting an application for renewed registration by brand or commercial name, a study may be requested if CNEDiMTS or CEPS consider that the product calls for special monitoring or that the study conducted or requested during the last registration stage needs continuing or taking further.

The stipulations in the Article above shall apply in this instance.

Article 12: Implementation of studies for products registered by generic category

Overseen by one or more signatory organisations or one or more companies, a coordinated study may be implemented at the request of CNEDiMTS or CEPS, for one or more products registered by generic category.

If the study request is made by CNEDiMTS, the meeting as provided for in Paragraph 2 of Article 10 is organised at the earliest possible opportunity. The organisation and follow-on arrangements are the same, but it does not have to be organised within the six-week timeframe.

The objectives, arrangements and conditions for conducting the study are agreed contractually between CEPS and the signatory organisation(s) or the company(ies) concerned. In the same way as for registrations by brand or commercial name, the study protocols are sent to CNEDiMTS for analysis.

Article 13: Implementation of studies for services subject to applications for registration by generic category, brand or commercial name

If it appears necessary to obtain information regarding the cost of a service subject to an application for registration by generic category, brand or commercial name, an agreement may be signed between CEPS and one or more signatory organisations. When the service is registered by brand or commercial name, the company concerned is involved in the study where necessary.

The agreement particularly sets out the conditions for collecting and processing data.

If the study request is made by CNEDiMTS, the meeting as provided for in Paragraph 2 of Article 10 is organised at the earliest possible opportunity. The organisation and follow-on arrangements are the same, but it does not have to be organised within the six-week timeframe.

Article 14: Consideration of data associated with a decision to remove a registration by generic category and replace it with a registration by brand or commercial name

When registration by generic category no longer appears appropriate, a notice of proposed removal of this registration is published, stating that the companies concerned must submit a registration application by brand or commercial name.

The number of days that companies have for submitting their registration application by brand or commercial name, together with existing data, is set in the notice of proposal. It is at least 90 days. If no application is submitted, a procedure to remove the registration by generic category is initiated in the month that follows.

Article 15: Studies requested for registration by brand or commercial name following the review of a registration by generic category

When a registration by generic category is reviewed, if replacing it with registration by brand or commercial name proves preferable, this objective is specified in the notice of proposed revision of the list of products and services mentioned in Article L 165-1 of the Social Security Code.

Unless required otherwise for public health purposes, the length of time that companies have for submitting their registration application by brand or commercial name, together with the studies, is set in the notice of proposal. It is at least eighteen months.

The notice of proposed revision specifies the objectives of the assessment and the points on which the studies must focus in particular. These objectives and points in particular are defined in consultation with CNEDiMTS.

Article 16: Monitoring of contractual provisions

For all contractual studies, the calendar stages are defined by agreements signed between CEPS and the companies or signatory organisations.

If the company or signatory organisation finds that the contractual timeframes cannot be met, it must inform CEPS as soon as possible. Failure to comply with this stipulation may give rise to the penalties provided for in Paragraph 3, II, Article L 165-3 of the Social Security Code pursuant to the procedure set out in Article 18, in accordance with Article R 165-35 of the Social Security Code (in the process of being signed).

Any difficulty likely to call the study arrangements into question and which arises after the signature of the agreement providing therefor must be reported to CEPS and CNEDiMTS for a possible re-examination.

Article 17: Study findings

The findings of contractual studies, including any interim findings when the agreement contains such provision, are sent to CEPS and CNEDiMTS.

The penalties provided for in Paragraph 3, II, Article L 165-3 of the Social Security Code should the studies not be conducted within the timeframes set in the agreement between CEPS and the company, are decided pursuant to the procedure set out in Article 18, in accordance with Article R 165-35 of the Social Security Code (in the process of being signed).

Article 18: Procedure for applying the penalties provided for in Paragraph 3, II, Article L 165-3 of the Social Security Code

Pursuant to the provisions of Articles R 165-34 and R 165-35 (in the process of being signed), if CEPS considers applying penalties for failure to comply with a study's obligations, failure to conduct a study or failure to submit interim findings as provided for in a contractual clause signed between CEPS and the company, the following procedure shall be applied:

- CEPS shall define the grievances and inform the company thereof;

- the company shall present its comments in writing within one month of receiving the notification and request a hearing with CEPS within the same timeframe;

- in all cases, the company shall send the necessary information, concerning its turnover, for determining the penalty, to CEPS at the earliest possible opportunity;

- once this one-month timeframe has passed, if a hearing was held, CEPS analyses the information supplied by the company and notifies the latter of its decision, specifying, where applicable, the penalty amount, the grounds on which this is based, the payment due date and the options and timeframes for appeal.

CHAPTER 3: THE CONTRACTUAL FRAMEWORK

Article 19: Signing agreements for registration and renewed registration on the list provided for in Article L 165-1 of the Social Security Code

The choice between registration by brand or commercial name and registration by generic category is down to the Ministers for Health and Social Security at CEPS' suggestion, after receiving an opinion from CNEDiMTS.

For first registrations or renewed registrations by brand or commercial name, CEPS signs an agreement with the company concerned.

For first registrations or renewed registrations by generic category, CEPS signs an agreement with one or more signatory organisations. That said, in special cases registrations by generic category may give rise to an agreement between CEPS and the companies concerned.

If an agreement cannot be reached with the company for a first or renewed registration by brand or commercial name, or with at least one signatory organisation concerned for a first or renewed registration by generic category, CEPS may suggest implementing the first or renewed registration by decision alone.

Article 20: Choosing whether to register by generic category, brand or commercial name

Registration by brand or commercial name on the list provided for in Article L 165-1 of the Social Security Code is particularly justified for:

- a product with innovative features pursuant to Article R 165-3 of the Social Security Code;

- a product that is unique and/or for which registration by generic category is not possible;

- monitoring the improvement in medical benefit.

Depending on the case, this allows for:

- regular assessment by CNEDiMTS of each product in a given category;

- contractual definition with the company of the conditions for implementing a price/volume clause, as provided for in Article 28, and its consequences;

- contractual definition with the company of the aspects on top of the tariff;

- recognition of a product for which the company has been tasked with demonstrating the service provided in new indications.

In other cases, registration on the list set out in Article L 165-1 of the Social Security Code is by generic category.

Article 21: Contents of applications submitted for first or renewed registration on the list set out in Article L 165-1 of the Social Security Code

For easier application examination and better compliance with the processing times as a result, companies or signatory organisations must ensure that their applications are complete, containing all the necessary information.

The application for a first or renewed registration of a product or service is sent both to CNEDiMTS for the medico-technical section, and CEPS for the medico-technical and pricing sections. The decisive date for beginning the procedure, i.e. the date on which the timeframes begin to run, is the date on which the application was submitted to CEPS' General Cabinet Office.

As far as possible, beyond studies justifying the medical qualities of the product or service which are likely to provide CNEDiMTS with invaluable information for its assessment, it is important that companies document their application in terms of tariff to a maximum. The applications must contain, in particular:

- cost analyses for the product or service with the most relevant breakdown;
- comparisons with existing products with the differences (particularly in terms of LPP codes) shown in their best light possible;
- indications concerning the current prices abroad with, naturally, all of the indications (VAT, volumes, distribution channels, special regulations, etc.) for determining correlations on a comparable basis;
- sales volume forecasts with, when justified, indications on the breakdown between user categories;
- the product's special features (diagrams or samples demonstrating specific aspects or characteristics for example).

Article 22: Statutory timeframes

For first or renewed registrations by brand or commercial name of the products and services mentioned in Article L 165-1 of the Social Security Code, CEPS ensures that the 180-day statutory timeframe is kept, including by keeping track of the timeframes for publishing the undertakings it signs.

To help meet such timeframes, the companies or signatory organisations shall do their utmost to respond to CEPS' proposals within eight working days.

There are no statutory timeframes for first or renewed registrations by generic category, but CEPS is aware of the current delay in signing this framework agreement and as such is working hard to make up for these delays.

Article 23: Tariff setting principles

Because new products are registered by generic category, they should, in principle, be placed in an existing category and therefore be given the existing tariff or price. In this case, the general rule that any new registration should enable savings to be made if they do not represent any improvement in expected service (ASA) does not apply.

However, when products in the same category are subject to registration by brand or commercial name, any new product which does not represent any improvement in expected service is recommended a tariff that, in relation to the tariff of the category in question, takes account of the diversity of the supply, how long ago the last registration took place and how long the category has existed. On this occasion, CEPS may have to review the tariff of comparable products or reference products already registered on the list set out in Article 165-1 of the Social Security Code.

Article 24: Consideration of innovations in the pricing of products and services

Pursuant to Article L 165-2 of the Social Security Code, an improvement in expected service (ASA) or improvement in service provided (ASR) concerning the products and services mentioned in Article L 165-1 of the Social Security Code is a necessary pre-requisite, but does not suffice on its own to warrant a price difference with their reference products.

CEPS' appraisal of this sufficiency factors in, for example:

- the savings, irrespective of the form they may take, that the product or service concerned can enable the national compulsory and top-up insurance systems to make;

- the significance for public health of the innovation provided by the new product or service (each new innovation does not necessarily justify a higher tariff).

Moreover, decisive and expensive innovations for some patient groups can justify a high price at the outset which may be assessed relative to international market constraints; in this case the registration agreement sets a maximum volume on the basis of the target patient group indicated by CNEDiMTS, beyond which a clawback payment is due.

Article 25: Setting the maximum purchase price

Whenever possible, CEPS sets a maximum purchase price for the products and services mentioned in Article L 165-1 of the Social Security Code.

Before it does this, or for any reduction in reimbursement tariff, CEPS examines with the signatory organisations concerned the specific conditions for using up stocks for the new maximum purchase price or tariff to come into force.

When a product category is concerned, any companies refusing to apply the maximum purchase price may ask for a reimbursement reclassification for their product. But CEPS shall, in its proposals to the Ministers, ensure that a supply of products benefiting from reimbursement by compulsory health insurance is maintained.

Furthermore, in the event that products would likely replace expenditure normally borne by patients, CEPS may consider keeping a co-payment, via a difference between the maximum purchase price and the tariff.

Article 26: Setting the prescription price

In the event that the products assigned a maximum purchase price or prescription price are distributed through pharmacies and/or service providers under Article L 5232-3 of the Public Health Code, as well as through other channels, the signatory organisations and/or companies concerned, if they have products registered by brand or commercial name, are consulted about the arrangements for such a price assignment and measures are taken when necessary to maintain the distribution margins. Such measures are assessed at least once a year.

When the market conditions for delivering to patients a product or service mentioned in Article L 165-1 of the Social Security Code experience supply difficulties or leave an insufficient profit margin for professionals who must apply the maximum purchase price, CEPS associates a prescription price with the maximum purchase price.

When the maximum purchase prices have been set for generic categories without a prescription price being set initially, in the event of demonstrated rises in manufacturer prices – even due to increases in cost prices – CEPS takes measures particularly by setting a prescription price by decision. If this default (rise in manufacturer prices) is limited to a small number of companies marketing their product under a generic category, CEPS recommends that the Ministers register by brand or commercial name the products concerned by these increases under the generic category tariff associated with a prescription price and maximum purchase price.

Article 27: Tariff and price revisions

Intentions to revise a tariff or price of a product or service mentioned in Article L 165-1 of the Social Security Code may be expressed by CEPS or a company or signatory organisation. CEPS may instigate such a revision at the request of the Ministers or National union of health insurance funds.

In this case it informs the company(ies) or signatory organisation(s) concerned so that they can present their arguments.

If a company would like to revise a tariff for a registration by brand or commercial name, CEPS must make its position known within 90 days. If no response is received within this timeframe, the company obtains the revised tariff which CEPS has published within 30 days.

However, if the company would like to revise a tariff or price concerning a registration by generic category, CEPS does not have to process this request within any particular timeframe, even if it shall do its utmost to do it as quickly as possible, given the complexity of the subject.

Article 28: Price/volume clauses

In the event that registration on the list set out in Article L 165-1 of the Social Security Code is subject to a contractual price/volume clause, CEPS sets the volume rebate that the company must owe should these quantities be exceeded. Such a clause may apply to several companies when their products belong to the same category. In this case, the volume rebate is generally calculated in proportion to the sales volumes of each of these companies.

If a company terminates the agreement that stipulated a clause concerning price/quantities – whether or not pooled – CEPS applies to the company's products concerned a price reduction corresponding to a reduction in the estimated turnover for the following year equivalent to that of the rebate that was owed. The agreement covering the product's first or renewed registration provides, to this end, that the product sales declaration obligations continue to apply even if one of the parties terminates the agreement.

The agreement covering the first or renewed registration of a product or service on the list set out in Article 165-1 of the Social Security Code may provide that CEPS will decide on a price reduction if the planned quantities are exceeded or if the targets set are not met.

Article 29: Notices of proposal

When, pursuant to Article R 165-9, the Ministers for Health and Social Security instigate a registration by generic category, CEPS ensures that consultations are held with the signatory organisation(s) concerned prior to the notice's publication.

If CNEDiMTS has issued an opinion prior to the Ministers instigating this registration, these consultations begin as soon as said opinion has been published.

The consultation parties are normally given 30 days for making their comments known. However, unless specifically required otherwise, this timeframe may be extended to factor in any holiday periods or the complexity of the subjects being commented on.

During this timeframe granted for making comments, a signatory organisation or company may ask to be heard by CEPS. This hearing may possibly be held once the timeframe granted for submitting comments has passed, in which case any comments received within ten days of said hearing are taken on board.

Article 30: Signing of agreements

When CEPS presents a company or signatory organisation with an agreement for first or renewed registration of a product or service by brand or commercial name or by generic category, the latter has one month in which to return the agreement signed. The draft agreement is sent along with the draft first or renewed registration ruling. The first or renewed registration ruling comes within the remit of the Ministers for Health and Social Security and, as such, the draft is likely to be amended before it is signed. In such a case, the agreement signatory is informed thereof before the ruling is published in the *Journal officiel de la République française* and confirms whether or not it will be signing the agreement.

That said, if one or more meetings or discussions in preparation of CEPS' decision have been organised, this timeframe may be reduced to ten working days so as to reduce the time it takes for decisions to come into force.

Moreover, the parties agree that, as far as possible, if a company or signatory organisation is sure that it does not wish to sign the agreement proposal, it makes this refusal known immediately.

Article 31: The possibility of companies joining signatory organisations as members

The formal establishment, through this framework agreement, of relations between CEPS and the signatory organisations and their development implies that the latter can accept the membership of any company, irrespective of its status or nationality, which manufactures or distributes the products or services within its scope as defined in Chapter 4. To this end, these organisations ensure that their status is such that companies registered in another EU Member State can join as members in particular. This stipulation is applied subject to the other general statutory restrictions as well as internal disciplinary measures which might be taken against another company for its non-admission or exclusion.

Any signatory organisations whose statuses would need adjusting in this regard undertake to submit a change in status proposal to their bodies within the year following the signature of this framework agreement.

If this change in status does not occur within this one-year timeframe, CEPS must be informed thereof.

Article 32: Information for member companies of signatory organisations

The signatory organisations undertake to provide their member companies with complete and sincere information about the negotiations and agreements signed with CEPS.

Article 33: Cooperative action to promote responsible use of the products and services mentioned in Article L 165-1 of the Social Security Code

The signatory organisations undertake to actively pursue, or to initiate, action undertaken with regard to the responsible use of the products and services mentioned in Article L 165-1 of the Social Security Code, with the competent bodies.

CHAPTER 4: REPRESENTATIVE SCOPES OF SIGNATORY ORGANISATIONS

Article 34: Participation of signatory organisations

Every time CEPS addresses subjects concerning registrations by generic category within the representative scope of a signatory organisation, it informs the latter thereof and invites it to take part in any consultation meetings it might organise. When needs be the signatory organisation is also informed and involved regarding a first or renewed registration by brand or commercial name.

For registrations by generic category, agreements within the representative scope of a signatory organisation are systematically presented to the signatory organisation for signature.

A signatory organisation that is only marginally concerned by a scope of the list set out in Article L 165-1 of the Social Security Code may share its viewpoint with CEPS, and even attend consultation meetings, even if it is not mentioned in Article 36 with respect to this scope.

Article 35: Competent persons of signatory organisations

As soon as possible after signing this agreement, the signatory organisations inform CEPS of the competent person or people to which meeting invitations and any documents forwarded by CEPS should be sent, along with their relevant contact details (postal address, email and telephone number).

They must also indicate the name of the person or people authorised in accordance with the regulations to sign the agreements with CEPS. Any general or one-off proxy must be reported in writing to CEPS.

The signatory organisations undertake to report to CEPS any change concerning said people or their contact details.

Article 36: Representative scope of each of the signatory organisations

According to the different categories in the list set out in Article L 165-1 of the Social Security Code, the table below presents the representative scope of each of the signatory organisations pursuant to Article L 165-2 of the Social Security Code.

CODE I: Medical devices for home care and daily living aids, dietary foods and dressing supplies

Chapter 1: Medical devices, equipment and products for treating specific illnesses

SECTION	DESCRIPTION	SUB-SECTION	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
1	MD for treating respiratory and ear-nose-throat illnesses	1	Aerosol generating equipment	CSRP, FSPF, SNITEM, SNADOM, SYNALAM, UNPDM, UNPF, USPO
		2	Medical devices for treating respiratory failure and associated services	SNITEM, SNADOM, SYNALAM, UFAT (§2, §4 et §5), UNPDM
		3	Other medical devices for treating respiratory failure	FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
2	Medical devices for home infusion therapy	1	Equipment and accessories for home infusion therapy	CSRP, FSPF, SNITEM, SNADOM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		2	Accessories necessary for using an implantable catheter port or a tunnelled central venous catheter	CSRP, FSPF, SNITEM, SNADOM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		3	IV drip stands and poles on castors	CSRP, FSPF, SNITEM, SNADOM, SYNALAM, UNPDM, UNPF, USPO
		4	Disposable infusion pumps	FSPF, SNITEM, SNADOM, SYNALAM, UNPDM, UNPF, USPO
		5	Active systems for home infusion therapy	FSPF (§1, §2, §3), SNITEM, SNADOM, SYNALAM, UFAT, UNPDM, UNPF (§1, §2, §3), USPO (§1, §2, §3)
3	MD for self-treatment and self-testing	1	Self-testing devices	CSRP, FSPF, SFRL, UNPF, USPO
		2	Self-treatment devices	APPAMED (§1), CSRP, FSPF,SFRL, UNPF, USPO
		3	Medical devices for self-measurement	CSRP, FSPF, SFRL, UNPF, USPO
4	MD for treating incontinence and urogenital disorders	1	Medical devices for urinary or faecal incontinent patients and ostomates and for treating colorectal problems caused by neurological disorders	APPAMED, CSRP, FSPF, SNADOM, SYNALAM, UNPDM, UNPF, USPO
		2	Medical devices for the urogenital system	CSRP, FSPF, SNITEM, SNADOM, SYNALAM, UNPDM, UNPF, USPO
5	Products for nutrition and administration equipment	1	Oral nutrition	CSRP, FSPF, SFNS, UNPF, USPO
		2	Products for enteral nutrition and associated services	FSPF, SFNS, SNADOM, SYNALAM, UNPDM, UNPF, USPO
		3	Medical devices for enteral nutrition administration	FSPF, SFNS, SNADOM, SNITEM, SYNALAM, UNPDM, UNPF, USPO
		4	Oral rehydration solutions	CSRP, FSPF, SFNS, UNPF, USPO

SECTION	DESCRIPTION	SUB-SECTION	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
6	MD for treating and maintaining the musculoskeletal system			AFIDEO, APPAMED (Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices, Materials for producing immediately applicable immobilisation devices, thermoformable at low temperature, moulded directly onto the relevant body parts, in a viscoelastic or rubber-like state, Liquid or paste resins polymerisable at room temperature, for a surface area above or equal to and below (> and <) the following dimensions, Jersey tube for producing these devices.), CSRP (High molecular weight viscoelastic hyaluronic acid solution for intra-articular injection), FSPF (Pulley physiotherapy device, Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices, Materials for producing immediately applicable immobilisation devices, thermoformable at low temperature, moulded directly onto the relevant body parts, in a viscoelastic or rubber-like state, Liquid or paste resins polymerisable at room temperature, for a surface area above or equal to and below (> and <) the following dimensions, Jersey tube for producing these devices, High molecular weight viscoelastic hyaluronic acid solution for intra-articular injection), SNITEM (Pulley physiotherapy device, High molecular weight viscoelastic hyaluronic acid solution for intra-articular injection, Equipment for treating pseudarthrosis), SNADOM (Pulley physiotherapy device, Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices), SYNALAM (Pulley physiotherapy device, Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices), UNPDM (Pulley physiotherapy device, Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices), UNPF (Pulley physiotherapy device, Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices, Materials for producing immediately applicable immobilisation devices, thermoformable at low temperature, moulded directly onto the relevant body parts, in a viscoelastic or rubber-like state, Liquid or paste resins polymerisable at room temperature, for a surface area above or equal to and below (> and <) the following dimensions, Jersey tube for producing these devices, High molecular weight viscoelastic hyaluronic acid solution for intra-articular injection), USPO (Pulley physiotherapy device, Off-the-shelf sling and swathe for support and immobilisation of the shoulder joint, Materials for producing immediately applicable immobilisation devices, Materials for producing immediately applicable immobilisation devices, thermoformable at low temperature, moulded directly onto the relevant body parts, in a viscoelastic or rubber-like state, Liquid or paste resins polymerisable at room temperature, for a surface area above or equal to and below (> and <) the following dimensions, Jersey tube for producing these devices, High molecular weight viscoelastic hyaluronic acid solution for intra-articular injection)

SECTION	DESCRIPTION	SUB-SECTION	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
7	MD for other treatments and misc. items	1	Bilirubin control and phototherapy devices for treating Crigler-Najjar syndrome type I	
		2	Transcutaneous electrical nerve stimulation equipment for treating stubborn pains and consumables	CSRP, FSPF, SNITEM, UNPF, USPO
		3	Medicines that became medical devices as of 14 June 1998	CSRP, FSPF, SNITEM, UNPF, USPO
		4	Misc. items	APPAMED, CSRP, FSPF, SNITEM, UNPF, USPO

Chapter 2: Medical devices and equipment for home care and daily living aids for people with medical conditions and disabilities

SECTION	DESCRIPTION	SUB-SECTION	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
1	Beds and equipment for beds	1	Beds and accessories	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		2	Pressure ulcer prevention medical aids	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
2	MD and equipment for daily living aids	1	Sit-to-stand adjustable equipment	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		2	Sticks and crutches	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		3	Off-the-shelf hip and knee positioning cushions for patients with multiple disabilities in lying-down position	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		4	Walkers and delivery service	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		5	Continuous and dynamic spinal traction device and delivery service	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UNPDM, UNPF, USPO
		6	Wheelchair for hire and delivery service	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		7	Seats that can be fitted to a frame on wheels	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		8	Equipment designed to lift up patients	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
		9	Misc. daily living aids	CSRP, FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO

Chapter 3: Items for dressings, compression equipment

SECTION	DESCRIPTION	SUB-SECTION	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
1	Items for dressings	1	Dressings	APPAMED, CSRP, FSPF, UNPF, USPO
		2	Silver dressings	APPAMED, CSRP, FSPF, UNPF, USPO
		3	Gauze pads and cotton	APPAMED, CSRP, FSPF, UNPF, USPO
		4	Securing and holding means	APPAMED, CSRP, FSPF, UNPF, USPO
2	Vascular compression and support equipment	1	Elastic compression straps	APPAMED, CSRP, FSPF, UNPF, USPO
		2	Foam straps for padding	APPAMED, CSRP, FSPF, UNPF, USPO
		3	Pressure relief cushions Elastic compression bandages	APPAMED, CSRP, FSPF, UNPF, USPO

Chapter 4: Accessories of products under Code III of the reimbursable products and services list	**SIGNATORY ORGANISATIONS CONCERNED:** SNITEM

CODE II: External prosthetic and orthotic devices

CHAPTER	DESCRIPTION	PARAGRAPH	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
1	Orthotic devices (e.g. small devices)	A	Hernia bandages	APPAMED, CSNO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, USPO
		B	Orthotics for feet	APPAMED, CSNO, CSNPO, CSRP, FNP, FSPF, SNOF, UFOP, UNPDM, UNPF, UPODEF, USPO
		C	Heel cups	AFIDEO, APPAMED, CSNO, CSNPO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, UPODEF, USPO
		D	Elastic compression orthotics for the limbs	AFIDEO, APPAMED, CSNO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, USPO
		E	Medico-surgical belts and orthopaedic corsets in reinforced material	AFIDEO, APPAMED, CSNO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, USPO
		F	Cervical collars	AFIDEO, APPAMED, CSNO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, USPO
		G	Misc. orthopaedic correction devices	AFIDEO, APPAMED, CSNO, CSNPO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, UPODEF, USPO
		H	Off-the-shelf therapeutic footwear (CHTS)	CSNO, CSNPO, CSRP, FSPF, SNITEM, SNOF, UFOP, UNPDM, UNPF, UPODEF, USPO
		I	Off-the-shelf non-therapeutic footwear designed to accommodate walking aids	CSNO, CSNPO, CSRP, FSPF, SNOF, UFOP, UNPDM, UNPF, UPODEF, USPO, SNITEM
		J	Made-to-measure pressure garments for severe burn victims	CSNO, CSRP, APPAMED, FSPF, SNOF, UNPDM, UNPF, USPO
2	Medical opticianry			AOF, SNFDO, SYNOM, UDO
3	Electronic devices for deafness correction			SYNAM
4	Non-orthopaedic external prosthetic devices	A	Breast prosthetic devices	CSRP, FSPF, SNOF, UNPDM, UNPF, USPO
		B	Tracheal cannulae	FSPF, SNITEM, UNPF, USPO
		C	Transtympanic ventilation tubes	
		D	Voice prostheses	CSRP, FSPF, SNITEM, UNPF, USPO
		E	Breathing prostheses for tracheostomy	CSRP, FSPF, SNITEM, UNPF, USPO
5	Eye and face prosthetic devices			UDOF
6	Foot orthotics			CNSPO, UPODEF
7	Orthotic prosthetic devices			UFOP

CODE III: Implantable medical devices, human-derived implants and human-derived tissue grafts

CHAPTER	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
1	Implantable medical devices not containing or not made from any biological tissue or biological derivatives	AFIDEO (Orthopaedic and trauma implants), SNITEM
2	Implantable medical devices made from or containing non-viable animal tissue or derivatives	AFIDEO, SNITEM
3	Human-derived tissue grafts	EFS
4	Active implantable medical devices	AFIDEO, SNITEM

CODE IV: Mobility equipment

CHAPTER	DESCRIPTION	SIGNATORY ORGANISATIONS CONCERNED
1	Wheelchairs	FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
2	Misc. vehicles	FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO
3	Additions, options and repairs applicable to wheelchairs	FSPF, SNADOM, SNITEM, SYNALAM, UFAT, UNPDM, UNPF, USPO

CHAPTER 5: FINAL STIPULATIONS

Article 37: Assessing the application of this framework agreement

CEPS organises a meeting for assessing this framework agreement with all of the signatory organisations at least once a year and, for the first meeting, no later than six months following its signature.

Should there be any proven difficulties in the application of this framework agreement, on an exceptional and justified basis a signatory organisation may ask for CEPS to organise a meeting with all of the signatory organisations in addition to the meetings and hearings it may request.

Article 38: Scope and term of the framework agreement

This agreement is a framework agreement in the meaning of II, Article L 165-3 of the Social Security Code.

It is applicable for three years from its signature date.

The agreement may be supplemented by riders. However, if a non-substantial amendment to legislation or the regulations automatically amends this framework agreement, the new version of the latter is submitted to the signatory organisations at the earliest possible opportunity. Said amendment is applicable straightaway, unless one of the signatories objects thereto in writing within one week. In such a case, Paragraph 3 of Article 39 shall apply.

Article 39: Terminating this framework agreement

CEPS may terminate this framework agreement, in which case its stipulations are extended for a maximum period of one year so that a new framework agreement may be negotiated.

A signatory organisation may unilaterally terminate this framework agreement, in which case it is removed from the list of signatory organisations three months after CEPS receives its notification.

If a significant amendment to legislation or the regulations, or a major change in ministerial policy, were to change the general economic conditions of this framework agreement, the parties would swiftly examine the possibility of a renegotiation. If such a renegotiation were to prove impossible, CEPS would terminate the agreement with immediate effect.

Article 40: Additional signatory organisations to this framework agreement and changes in name or acronym of the former.

If an organisation representing companies that manufacture or distribute products or services on the list mentioned in Article L 165-1 of the Social Security Code wish to follow this framework agreement after its signature, along with CEPS it shall sign a rider adding it to the list of signatory organisations and updating the Table in Article 36. This rider shall come into force on the date it is signed. It does not need to be signed by the other signatory organisations, whom CEPS shall inform at the earliest possible opportunity.

If a signatory organisation changes its name or acronym, along with CEPS it shall sign a rider updating the list of signatory organisations and the Table in Article 36. This rider does not need to be signed by the other signatory organisations, whom CEPS shall inform at the earliest possible opportunity.

Signed in Paris, in 27 copies, on 16 December 2011.

For CEPS, Gilles Johanet		**For SNFDO,** Pascal Rétif	**For SNITEM,** Christian Seux
For AFIDEO, by proxy, Marc Morel	**For AOF,** Philippe Verplaetse	**For SNOF,** Guy Capron	**For SYNALAM,** Olivier Lebouché
For APPAMED, Damien Peras	**For CSNO,** Patricia Pisanu	**For SYNAM,** by proxy, Kulmie Samantar	**For SYNOM,** by proxy, Kulmie Samantar
For CSNPO, Raymond Massaro	**For CSRP,** by proxy, Emmanuel DÉCHIN	**For UDO,** by proxy, François Chevet	**For UDOF,** Michel Durand
For EFS, by proxy, Anne Legendre	**For FNP,** by proxy, Serge Coimbra	**For UFAT,** by proxy, Anne-Laure Marcelin	**For UFOP,** Cyril Lecante
For FSPF, Philippe Gaertner	**For SFNS,** Hervé Le Henand	**For UNPDM,** by proxy, Frédéric Piant	**For UNPF,** Michel Caillaud
For SFRL, Élisabeth Campagne	**For SNADOM,** Bernard Paramelle	**For UPODEF,** Marie-Line Boucharenc	**For USPO,** by proxy, Paul Gelbhart

Appendix to the framework agreement between the Healthcare Products Pricing Committee (CEPS) and the signatory professional organisations concerned by the products and services on the list provided for in Article L 165-1 of the Social Security Code: General principles governing tariff and price setting

CEPS determines the prices and tariffs of the products and services mentioned in Article L 165-1 of the Social Security Code together with the company(ies) concerned for registrations by brand or commercial name, or with one or more signatory organisations for registrations by generic category. This approach is based on three rules.

Two of these relate to tariffs:

Article R 165-4 of the Social Security Code stipulates that "*products and services (...) that represent neither an improvement to the service expected or the service provided, nor savings on treatment costs, or that are likely to entail unjustifiable national health insurance spending, may not be registered on the list provided for in Article L. 165-1 of the code"*.

Article R. 165-14 provides that "*the primary considerations when setting tariffs should be: the service expected or provided; any improvement to this service; the tariffs and prices of comparable products or services already included on the list; the sales forecasts and the foreseeable conditions surrounding actual use in practice."*

As regards prices, they should be determined on the basis of the very broad provisions of Article L. 162-38 of the same code, according to which the setting of prices or markups for products or services that are to be covered by compulsory national health insurance plans "must take into account changes in costs, income and business for the practitioners or companies concerned".

When the same figure is set for a tariff and a maximum purchase price at the same time, this figure must be in keeping with the rules on both tariffs and prices.

APPENDIX 4: METHODS FOR SETTING MEDICINE PRICES

I Setting and changing the prices of medicines sold in community pharmacies

1. Methods for setting the initial prices of medicines sold in community pharmacies

1.1. General criteria and principles governing price setting

Article L.162-16-4 of the Social Security Code sets out the rules governing price setting for medicines that are reimbursable under the social security system:

"*The public sales price for each of the medicines mentioned in Article L. 162-17, Paragraph 1, shall be set by means of an agreement between the company selling the medicine and the French Healthcare Products Pricing Committee (CEPS), pursuant to Article L. 162-17-4 of the code, otherwise they shall be set by ruling of the ministers for social security, health and the economy after consultation with CEPS. The primary considerations when setting the prices are any additional medical benefit which the product provides, the prices of other products providing the same treatment, the forecast or recorded sales volumes of the product, and the foreseeable and actual circumstances surrounding use of the medicine."*

Article R.163-5, I, Paragraph 2, stipulates that "*medicines that provide no additional medical benefit as assessed by the commission provided for in Article R.163-15 and no savings on medical treatment costs*" may not be included on the list provided for in Article L.162-17 of the Social Security Code.

The product's additional medical benefit is assessed in an opinion from the Transparency Commission. CEPS makes its decision on the basis of this opinion in almost every case. However, in keeping with case law, as an exception CEPS may base its decision on a different assessment than that of the Commission. It may consider that a medicine does not have an ASMR rating when the Transparency Commission had previously attributed one to it, or may attribute an ASMR rating to a medicine which previously did not have one.

This happens in particular in the case of illnesses for which the medicine requirements are partially unmet, due to some patients not being able to benefit from existing treatments (intolerance or contraindications) or not (no longer) responding to the latter, where medicines come forward that have a different mechanism of action and are therefore likely to go at least some way towards fulfilling the unmet needs, and yet which are not – and probably cannot be – shown to be superior to the reference products. In light of the results available, the Transparency Commission considers that it cannot grant an ASMR rating to these products, whilst at the same time sometimes indicating that they are "useful alternative treatments". When, on top of this, the treatment costs of the old reference products are very low and hence incompatible with the costs required to market more recently developed medicines, CEPS is sometimes obliged to make an exception, as it is allowed to do according to the case law, and to grant an ASMR rating in order to make a medicine available to patients, without disregarding the fundamental rule of the Social Security Code (for example, Pradaxa and Xarelto in 2012).

In compliance with the above provisions, CEPS' task is to obtain the most advantageous price and financial conditions for the national health insurance system, whilst taking into consideration both the pharmaceutical market as a whole and the limitations of the ONDAM budget, as well as public health needs and the obligation to treat all the companies equally.

Consideration of the pharmaceutical market as a whole requires that all discussions about an individual medicine price should look beyond the bilateral negotiating framework and take into consideration the economic consequences the price may have on **development of the market and national health insurance spending**: the direct, immediate consequences on price structures within therapeutic groups; indirect consequences on the relative growth among the different groups; medium-term consequences in terms of estimating the financial burden which the associated reimbursements will have on the ONDAM budget; and more long-term consequences if it is foreseeable that medicines with the same indications may be developed at a later date.

The goal of **fulfilling health needs** requires CEPS to ensure through its actions that patients have access to the medicines they need, and in this respect price setting is merely a means to an end.

Upholding the principle of **equal treatment between medicines** must apply regardless of which companies are selling them. Among other things, this principle dictates specifically that CEPS should not see it as part of its role, regardless of the benefit that this may bring to research and innovation, to finance research up-front through its pricing of medicines that are not themselves the results of this research, and even less, to treat innovative medicines differently depending on the country of origin of the innovation.

1.2. **Medicines with no ASMR rating**

With regard to setting prices for medicines with no ASMR rating, the rule in Article R.163-5, I, Paragraph 2, implies that the committee should address two questions: Saving in relation to what? What is the size of the saving?

1.2.1. Saving in relation to what?

In some cases, the choice of reference treatment against which to measure the saving is obvious and indisputable in light of the Transparency Commission's opinion. However, this is not always the case by any means.

For example, **when a new product in an existing range is registered**, CEPS must often decide whether the most appropriate way to determine the impact of the product's registration on social security expenditure is to compare it against the range to which the new product belongs and which it will, to a certain extent, replace, or to compare it against equivalent products being sold by other companies (possibly at a lower price). In most cases, CEPS decides to compare the new product with cheaper rival medicines, so as not to perpetuate any unjustified price variations between different products that provide the same service. Sometimes, when an agreement cannot be reached at that price, and especially when the new product is intended to replace an existing product en masse, CEPS agrees to set a price mid-way between the price of the product being replaced and that of the cheaper rival product.

Another common problem encountered relates to the choice of **measurement criterion**: **between daily treatment cost, course of treatment cost or pack cost.** While the daily treatment cost is the one used most often, especially for solid or injectable treatments for chronic conditions, the solution can be less obvious for short-term treatments or when there is no fixed dose (topical applications, liquid forms, etc.). Arguments in favour of the course of treatment cost are rarely accepted by CEPS, as it is aware that prescription practices frequently fail to comply with clinical trial protocols or with the SPC (Summary of Product Characteristics). Therefore, in some cases, when it is clearly inappropriate to use the daily treatment cost but the course of treatment cost is far too unclear, CEPS decides to compare boxes or bottles, on the basis of comparable average prescriptions.

Finally, in very rare cases CEPS agrees to take into consideration, for purposes of cost comparison, assertions that the number of co-prescriptions with other medicines will fall, even if this seems to be borne out by the clinical trials. Past experience has shown that these forecasts are almost always disproved in practice.

1.2.2. Size of the saving?

Generally speaking, the price markdown compared with the last product registered should be relatively greater the higher the price of the reference product and the more time that has elapsed between the two registrations.

However, the expected saving is not measured in terms of the difference in unit price between the new medicine and the already registered product with which the Transparency Commission is comparing it. It is measured in terms of overall saving, which is obtained by calculating treatment cost differentials by volumes. This general observation leads to two main consequences.

The first results from the distinction between medicine groups in which prescription volumes are stable in theory (definite diagnoses; clear, restricted indications) and groups in which there is a risk of unjustified growth in sales volumes. In the first instance, the only possible effect of a new competitor is to shift market shares, and therefore it is welcome, even if the price advantage is relatively insignificant. In the second instance however, the relative price advantage gained from the arrival of a new competitor could be offset or even cancelled out by the overall increase in volumes resulting from greater promotional pressure on prescribers. Hence CEPS is more exacting in this case.

A second consequence is that savings will only really be achieved if the new product wins a share of the market, and these savings will be proportional to the market share. CEPS can therefore ensure that the price difference does not hamper the product's access too significantly so as to be able to gain sufficient savings in the treatment cost. Finally, in the case of novel pharmaceutical products with no ASMR rating, CEPS is careful to make sure that registration of these new products will not inadvertently – or indeed purposely, where products coming to the end of their patents are concerned – prevent the development of generics for commercial or legal reasons. In such a case, in accordance with ministerial guidelines, CEPS will only approve the registration at a price equal to or lower than that of the corresponding generics.

1.2.3. Generic medicines

At the start of 2012, the generic markdown in relation to the original product price was increased from 55% to 60% for patents that lapsed from January 2012. When it is not possible to place a generic medicine on the market at a price based on a 60% markdown on the original medicine's ex-manufacturer price, because of the restricted size of the market concerned, the generic production cost or the low price of the original product due to the length of time it has been on the market, CEPS may agree to apply a smaller markdown, provided that the company provides circumstantial evidence to back up its application and in line with a price difference after tax of at least 10% with the original product. CEPS stipulates that it will increase the markdown if new generic-producing laboratories enter the market.

Once the first generic versions of a group registered on the list come onto the market, the general rule is a reduction in the original product price, which was increased from 15 to 20% for products which have gone off-patent since January 2012. Where the manufacturing costs are such that the price of the generic cannot be marked down significantly in comparison with the price of the original product and the 20% markdown rule results in too small a difference between the respective retail prices of the original product and the generic, which compromises the legitimacy of generic substitution by pharmacists and the credibility of the policy on generics, CEPS can, on an exceptional basis, grant partial or full exemption from the markdown. A minimum difference of 10% in retail price after tax is maintained between the original product and generic.

Attribution of a fixed accountability tariff (TFR)[41] to generic groups depends on the generic market share targets being met. The substitution thresholds of 55% at 12 months, 60% at 18 months and 65% at 24 months have been increased to 60%, 65% and 70% respectively. An 80% substitution threshold at 36 months has also been introduced. Below the substitution thresholds set at these intervals, after examination by the generics surveillance committee CEPS can decide not to attribute the TFR to the generic groups concerned. That said, when CEPS decides not to attribute a TFR because the generic supply is not sufficient for example, it applies the ministerial policy whereby reducing the original product price makes savings that have the same effect as if there had been generic substitution at 80%.

Moreover, with no decision to attribute a TFR at 18 months because the substitution targets have been met, CEPS has continued to request price reductions of 12.5% for original products and 7% for generics.

In 2013, CEPS implemented a new ministerial guideline in terms of "price convergence", with the aim of bringing the treatment cost of generics on the one hand and that of original products on the other into line with the lowest prices, in homogeneous pharmacotherapeutic groups in which generic substitution is high.

1.3. Medicines with an ASMR rating

Registering these medicines on the lists can lead to additional expenditure by national health insurance, but the decision as to what constitutes an acceptable extra cost is a difficult matter and it is impossible to devise a standard formula.

[41] TFR: to foster development of the generic market, the 2003 Social Security Financing Act provided for the possibility of limiting the reimbursement of medicines in a generic group on the ANSM list. Products belonging to a generic group stipulated in the Ruling of 29 July 2003 are reimbursed on the basis of this fixed accountability tariff (TFR) if their sales price is more than or equal to said tariff. If a product costs less than the TFR of the group it belongs to, the reimbursement base is limited to the sales price of the product.

There is no scale of acceptable price differences that corresponds to the ASMR rating scale. Discussions on the price for an ASMR-rated medicine are therefore open to negotiation and the company's demands need to be weighed up against the need or urgency for the medicine to be registered on the reimbursable list, in terms of healthcare needs.

However, ministerial policy does provide a framework for these negotiations on two particular points.

The first relates to **medicines with an ASMR rating of III or higher**, for which CEPS should accept an initial listing price that is consistent with the prices in force in the main EU Member States, in accordance with ministerial guidelines and under the terms provided in the framework agreement. This principle does not imply that all medicines with these ASMR ratings should automatically be registered on the reimbursable lists at a European level price, but rather that if they are accepted onto the lists, it should be at this price. If the expenditure that this price level will entail is out of proportion with the anticipated benefit for patients or for public health, it cannot be ruled out that the product will not be accepted onto the reimbursable medicines lists.

In particular, more often than not the discussions regarding the initial listing price for these medicines go hand-in-hand with a discussion on contractual conditions, which are as important as the price itself, since they are usually drawn up to ensure that the medicine is used appropriately in relation to the identified needs, or to anticipate rebates on volumes sold, depending on the size of the sums in question (see 2.3). Registration of these medicines on the respective lists is also often subject to an undertaking to conduct studies, under the terms set out in Articles 10b and 11 of the framework agreement.

CEPS has also sought to put a stop to the uninterrupted rise in the prices of the most expensive medicines. In most countries, for a very long time there had been the tacit acceptance that a higher price could be asked for medicines that represented a significant improvement in treatment compared with that of the reference medicine, as authorised in France by the Social Security Code. In some medicine groups, and anti-cancer drugs in particular, in which new products have succeeded each other at a fairly constant rate, this system has sometimes resulted in prices that translate as high treatment costs: up to around EUR 50,000 per year per patient for some products. CEPS considers that at these price levels, access to the French market is enough of a benefit for the innovating companies, whilst it is not necessary or justifiable for *l'Assurance Maladie* to take on further costs.

For ASMR IV-rated medicines, price negotiations must take into account the nature of the target patient group. For example, where a medicine has the same target patient group as the reference medicine, CEPS may quite easily decide that an increased market share will be adequate reward for the company's innovation, without the need for a price advantage on top of this. The decision may be different if the ASMR rating is based on a specific benefit for a restricted patient group.

1.4. Setting prices for 'me too' and 'follow-on' medicines

As regards price setting for 'me too' and 'follow-on' medicines, it is important to first clarify what is meant by these terms.

For a medicine with no ASMR rating (ASMR V) which a company is applying to have registered on the reimbursable medicines list, it is important to distinguish whether the new product is sold by the same company that sells the already listed product compared with which the new product has no additional medical benefit, or by a rival company.

In the first situation, in practice the new product will be a substitute for the existing product where the latter has gone off-patent or will be going off-patent in the near future. In these instances the new medicine is referred to as a 'follow-on'. It is a simple matter of fact and CEPS is not concerned with what the company's intentions may be. The new medicine is usually a variation on its predecessor: an enantiomeric form, new pharmaceutical form, prodrug, etc. Levocetirizine, prolonged release tamsulosin and pregabalin are some examples. In such cases, the rule set in the ministerial guidelines is straightforward: the price of the new product must be the same as the price of generic versions of the original product. CEPS applies this rule to daily treatment cost and to the retail price after tax. When the new product is developed well before its predecessor is due to go off-patent, CEPS may agree to list it at the same price, under the contractual condition that once the generics of the original product come onto the market, if the second product has not been genericised itself, its price will be reduced to that of the generics of the original. Some examples of this are desloratadine and lansoprazole oral suspension.

When the new product has been given an ASMR IV rating in relation to the original, it is still classed as a follow-on, but the price-setting rule is more favourable. The price is set in such a way that the prescription costs of the new medicine are no higher in retail price including VAT than the prescription cost of the original, taking the degree to which it is substituting the original into account. In this case, the registration agreement stipulates that the price will be reduced at a later date, to reflect progress in the market share held by generics, where applicable. One example of this is esomeprazole.

In the latter situation, when the new product is sold by a rival company to the company selling the reference product, a distinction is made on the basis of the length of time since the reference product came onto the market. If this period is sufficiently short – up to just a few years – and even if the modes of action of the two medicines in question are very similar, it indicates that the two medicines are each the product of independent research, and the companies have incurred the same level of risk. These are not 'me-too' medicines, but competing medicines that have arrived on the market at different times. CEPS considers that restricting the number and diversity of competing products in principle would only bring disadvantages, both in terms of cost (new products represent savings for national health insurance under the terms of the Social Security Code) and for medical reasons (even a product which is not given a ASMR rating can be a preferable choice for some patients). Another reason is that if all healthcare systems only allowed the very first or first few comers access to the market, this would create an unsustainable burden of 'all or nothing' on the companies' research work.

The term 'me-too' is therefore only used for medicines that have been inspired by the success of their predecessors and have entailed a relatively low level of risk for the company. By definition, the marketing of 'me-too' products takes place many years after the leaders in the group first came onto the market. Some examples of this are olmesartan, rosuvastatin and lercanidipine. There is no simple price setting rule for such medicines. CEPS' aim is to obtain the greatest possible saving; therefore it seeks to find a happy medium between the saving per pack sold, where the lower the pack price the greater the saving, and the number of packs sold instead of a more expensive rival, where the number of packs sold will be greater if the price is set at a level that will allow resources for more intense advertising.

The above principles apply to the initial registration of the medicines in question.

2. Methods for revising the prices of medicines sold in community pharmacies

2.1. Contracts based on performance criteria

Contracts are currently being used in several European countries, though in widely differing forms. Their purpose is to seek an acceptable compromise when taking on the costs of medicines that are likely to involve considerable extra costs, but whose conditions of use or efficacy are still uncertain. Most of these contracts are in fact simple price-volume contracts or contracts based on the posology or treatment duration used in practice, such as those often used by CEPS.

Genuine contracts based on performance criteria could be considered for medicines with a high ASMR rating. They may also be considered when a medicine is put forward accompanied by clinical documentation that does not warrant a high ASMR rating, even though it may have strong potential as an improvement on existing products. In the majority of cases, CEPS relies on what has already been proven, at the risk that the medicine may not be registered on the reimbursable medicines list if no price agreement can be reached under the terms of the Social Security Code. However, in some very rare instances, CEPS agrees to give these medicines a chance, even though in principle the assessment would not warrant the price requested; however this is done on very strict conditions. In the first place, the anticipated, but unproven, benefit must be such that it could not reasonably have been proven during the clinical trials carried out prior to marketing authorisation; or, for example, that it can only be proven in real-life practice. In the second place, if this benefit exists, it must represent a clear advantage and be preferable in public health terms. In the third place, a study must be devised that, by the end of the fixed-term trial period (generally no more than three years), will unequivocally prove that the benefit both exists and is considerable. Finally, the company marketing the medicine must enter into an agreement whereby it undertakes among other things to bear the financial costs in the event of failure of the product.

It goes without saying that the risk involved in this approach relates to profit levels, not to tolerance of the medicine.

Article 10b of the framework agreement thus sets out the terms for setting a "conditional price" which can only be confirmed if the expected improvement of the medicine is "demonstrated and quantified by an appropriate study, backed up by specific findings associated with indicators that are set by agreement". Otherwise, the price obviously will not be maintained at the level initially and conditionally set.

2.2. Price review clauses

Price review clauses are introduced at the time of price setting in three main situations:

- Where certain assumptions are made when setting the initial price that only time and usage will confirm or negate, and it is necessary to guarantee that the actual cost per patient of use of the medicine remains consistent with the level that was agreed with the company at the time of registration: in essence, this is the situation that 'daily treatment cost clauses' are designed to cover.

Where it is necessary to ensure that the sales volumes achieved by the medicine remain consistent with its medically established target patient group: these situations are covered by volume clauses.

- Where the price level and the likely sales volumes, especially for medicines that have been listed at a protected European-level price because of their ASMR rating, warrant a price reduction at the end of the period guaranteed in the framework agreement. In these cases, unconditional price reduction clauses may be drawn up that become effective on a set date.

2.2.1. Daily treatment cost clauses

Daily treatment cost clauses are split into two categories: 'range of dose' clauses and 'posology' clauses. Where a dose-related effect has been established in their use, many medicines are sold in several different dose sizes, either from the time they are authorised, or at a later date when additional dose sizes are added. In these cases, CEPS decided that the best way to ensure both that the different dose sizes of the medicine were properly used and that rival companies in the medicine group in question were treated fairly, was for all dose sizes of the same medicine to be sold at the same price per pharmaceutical unit. With these uniform prices, it is not in the pharmaceutical companies' interest to specifically promote the sale of the highest, most expensive dose sizes. It also means that the treatment cost and the balance of relative prices between rival companies can be maintained at the same level over time, since the actual treatment costs are independent of the distribution of sales volumes between the different dose sizes.

When it is not possible to set uniform prices, for example for the sake of international price consistency, a 'range of dose' daily treatment cost clause is signed instead, with a view to producing a more or less similar effect. In these cases, what is agreed with the company at the time of the medicine's registration is actually a daily treatment cost reflected in the prices of the different dose sizes, on the basis of an assumed distribution pattern of prescriptions. If the statistics show that the actual distribution is different from the assumed distribution, the prices are revised to establish a new agreed treatment cost.

The purpose and the mechanism of 'posology' clauses are exactly the same as those for the 'range of dose' daily treatment cost clauses. At the time of the product's registration, a daily treatment cost is agreed on, based on an assumed average posology (as stated in the MA or as demonstrated in studies conducted prior to registration, including in countries where the product has already been marketed). If the actual posology observed in real life is different from the posology used to establish the selling price, the price is revised to establish a new agreed treatment cost.

2.2.2. Volume clauses

CEPS considers that volume clauses are not warranted when their main effect would be to distribute market shares between competing companies. Except in a few cases, they also do not make sense when registering non ASMR-rated medicines on the lists, as sales of such medicines represent savings for national health insurance and the larger the volumes sold instead of more costly products, the greater the savings. In these instances, CEPS feels that the system of end-of-year quantity clawbacks per category of pharmacotherapeutic groups is more appropriate.

However, volume clauses are essential in the relatively common situation where an innovative medicine's ASMR rating is only applicable to some of its indications or to a small patient group, or where, regardless of any financial considerations, public health requirements dictate that a product should only be used for a limited number of indications for which it is absolutely essential, as is often the case for antibiotics, for example.

CEPS has insisted on not signing any more agreements containing daily treatment cost or volume clauses that would only be implemented via volume rebates. However, to prevent minor and potentially reversible excess sales above the contractual thresholds from leading to a series of marginal price alterations entailing high administrative costs, CEPS frequently agrees in practice to make the implementation of price reductions subject to exceeding a variation threshold, where price reductions that are not implemented are compensated for by an equivalent amount of volume rebates. Above all, in accordance with the framework agreement, price variation clauses entered into for medicines rated at ASMR levels III or higher usually stipulate that the reductions will be converted into clawback payments for the product's first five years on the market.

2.3. Price changes within genericised groups

Once the first generic versions of a group registered on the list come onto the market, the general rule is a reduction in the original product price, which was increased from 15 to 20% in 2012. Where the manufacturing costs are such that the price of the generic cannot be marked down significantly in comparison with the price of the original product, and the original product price markdown rule results in too small a difference between the respective retail prices of the original product and the generic – which compromises the legitimacy of generic substitution by pharmacists and the credibility of the policy on generics – CEPS can, on an exceptional basis, grant partial or full exemption from the markdown. A minimum difference of 10% in retail price after tax is generally maintained between the original product and generic.

The principle of a 20% markdown on the original product price when the patent lapses must now apply, whether or not the generic is indeed marketed, and even if this comes onto the market – for whatever reason – more or less a long time after the lapse in patent.

Furthermore, and this has been the case since 2008, the price of original products is now lowered by 12.5% (as opposed to 10% before) and that of generics by 7% (4% before) once the first generic versions have been on the market for 18 months (as opposed to 24 months before) – unless the generic group is attributed a fixed accountability tariff (TFR). The reduction in generic prices may therefore be discussed when the generic supply in the group is insufficient. Lastly, the competitive context of the therapeutic group may change when the market share and price of medicines on the list change. CEPS therefore applies ministerial policy (covered in Article 13a of the framework agreement) as regards "price consistency" which, for groups where generic versions are being introduced and developed, gradually narrows the price differences between these generics and medicines providing the same treatment that are still on-patent.

At the end of 2012, in line with new ministerial policy, CEPS undertook a "price convergence" policy with the aim of bringing the price of generics on the one hand and that of original products on the other more into line with the lowest prices for homogeneous pharmacotherapeutic groups in which generic substitution is high – where applicable by arguing in favour of daily treatment cost.

2.4 Other price changes

In addition to price reductions introduced in implementation of specific clauses, which do not require further commentary, prices may also be reduced at CEPS' initiative in several situations.

With regard to products covered by a European-level price guarantee, the prices and associated clauses can nevertheless be revised if the conditions that justified them are amended: European prices, significant variation in production costs, assessment of the product, medico-economic analysis and sales volumes recorded.

Pursuant to Article 13b of the framework agreement, CEPS is also authorised to ask that contractual clawback payments be transformed into price reductions three years after registration, once the product is not covered by a European-level price guarantee (five years).

Pursuant to Article L. 162-17-4 of the Social Security Code, when the growth in medicine spending is clearly inconsistent with the ONDAM target, even if it is consistent with ministerial policy and the provisions of the framework agreement, CEPS recommends price reductions via agreement.

Reductions may also be warranted once the findings of the follow-up studies on real-world use of the products, conducted in accordance with Articles 10b and 11 of the framework agreement, are known, and more generally, when the scientific and epidemiological data used as a basis for the agreements change significantly.

Prices can also be reviewed when a product is due to have its registration renewed. This is an opportunity for looking at the position that the product has actually gained in the market, which can vary widely from what may have been anticipated at the time of the product's first registration. This is the case in particular, even where there has been no improper use of the product, when its prescription volumes have risen significantly since it was registered, in particular following an extension of its indications. A price reduction may also be justified, in accordance with the Social Security Code, when equally effective and less costly rival products have come onto the market since the product in question was first registered.

Lastly, companies are of course free to propose price reductions themselves. By definition, these are competitive price reductions, which to date have usually been for the original products of generic groups that have been put on a fixed accountability tariff (TFR). CEPS is not without hope that this type of reduction could be extended to medicines still on-patent, as prescribers' and patients' price awareness grows and as companies are obliged to use low price as a marketing lever for their product where it has no added medical benefit.

CEPS accepts price increases for essential medicines that meet healthcare needs and were registered at a price that did not allow the companies to cover their manufacturing and marketing costs. These are generally long-standing products whose market has progressively diminished, orphan medicines, or medicines which – although not strictly defined as orphan medicines – can be classed along with them for financial purposes.

However, CEPS rejects companies' proposals for so-called 'win-win' price changes, since although their immediate effect may be neutral or beneficial for national health insurance, they tend to prove more costly in the long term and always upset the relative price balance within pharmacotherapeutic groups.

II . Setting hospital medicine prices and tariffs

Chapter 3 of the CEPS-LEEM hospital medicines framework agreement now stipulates the procedures, forms and conditions for the setting and reviewing of prescription fees for medicines on the outpatient medicines list and of accountability tariffs for products on the list for invoicing on top of “T2A” (DRG-based funding).

Medicines for patients in hospital are intended to be financed under the hospital service tariffs.

By special dispensation, some medicines are funded on top of these tariffs so as to improve patients' access to expensive medicines. These products that can be invoiced on top of such tariffs are reimbursed on the basis of an accountability tariff, which the company submits to CEPS, who may then oppose it where applicable. If CEPS does oppose a company's proposal, it sets an accountability tariff itself.

Moreover, medicines that can be sold to outpatients via hospital pharmacies are reimbursed on the basis of a prescription fee that the company submits to CEPS, who may then oppose it where applicable. If CEPS does oppose a company's proposal, it sets a prescription fee itself. Some so-called "dual channel" outpatient medicines, incidentally, can be acquired by patients from community or hospital pharmacies alike. CEPS has been obliged to set specific pricing rules in this instance.

Lastly, products listed as able to be invoiced on top of "T2A" can also be registered in the community sector.

Medicines listed as able to be invoiced on top of "T2A" (DRG-based funding)

Legislative criteria for setting accountability tariffs

Article L. 162-16-6 of the Social Security Code concerning medicines that can be invoiced on top of hospital services primarily factors in the sales prices practised for the product, sales prices for medicines providing the same treatment, forecast or recorded sales volumes, foreseeable and actual circumstances surrounding use of the product, any additional medical benefit which the product provides as assessed by the Transparency Commission and, where applicable, the medico-economic assessment findings.

Contractual criteria

In accordance with the abovementioned Article of the Social Security Code, Article 8 of the hospital medicines framework agreement of 5 December 2012 sets out the criteria governing opposition by CEPS to a company's submitted price.

CEPS may oppose the proposed price on the grounds that it is exceptionally high in relation to the prices in force in the main EU Member States, or in relation to prices in force in the French market, where directly comparable products are already being sold on the French market. It may also oppose the price due to the product's medico-economic analysis, the inadequacy of the undertakings made by the company, where the proposed price is only justified for some of the indications included in the marketing authorisation, and when the quantities sold will incur exceptionally high spending by the national health insurance system. CEPS may lastly oppose the price if the product's inclusion on the list of products that can be invoiced on top of hospital services leads to sales volumes that give rise to volume discounts on the company's proposed price.

CEPS' approach

CEPS' acceptance of or opposition to the company's submitted accountability tariff is therefore based on either the Social Security Code criteria, the criteria contained in the framework agreement, or a combination of the two.

For all the products concerned, CEPS bases its examination on two main sets of information[42]:

- the first being information derived from processing the companies' sales declarations to CEPS and ANSM, which provide a picture of the volumes sold to healthcare establishments, average prices used and growth in both prices and volumes;

- the other being information concerning prices of some medicines abroad, obtained from the database of the specialist service provider that has signed an agreement with CEPS.

CEPS therefore compares both sets of information when making its decisions, and also takes into consideration the fact that financing on top of hospital services could act as a growth stimulus for the products concerned.

Finally, it pays close attention to avoiding price discrepancies within the various groups of comparable medicines.

CEPS is also extremely vigilant as to current prices elsewhere in Europe which might prove to be a basis for opposition. It bases its analysis on the comparison of forecast or recorded sales volumes in France for the product concerned, in relation to the comparable European markets.

On an exceptional basis, for essential medicines, reference to European prices has resulted in CEPS agreeing to higher submitted tariffs than the current prices in France, for products with a temporary authorisation (ATU), when it appeared that these French prices were much lower than most of the other prices across Europe.

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[42] ATIH data, which provides a picture of the volumes sold to healthcare establishments of only medicines listed as able to be invoiced on top of hospital services ("T2A"/DRG-based payment model), their average prices and growth in both prices and volumes, can also be used when reviewing accountability tariffs.

In order to maintain an incentive for hospital purchasers to negotiate prices, invoicing by *l'Assurance Maladie* is carried out on the basis of the establishment's purchase price, increased by an interest margin equal to 50% of the difference between the establishment's purchase price and the accountability tariff set by CEPS.

More generally, CEPS believes that the difference between the tariff that is reimbursed by *l'Assurance Maladie* and the prices actually paid by the healthcare establishments could lead to inappropriate buying practices by the hospitals and that therefore the difference should be restricted to the usual price differences based on the quantities bought by the establishments or specific services they can provide for the sellers.

Medicines that can be sold to outpatients in hospital pharmacies

Legislative criteria for setting prescription fees

Article L.162-16-5 of the Social Security Code concerning outpatient medicines stipulates the same criteria for setting the prescription fees of outpatient medicinal products as for setting the accountability tariff of medicines that can be invoiced on top of hospital services (see above).

Contractual criteria

In accordance with the abovementioned Article of the Social Security Code, Article 8 of the hospital medicines framework agreement of 5 December 2012 sets out the criteria governing opposition by CEPS to a company's submitted price.

The submitted price can be opposed according to the same criteria as mentioned for medicines that can be invoiced on top of hospital services.

CEPS' approach

CEPS' acceptance of or opposition to the company's submitted accountability tariff is therefore based on either the Social Security Code criteria, the criteria contained in the framework agreement, or a combination of the two.

For all the products concerned, CEPS bases its examination on two main sets of information[43]:

- the first being information derived from processing the companies' sales declarations to CEPS and ANSM, which provide a picture of the volumes sold to healthcare establishments, average prices used and growth in both prices and volumes;

- the other being information concerning prices of some medicines abroad, obtained from the database of the specialist service provider that has signed an agreement with CEPS.

CEPS therefore compares both sets of information when making its decisions,

For the rest, CEPS takes exactly the same approach regarding outpatient medicines as has been described above for medicines listed as able to be invoiced on top of "T2A" (DRG-based funding). The only difference is the interest mechanism applicable when invoicing the latter.

[43] French national health insurance (*Assurance Maladie*) data called Rétrocéd'AM, which provides a picture of the amounts presented for reimbursement, amounts reimbursed and the number of units reimbursed by the general scheme for outpatient medicines alone, can also be used when reviewing prescription fees.

Special cases

Some so-called "dual channel" medicines can be issued to patients either by community pharmacies or hospital pharmacies. Other medicines that can be invoiced on top of "T2A" (DRG-based funding) are also available in community pharmacies.

For biosimilars and generics, CEPS' approach is to set a community price, marked down in relation to the reference product (original product or so-called "benchmark" biological medicine). This pricing method is not applied in the hospital sector however, for which CEPS sets exactly the same tariffs for comparable hospital medicines (see above).

This means that different prices can be observed between the community and hospital sectors when the same generics or biosimilars are listed on both the community list and the outpatient medicine list or list of products that can be invoiced in top of "T2A" funding.

Thanks to these equal accountability tariffs or prescription fees for comparable medicines, manufacturers or generics and biosimilars can submit tenders to calls for tenders on an equal footing with manufacturers of "benchmark" products. The point of this mechanism is so as not to discourage prescriptions of generics and biosimilars in hospitals, and to benefit from savings when issuing a hospital prescription in the community.

APPENDIX 5: TARIFF AND PRICE SETTING FOR MEDICAL DEVICES

An overview of the rules governing tariff and price setting for medical devices and their new versions used to feature in Appendix 3 of CEPS' previous annual reports, but it now only covers the rules not set out officially in the Medical Devices (MD) Framework Agreement or any clarifications that may prove necessary.

As such, Article 20 of the MD framework agreement represents an update in CEPS' doctrine as regards its proposals to the ministers on the choice between registering by brand or commercial name and registering by generic category. Indeed, when one of the criteria stipulated in this Article is met, registration by brand or commercial name is chosen.

Likewise, the pricing principles encompassing category-based pricing and consideration of innovations are addressed in Articles 23 and 24 of the MD Framework Agreement.

CEPS' doctrine on tariff and price setting, meanwhile, is covered in the appendix to the MD framework agreement. This text position indicates that it concerns an overview of this doctrine applied by CEPS, without it being contractualised.

However, two points still merit clarification for all that: differences between prices and tariffs (1) and tariff revisions by profession (2). Concerning the latter point, Article 27 of the MD framework agreement (tariff and price revisions) only addresses the procedure for processing applications, rather than the doctrine content.

1. Discrepancies between prices and tariffs

The reimbursement system for medical devices, unlike the system for medicines that was in force before ‘fixed accountability tariffs’ were introduced, is such that in general situations, there can be discrepancies between the tariff, which is the national health insurance reimbursement base, and the actual price.

When CEPS considers it necessary, for reasons of equal access to care or disability support, to prevent such a discrepancy from being established, the only means available since the new rules were introduced is to set a maximum purchase price (see CEPS 2001 annual report). CEPS aims to set maximum purchase prices on an almost routine basis, for it considers that the contribution made by medical devices to the preservation or restoration of individuals’ health or quality of life is as important as that of the other elements of care provision, including medicines. It therefore considers that patients’ out-of-pocket expenses that are not kept under control can constitute a threat to their equality of access to care.

In particular, when tariff reductions are introduced, CEPS is keen to ensure that these go hand-in-hand with a maximum purchase price, and where applicable a prescription price, in order to avoid a situation where savings are made at the patient’s expense and act as a reduction in their reimbursement, an area over which CEPS has no jurisdiction.

It is safe to say that at present, with the notable exception of adult opticianry and hearing aids, the vast majority of devices or services included on the reimbursable medical devices and services list have a maximum purchase price and for those which do not have one, or are yet to have one, the prices in force are in any case identical or very close to the tariffs.

However, setting a maximum purchase price presupposes that a solution must be found to the issue of the extra costs charged for services or accessories that go beyond the definition of the reimbursable product or service as stipulated on the list. This is often the case for external prosthetic devices and orthotic devices, where patients may request, and the operators involved may offer, extra aesthetic or technical features; however these are not the only cases. For example, in the area of hearing devices for young children, those working in the profession have highlighted the fact that the discrepancy between the tariff and the price left room to pay the salaries of the hearing device personnel, who might be needed for a number of sessions, to adapt the appliance to the patient, especially very young patients or patients with multiple disabilities. In the event, the patient's share of the costs was usually taken care of by universal health cover (CMU), top-up insurance or help provided by regional or municipal aid bodies approached by the support personnel themselves. The difficult, sometimes impossible task of determining a maximum purchase price according to logical criteria, and the possibilities available for funding patients' out-of-pocket expenses led CEPS to opt for setting a maximum purchase price for these hearing devices that was higher than the reimbursement tariff.

For extras of an aesthetic nature, when they are easy to separate from the defined reimbursable product or service per se, there is no reason why the operators involved should not produce separate bills for the patient's out-of-pocket share, whilst adhering to the maximum purchase price for the main element. When these extras cannot be separated from the reimbursable device, it is important to avoid exemptions, which could gradually lead to a strong risk of all satisfactory products being taken off the reimbursable list and thus to access problems for less well-off patients. However, in 2003, the French Council of State ruled that in the case of customised orthopaedic footwear a complete ban on exemptions was illegal. In this instance, after taking advice from the national consumer's association, CEPS replaced the ban with a strict procedure requiring patients to be given information in advance. Whether or not the extras can be separated from the main product, if they are legal, patients must be given information regarding the non-reimbursable elements in advance.

2. Price revisions by profession

The medical devices sector covers several different professions, many of which are made up of small or very small businesses whose operations are more comparable to those of private service providers or small-scale craft industries than those of companies carrying out research and industrial-scale production. A large proportion of the tariffs and maximum purchase prices applicable to the reimbursable services provided by these professions often goes towards salary costs.

In these cases, the issue surrounding tariffs is somewhat different than in the other medical device fields. In particular, the criteria on price setting provided in Article L. 162-38 of the Social Security Code (overall cost, income, business operations) play a key role.

As regards the tariff-setting proposals it formulates and above all periodic tariff reviews, CEPS feels it is important to adhere to two objectives:

- the tariff and price levels must be high enough to guarantee a continuous, uniform supply across the whole country, and a quality level consistent with the service expected or provided that warranted inclusion on the list.

- these price levels should not, however, be such as to unduly favour unproductive operations, which would effectively turn the products of more competitive businesses into a bargain.

CEPS has decided that the most effective way of achieving these objectives is by regular tariff revisions, and has therefore proposed annual set tariff revision mechanisms in several cases, based on medium-term cost increases. This procedure goes hand-in-hand with regular monitoring of actual costs and profits, so that the fixed rates adopted can be altered if necessary, either at CEPS' instigation or at the initiative of the trade associations concerned.

APPENDIX 6: TABLE OF CLAWBACK PAYMENT THRESHOLDS PER CATEGORY OF PHARMACOTHERAPEUTIC GROUPS FOR 2012-2015

For the 2014 financial year, the table of pharmacotherapeutic groups was not updated. The scope and different coefficients and thresholds have been kept as they were in 2012. The coefficient provided in Article 17a) of the framework agreement is set at 25%. For each group, the portions of the overall clawback figure based respectively on turnover and excess are set at 65% and 35%.

NB: Products issued to outpatients or invoiced on top of T2A funding are marked in italics, except for categories made up primarily of these products.

Category	clawback payment threshold 2013	2013 rate (K rate not included)	2014 rate (K rate not included)	2015 rate (K rate not included)
A02 (antiacids and anti-flatulent agents) other than A02B2 + A03 (antispasmodics, anticholinergics and gastro-intestinal motility treatments) + Vogalene (A04A9) (*incl. Prepulsid and Debridat inj.*)	0.4%	0.0%	0.0%	0.0%
A02B2 (proton pump inhibitors)	-9.6%	-10.0%	-5.0%	0.0%
A04 (antiemetics) except Vogalene (A04A9)	0.4%	0.0%	0.0%	0.0%
A05A1 (bile therapy and cholecystokin) + A05B (hepatic protectors, lipotropics) + A06 (laxatives) incl. Relistor + A07 (anti-diarrhoeals) except A07E + A09 (digestives including enzymes)	0.4%	0.0%	0.0%	0.0%
A05A2 (bile stone therapy) + A07E (intestinal anti-inflammatory agents) + budesonide (H02A2)	0.4%	0.0%	0.0%	0.0%
A10 (antidiabetic agents)	4.4%	4.0%	0.0%	0.0%
A11 (vitamins *incl. Un alfa inj.*) + A12 (calcium) other than A12C1 + C05 (haemorrhoid and varicose vein treatments) + C10B (natural anti atheroma preparations) except Calcium sorbisterit and Phosphoneuros + Zymaduo and Fuosterol + V06 (dietetic agents) + V07 (other products)	0.4%	0.0%	0.0%	0.0%
B01A (non-injectable anticoagulants) + B01B (injectable anticoagulants: heparins) + B01E (direct thrombin inhibitors) + B01X (other anti-thrombotic agents) except Ceprotin and Protexel (*incl. Orgaran and Xigris*)	25.4%	25.0%	10.0%	2.0%
B01C (antiplatelet agents) except Xagrid	-4.6%	-5.0%	0.0%	0.0%
B02A and B (haemostatic agents) + B03 (anti-anaemic preparations) except B03C and Eporatio (B03X) + A14A1 (anabolic hormones) + Lederfoline, Elvorine and Folinoral (V03D) (*incl. injectable iron*)	0.4%	0.0%	0.0%	0.0%
B02C and D (clotting factors) + Ceprotin and Protexel (B01X) + J06 (sera and gamma-globulin) except Synagis (J06H9)	3.4%	3.0%	3.0%	0.0%
B03C (erythropoietin products incl. Retacrit) + Eporatio (B03X)	0.4%	0.0%	0.0%	0.0%
C01A + B + C (cardiac glycosides, anti-arrhythmics and cardiac stimulants) + injectable magnesium (A12C1)	0.4%	0.0%	0.0%	0.0%
C01D + E + X (coronary arterial disease treatments) + C02 (antihypertensives) + C03 (diuretics) + C07 (beta blockers) + C08 (calcium channel blockers) + Caduet (C10A1)	0.4%	0.0%	0.0%	0.0%
C04 (vasodilators) + N6D (nootropics) + Olmifon (N07X)	0.4%	0.0%	0.0%	0.0%
C09 (renin-angiotensin-system acting agents)	-2.6%	-3.0%	0.0%	0.0%
C10A (cholesterol and triglyceride regulating agents) + C10C (lipid regulating agents for use in combination)	-4.6%	-5.0%	0.0%	0.0%
D (dermatologicals) + Terbinafine (J02A) + Metvixia (L01X9) + Efudix (L01B)	0.4%	0.0%	0.0%	0.0%
G01 (gynaecological anti-infectives) + Florgynal (G02F)	0.4%	0.0%	0.0%	0.0%
G02 (other gynaecologicals) except Florgynal (G02F) + G03 (ovulation inhibitors) except G03B, G and J	0.4%	0.0%	0.0%	0.0%
G03B (androgens), G04 (urologicals) except G04A (*except Revatio and Adcirca, G04E*)	2.4%	2.0%	2.0%	0.0%
G03G (gonadotrophins/ovulation stimulants) + H01C1 and C3 (hypothalamic hormones) (*incl. Salvacyl*)	0.4%	0.0%	0.0%	0.0%
H01A (ACTH) + H01C2 (anti hGH antibodies) + H02 (oral corticosteroids) except budesonide (H02A2) + H04A, B and D (calcitonin, glucagon and antidiuretic hormones) + A16A (other digestive treatments: *Proglicem*) + Alkonatrem (J01A) (*incl. Minirin inj.*)	0.4%	0.0%	0.0%	0.0%

Category	clawback payment threshold 2013	2013 rate (K rate not included)	2014 rate (K rate not included)	2015 rate (K rate not included)
H03 (thyroid treatments) (*incl.Proracyl*)	0.4%	0.0%	0.0%	0.0%
H4C (growth hormones)	-0.6%	-1.0%	-1.0%	0.0%
J01 (systemic antibacterials) except Alkonatrem (J01A) + J02A (systemic antifungal agents) except Terbinafine + J03A (systemic sulphonamides) + J05B (antivirals excl. anti-HIV agents) except J05B1 + G04A (antiseptic agents and urinary tract anti-infective agents)	-1.6%	-2.0%	-2.0%	0.0%
J05B1 (hepatitis antivirals) incl. Incivo and Victrelis + J05C (HIV antiretrovirals) incl. Edurant and Eviplera + L03B1 (alpha interferons)	7.4%	7.0%	4.0%	0.0%
J07 (vaccines) + V01A (allergy treatments) + Synagis (J06H9)	0.4%	0.0%	0.0%	0.0%
K (solutions for hospital use) + Nonan, Decan, Tracutil and Tracitrans (A12C2)	0.4%	0.0%	0.0%	0.0%
L01 except Metvixia (L01X9) and Efudix (L01B) + L02 (anti-cancer agents and cytostatic hormone therapy) + L03A (growth factors) except Copaxone (L03A9)	0.4%	0.0%	0.0%	0.0%
L03B2 (beta interferons) + Copaxone (L03A9) and Gylenia and Tysabri (L04X)	5.4%	5.0%	5.0%	0.0%
L04X (other immune suppressants) except Gylenia, Ilaris and Tysabri	0.4%	0.0%	0.0%	0.0%
M01A1 (anti-rheumatics, non-steroidal plain) except diacerein and glucosamine based products + M01A3 (Coxibs, plain) + M04 (anti-gout preparations)	0.4%	0.0%	0.0%	0.0%
M01A2 (anti-rheumatics, non-steroidal in combination) + M02 (topical anti-rheumatics and analgesics) + M03 (muscle relaxants)	0.4%	0.0%	0.0%	0.0%
M01C (disease-modifying anti-rheumatic drugs) + Acadione (M05X) + L04B (Anti TNF) + Stelara (L04X) (*incl. Orencia, Remicade and Roactemra*)	0.4%	0.0%	0.0%	0.0%
M05B (Biphosphonates) + G03J (Oestrogen receptor modulators) + Forsteo (H04E), Protelos, Osigraft and Inductos (M05X)	0.4%	0.0%	0.0%	0.0%
M05X (other musculoskeletal treatments) except Acadione and Protelos, Osigraft and Inductos + diacerein and glucosamine based products (M01A1)	0.4%	0.0%	0.0%	0.0%
N01 (anaesthetics) (incl. Naropeine and Versatis)	0.4%	0.0%	0.0%	0.0%
N02 (analgesics) except Buprenorphine and Methadone + N07C (antivertigo preparations)	0.4%	0.0%	0.0%	0.0%
N03A (antiepileptics) (*incl. Taloxa*)	2.4%	2.0%	2.0%	0.0%
N04A (antiparkinson drugs) + Adartrel (N07X)	2.4%	2.0%	2.0%	0.0%
N05A1 (atypical antipsychotics)	-1.6%	-2.0%	0.0%	0.0%
N05A9 (conventional antipsychotics) + N06A3 (mood regulators)	0.4%	0.0%	0.0%	0.0%
N05B (hypnotics and sedatives) + N05C (tranquillisers)	0.4%	0.0%	0.0%	0.0%
N06A (antidepressants) except N06A3 and Levotonine (N06A9)	0.4%	0.0%	0.0%	0.0%
N06B (psychostimulants) + N07E (alcohol dependence treatments) + N07F (opioid dependence treatments) + Rilutek (N07X), Levotonine (N06A9), Buprenorphine and Methadone (N02A)	0.4%	0.0%	0.0%	0.0%
N07D (anti-Alzheimer's products) + Mestinon, Prostigmine and Mytelase (N07X)	0.4%	0.0%	0.0%	0.0%
P (anti-parasitic products) + J04 (tuberculosis and lepra treatments) (*incl. Eskazole, Lamprene and Notezine*)	0.4%	0.0%	0.0%	0.0%
R01A1 + A6 (nasal corticosteroids and other topical nasal preparations) + R06A (systemic antihistamines)	-4.6%	-5.0%	0.0%	0.0%
R01A4 + A7 + A9 + B (nasal anti-infectives) + R05 (cough preparations) + R07 (other respiratory products) + A01 (stomatologicals) + Pulmozyme (V03H)	-4.6%	-5.0%	0.0%	0.0%
R03 (anti-asthma and COPD products)	-2.6%	-3.0%	0.0%	0.0%
S01 (ophthalmologicals) except S01E and S01P + S02 (ear treatments)	0.4%	0.0%	0.0%	0.0%
S01E (miotics and antiglaucoma preparations)	-0.6%	-1.0%	0.0%	0.0%
S01P (ophthalmological anti-neovascularisation products)	0.4%	0.0%	0.0%	0.0%
T01 (diagnostic imaging products) + T02X (other diagnostic tests) + Helikit (V03X), Lipiocis and Quadramet (V03C)	2.4%	2.0%	2.0%	0.0%
V03 (miscellaneous treatments) except Lederfoline, Elvorine, Folinoral, Pulmozyme, Helikit, Lipiocis and Quadramet + Mimpara, Phosphore, Phosphoneuros, Phosphosorb and Calcium sorbisterit (*incl. Cardioxane, Uromitexan, Ferriprox, Fasturtec and Ethyol*)	0.4%	0.0%	0.0%	0.0%
Z (orphan drugs < €30M)	0.4%	0.0%	0.0%	0.0%

Category	**clawback payment threshold 2013**	**2013 rate** (K rate not included)	**2014 rate** (K rate not included)	**2015 rate** (K rate not included)
Z' (orphan drugs >= €30M)	0.4%	0.0%	0.0%	0.0%
TOTAL	**0.4%**	**0.0%**	**0.0%**	**0.0%**

APPENDIX 7: PRICE AGREEMENTS AND PRO-FORMA CLAUSES

1. Price agreements for medicines

RIDER TO THE AGREEMENT OF
between the Healthcare Products Pricing Committee (CEPS)
and *X*

Having regard to the Social Security Code, in particular Articles L 162-16-4 and L 162-17-4,
Having regard to Decree No. 99-554 of 2 July 1999 amending the Social Security Code regarding the registration of medicines on the lists provided in Articles L. 162-17 of the Social Security Code and L. 618 of the Public Health Code and the setting of prices for such products,
Having regard to the ruling of 4 August 1987, amended, regarding prices and markups on reimbursable medicines,
Having regard to the General Tax Code, in particular Article 281-8,
Having regard to the Public Health Code, in particular Articles L 5123-1, L 5121-8, L 5121-13, 5121-1,
Having regard to the multiannual agreement made on *dd*/*mm*/*yy* between CEPS and *X*;

CEPS and *X* now agree on the following provisions:

ARTICLE I:

The prices stated in the table below shall be applicable as of the effective date of the decision.
Price registration or price change

Product	EphMRA/ATC category	Ex-manufacturer price	Retail price after tax	TFR (fixed accountability tariff)	Effective date
CIP code, name, dose (of active ingredient), pharmaceutical form, packaging, (company marketing the product)					Date of publication in the *Journal Officiel* or later date

ARTICLE II: (see below: pro-forma clauses)

ARTICLE III:

Appendix 3 to the above-mentioned agreement shall be amended pursuant to Article I.
Appendix 4 to the above-mentioned agreement shall be amended pursuant to Article II.

Signed in Paris, on

First name, Surname
Position
Company *X*

First name, Surname
Chairman of the French Healthcare
Products Pricing Committee

2. Pro-forma clauses regarding medicines

2.1. Pro-forma posology clause

Article 2

2.1. The price set in Article I (reference ex-manufacturer price: $PFHT_R$) is set on condition that the posology observed ($Poso_n$) is equal to or less than ……. (Reference posology: $Poso_R$).

2.2. The posology ($Poso_n$) shall be monitored every year and, on the first occasion (dd/mm/yy) with reference to the most recent EPPM published before this date.
If the posology observed ($Poso_n$) is greater than the reference posology ($Poso_R$) in a given year (n), the ex-manufacturer price as set in Article I shall be changed ($PFHT_{n+1}$) as follows:

$$PFHT_{n+1} = \frac{Poso_R}{Poso_n} \times PFHT_n$$

If there has already been one price change on the basis of this clause, a further price change may only be introduced on the basis of this clause if the posology observed is higher than the posology observed at the time of the first price change.
If ($Poso_n$ - $Poso_R$) / $Poso_R$ is less than x %, the $PFHT_n$ shall not be changed and the company shall instead owe a clawback payment (R_n) calculated according to the formula mentioned in 2.3 herebelow.

2.3 If the posology observed ($Poso_n$) is greater than the reference posology ($Poso_R$), the company may also be liable for a clawback payment (R_n) calculated according to the following formula:

$$R_n = CAHT_n - (PFHT_{n+1} \times V_n)$$

where:

- ($CAHT_n$) equals the sales figure established by GERS over the 12 months preceding the date given in 2.2 hereabove;
- (V_n) equals the product format sales volume of which GERS has been informed for the same period.

2.4. The company shall be notified of the clawback amount by CEPS, who will inform the relevant local URSSAF branch of the payment owed (Paris-RP branch for the Ile de France region and Lyon branch for all other regions). The company shall make this clawback payment upon receipt of the contribution request from the relevant URSSAF branch. The company shall inform CEPS by post of the payment amount and date.

(The clawback amount may be deducted by agreement from the sum used to work out the corresponding end-of-year clawback by pharmacotherapeutic class grouping owed by the company).

2.2. Pro-forma product range daily treatment cost clause

Article 1

The initial listing prices (or price changes) given in the table below shall be applicable as of the date they are published in the *Journal Officiel* (or shall be effective as of *dd*/*mm*/yy).

Product	**Category**	**Ex-manufacturer price**	**Retail price after tax**
First listing – CIP code, product aaa, …	……	€… ..	€… ..
First listing – CIP code, product bbb, …	……	€… ..	€… ..
Price change – CIP code, product ccc, …	……	€… ..	€… ..

Article 2:

2.1. The prices set in Article 1 are done so on the condition that the observed daily treatment cost for the product range ($CTJG_n$), calculated for the range comprising aaa, bbb, ccc, …, is equal to or less than € ---.--: the reference product daily treatment cost ($CTJG_R$).

2.2. The $CTJG_n$ value shall be monitored every year (n) and the first monitoring shall cover the 12 months preceding dd/mm/yy. It shall be calculated on the basis of the average yearly cost of the number of treatment days (NJT_n) and of the posologies of each of the products mentioned in 2.1 hereabove, which are included in the EPPM (IMS) data available on dd/mm/yy and the 12-month sales figure stated in the most recent GERS data available at this date.
$CTJG_n$ shall be calculated by dividing the sales figure for the whole range ($CAHTG_n$) as declared to GERS, by the number of days' treatment using products in the range ($NJTG_n$), so:

$$CTJG_C = CAHTG_n / NJTG_n$$

where $NJTG_n$ equals the sum of the number of days' treatment with each of the products in the range, i.e.:

$$NJTG_n = \Sigma NJT_{in}$$

The number of days' treatment, NJT_{in} is equal to the number of tablets (doses/units) sold for each product or product format (i) in the range divided by the corresponding posology (P_i) reported in the EPPM (IMS), so:

$$NJT_{in} = (\textit{number of units per pack} \times \textit{number of packs}_i) / Poso_{in}$$

If $CTJG_C > CTJG_R$, the ex-manufacturer price of each of the products or product formats in the range mentioned in 2.1. hereabove shall be uniformly changed ($PFHT_{n+1}$) with the result that $PFHT_{n+1} = PFHT_n \times CTJG_R / CTJG_n$ and the company shall be liable for a clawback payment R_n where $R_n = NJTG_n \times (CTJG_n - CTJG_R)$.

However, if $PFHT_{n+1} / PFHT_n > x$ %, no price reduction shall be carried out and the company shall still owe the clawback payment.

2.3. Pro-forma unit volumes clause

Article 2

2.1. The price (ex-manufacturer price) mentioned in Article 1 (reference ex-manufacturer price: ($PFHT_R$)) is set on condition that the annual sales volume (V_n) is less than or equal to the reference sales volume (V_R).

2.2. The sales volume (V_n) shall be reported every year in the GERS data for month *M*, the first occasion being the GERS data published in month *M* of year *A*.

2.3 If the annual sales volume reported (V_n) is greater than the reference sales volume (V_R), the ex-manufacturer price shall be changed ($PFHT_{n+1}$) as follows:

$$PFHT_{n+1} = [V_R \times PFHT_n + (V_n - V_R) \times a \times PFHT_n] / V_n$$
$$= [1 + a \times (V_n - V_R) / V_n] \times PFHT_n \text{ where } 0 < a < 1.$$

in addition, the company shall owe a clawback payment:

$$R_n = (V_n - V_R) \times a \times PFHT_n$$

2.4 However, if $PFHT_{n+1} / PFHT_n > x$ %, no price reduction shall be carried out and the company shall still owe the clawback payment.

2.5 Subsequent to any price change introduced pursuant to 2.2 hereabove, the current price in force ($PFHT_n$) shall only be reduced if the annual sales volume reported (V_{n+i}) is higher than both V_R and the sales volume which led to the previous price change (V_n).
If $V_{n+i} > V_n > V_R$, the company shall also be liable for a new clawback payment:

$$R_n = (V_{n+i} - V_n) \times a \times PFHT_n$$

2.6 CEPS reserves the right to revise the price and the above-mentioned provisions in the event of an extension of the product's indications.

2.7 The company shall be notified of the clawback amount by CEPS, who will inform the relevant local URSSAF branch of the payment owed (Paris-RP branch for the Ile de France region and Lyon branch for all other regions). The company shall make this clawback payment upon receipt of the contribution request from the relevant URSSAF branch. The company shall inform CEPS by post of the payment amount and date.

2.3. Pro-forma pooled sales turnover clause

Article 2

2.1. The price (ex-manufacturer price) mentioned in Article 1 (reference ex-manufacturer price: ($PFHT_R$)) is set on condition that the annual pre-tax turnover ($CAHT_n$) is less than or equal to the reference annual pre-tax turnover ($CAHT_R$).

2.2. The annual pre-tax turnover of the product range mentioned in Article 1 ($CAHT_{Xn}$) and the annual pre-tax turnover of this range and new proprietary products sharing the same indications ($CAHT_n$) shall be reported every year (n) in the GERS data for month M, the first occasion being the GERS data published in month M of year A.

2.3 On the basis of the turnover for one year (n), beyond a reference annual turnover ($CAHT_R$) for all the products mentioned in Article 1 and the new proprietary products sharing the same indications, the company shall be liable for a clawback payment:

$$R_{Xn} = (CAHT_{Xn} / CAHT_n) \times [(CAHT_n - CAHT_R) / PFHT_n] \times a \times PFHT_n \text{ where } 0 < a < 1$$
$$= (CAHT_{Xn} / CAHT_n) \times (CAHT_n - CAHT_R) \times a$$

where ($PFHT_n$) is the current ex-manufacturer price per tablet / mg / capsule, etc.
Furthermore, the ex-manufacturer price per tablet / mg / capsule, etc. of the products mentioned in Article 1 shall be changed ($PFHT_{n+1}$) as follows:

$$PFHT_{n+1} = ((CAHT_{Xn} - R_{Xn}) / CAHT_{Xn}) \times PFHT_n$$

2.4 However, if PFHTn+1 / PFHTn > x %, no price reduction shall be carried out and the company shall still owe the clawback payment.

2.5 Subsequent to any price change introduced pursuant to 2.3 hereabove, the current price in force ($PFHT_n$) shall only be reduced if the turnover reported ($CAHT_{n+i}$) is higher than the turnover which led to the previous price change ($CAHT_n$).
If $CAHT_{n+i} > CAHT_n > CAHT_R$, the company shall also be liable for a new clawback payment:

$$R_{Xn+i} = (CAHT_{Xn+i} / CAHT_{n+i}) \times (CAHT_{n+i} - CAHT_n) \times a \text{ where } 0 < a < 1$$

2.6 CEPS reserves the right to revise the price and the above-mentioned provisions in the event of an extension of the product's indications.

2.7 The company shall be notified of the clawback amount by CEPS, who will inform the relevant local URSSAF branch of the payment owed (Paris-RP branch for the Ile de France region and Lyon branch for all other regions). The company shall make this clawback payment upon receipt of the contribution request from the relevant URSSAF branch. The company shall inform CEPS by post of the payment amount and date.

3. Agreement regarding medical devices (including study clause)

AGREEMENT

between the Healthcare Products Pricing Committee (CEPS)

and the company (*X*)

Having regard to the Social Security Code, in particular Articles L. 165-2, L. 165-3, and L. 165-4;

Having regard to the opinion of the Products and Services Assessment Committee;

CEPS and the company (*X*) now agree on the following provisions:

Article 1: This agreement is made under the condition precedent that the ruling relating to the registration of device(s) (*Y*) shall be signed by the relevant ministers. This agreement shall be effective as of the corresponding effective date of publication of the decree in the *Journal Officiel*.

Article 2: The tariffs and maximum purchase price in € after tax given in the table below are set as follows:

Code	**Category**	**Tariff in € after tax**	**Max. PP in € after tax**
aaa, …	……	€… ..	€… ..
bbb, …	……	€… ..	€… ..
ccc, …	……	€… ..	€… ..

Article 3: (see below: pro-forma clauses)

Article 4: The company (*X*) undertakes to conduct and fund a study …. The aim of this study will be: …. The study findings shall be sent to CNEDiMTS and CEPS.

Paris, date

MM	Chairman of the French Healthcare
Company *XXXX*	Products Pricing Committee

4. Pro-forma clause for medical devices

4.1. Pro-forma unit volumes clause

Article 3:

3.1 The company (*X*) undertakes to inform CEPS every year, during the course of month *mm* for the year finishing in said month *mm* – and for the first time during the month *mm*/*yyyy* – of the total number of devices (*Y*) it has sold in France during the previous year.

3.2 If the number (*N*) of devices (*Y*) sold in the year exceeds a certain number (*n*), the prices/tariffs (*P*) stated in the ruling mentioned in Article 1 hereabove shall be changed (P_M) according to the formula:

$P_M = (a \times P) + [(1 - a) \times P \times (n / N)]$, *where* $0 < a < 1$

and the company shall be liable for a clawback payment (*R*) calculated according to the fomula:

$R = (P_V - P_M) \times N$

where (P_V) is the current price of the device in question.

However, if $P_M / P_V > x\%$, the price shall not be reduced but the company shall still be liable for the clawback payment (*R*).

3.3 Where there has already been one price reduction under the terms of Paragraph 3.2 hereabove, no new price reduction may be introduced on the basis of Paragraph 3.2, unless the number (*N'*) of devices (*Y*) sold established on this occasion is greater than the number (*N*) on which the previous reduction was based and if $P_M / P_V > x\%$.

If $N' > n$ and $P_V > P_M$, the company shall be liable for a clawback payment $R = (P_V - P_M) \times N'$.

3.4 The company shall be notified of the clawback amount by CEPS, who will inform the relevant local URSSAF branch of the payment owed (Paris-RP branch for the Ile de France region and Lyon branch for all other regions). The company shall make this clawback payment upon receipt of the contribution request from the relevant URSSAF branch. The company shall inform CEPS by post of the payment amount and date.

4.2. Pro-forma pooled sales turnover clause

Article 3:

3.1 In the same way as each of the companies marketing devices (*Y*) in France, the company (X) undertakes to inform CEPS every year, during the course of month *mm* for the year finishing in said month *mm* – and for the first time during the month *mm/yyyy* – of the total number of devices (Y) it has sold in France during the previous year.

3.2 On the basis of these declarations, the annual sales of device (*Y*) by company (*X*) and those of each of the companies marketing (*Y*) in France shall be estimated by multiplying the number of (*Y*) sold by the current LPPR tariffs, giving a theoretical annual turnover after tax for each of the companies: so $CATTTCy_x$ for company (*X*) and *CATTTCy*, the sum of the theoretical annual turnovers after tax obtained for each of the companies marketing (*Y*) in France.

If $CATTTCy > CATTTCy_{Ref1}$, the company shall be liable for a clawback payment according to the table below:

CATTTC threshold	Clawback payment owed
If $CATTTCy \leq CATTTCy_{Ref2}$	$R_x = a \times (CATTTCy - CATTTCy_{Ref1}) \times (CATTTCy_x / CATTTCy)$ where $0 < a < 1$
If $CATTTCy > CATTTCy_{Ref2}$	$R_x = [a \times CATTTCy_{Ref1} + b \times (CATTTCy - CATTTCy_{Ref2})] \times (CATTTCy_x / CATTTCy)$ where $0 < a < b \leq 1$

Furthermore, if $CATTTCy > CATTTCy_{Ref2}$, the prices/tariffs (P_V) stated in the ruling mentioned in Article 1 hereabove shall be changed (P_M) according to the formula: $P_M = [(CATTTC_y - R_x) / CATTTC_y] \times P_V$.

However, if PM / PV > x%, the price shall not be reduced but the company shall still be liable for the clawback payment (R).

3.4 In the event that a price reduction is implemented pursuant to 3.2 above, the conditions of the agreement shall be revised.

3.5 The company shall be notified of the clawback amount by CEPS, who will inform the relevant local URSSAF branch of the payment owed (Paris-RP branch for the Ile de France region and Lyon branch for all other regions). The company shall make this clawback payment upon receipt of the contribution request from the relevant URSSAF branch. The company shall inform CEPS by post of the payment amount and date.

APPENDIX 8: INTERNATIONAL PRICE REFERENCING FOR MEDICINES

International price referencing for medicines has been carried out on relatively few occasions, and interpreting the results is no easy matter[44]. It is based on complex methods and various precautions must therefore be taken when making use of it.

International price referencing must ideally compare the prices of pharmaceutical product formats that are exactly the same in all respects (pharmaceutical, dosage, size of pack and so on) in the different reference countries. But pharmaceutical product formats differ from one country to the next in practice, and this means that a balance must be struck between the extent to which the products are comparable and the extent to which the sample is representative of the medicines being studied: if the price referencing is limited to strictly comparable products then the medicine sample is small and not representative. What's more, the medicine sample must be representative for each reference country.

There is no one-size-fits-all, correct measure for estimating price differences between countries. The results particularly depend on the sample size, product comparability criterion and the weight attached to each product when establishing the price index. As such, international price referencing studies must test the sensitivity of the results to the chosen method.

CEPS has added two price referencing studies to its annual report for the first time. One concerns the prices of major generic groups and the other the prices of high-turnover (blockbuster) on-patent medicines. Moreover, as it has done every year since 2012, this annual report presents a summary of the results of a few benchmark studies in this field.

I/ Methodological questions

1/ Which prices are compared?

Medicine retail prices are not very comparable between countries: the differences in applicable tax systems, particularly VAT rates, as well as the distribution remuneration arrangements (in France, wholesaler-distributors' and community pharmacists' profit margins) introduce too much of a reference bias.

Preference is therefore usually given to ex-manufacturer price (PFHT) referencing. That said, as far as generics are concerned it can also be noted that a significant proportion of French ex-manufacturer prices is currently given over to remuneration of community pharmacists in the form of commercial rebates granted by generic-producing laboratories, and this seems to apply less for the manufacturer prices before tax in the UK and Germany.

The prices compared in the studies are ex-manufacturer prices at face value. But the authorities often set up clawback systems (linked to product sales volumes for example), and this has an impact on referencing of real prices paid by health insurance coverage schemes.

Lastly, depending on national system, a medicine may have one price or, on the other hand, several different prices: regional prices, prices negotiated by health insurance funds and so on.

[44] Pharmaceutical Pricing Policies in a Global Market OECD 2008, particularly Chapter 2, Appendix 2

2/ What are the referencing procedures?

Direct referencing of the national prices of one or more products between themselves are but of limited interest. It will always be possible to find medicines that cost more or less in one country than in another. A selection of products available in France and Italy has therefore been presented, with lower Italian prices, without it being possible to draw any general conclusions[45]. Likewise, it would be unwise to make a generalisation concerning the results of a study comparing the prices of 150 product formats, of which 95 are reimbursable in France, with higher German prices[46].

Using an index of the prices of a basket of representative medicines, weighted by their sales volumes, is the only way we can compare prices over time or between countries. This weighting factors in the importance of different medicines in terms of sales volumes. If weighting by volumes is not carried out, the price of a product with little or no volume would influence the average price in the same way as the price of a product with a high volume.

The type of weighting used is likely to affect the referencing results quite markedly. Accordingly, weighting by sales volumes achieved in one country will help to offset the influence of the different market compositions between the countries and to answer the question: what would spending amount to if the medicines sold were paid at the price of another?[47] This is an important question for the public authorities in the country considered.

3/ Which medicines are compared?

For "pack-based" referencing, the medicines must obviously be selected to ensure strict comparability between one State and another: same format, same dosage, same number of units. Referencing by defined daily dose[48], more complex in theory, is nonetheless likely to get round the differences in packaging and dosage. These units of measurement do not seek to be exhaustive as the international price referencing studies also use milligrams or average daily posologies as units of measurement.

Estimated price differences vary depending on which unit of measurement is used. As a result, the sensitivity of the results to the chosen unit of measurement must be analysed in the studies.

Lastly, the chosen referencing guidelines can be noted via several questions: products used in the community/hospital sector or composite basket of products, old, recent or innovative products, on-patent or genericised products, etc.

4/ Other methodological questions

The referencing period must be noted. For a one-off analysis, the most recent data must be used to make sure it is still applicable as prices are often changed. It may be worthwhile rounding off an analysis of a given year with repeated referencing over time, so that changes in pricing policy can be detected.

Bilateral referencing between two States should be distinguished from multilateral referencing which compares one State to a group of other States. In principle, the latter type restricts the number of products concerned as long as the constraint of exact pack similarity is complied with.

Different marketing dates between countries influence the estimated price differences since the price of a medicine varies throughout its life cycle. This effect must be ironed out.

[45] http://fr.scribd.com/doc/149864370/Cout-des-medicaments-en-France-la-gabegie-se-poursuit-Dossier-de-presse

[46] http://www.europe-consommateurs.eu/fileadmin/user_upload/eu-consommateurs/PDFs/publications/etudes_et_rapports/medicaments-etude_complete-FR-FINAL.pdf

[47] Ex-manufacturer prices can be weighted by the volumes consumed in each country considered; the differences observed may then stem from the differences in consumption between countries. Alternatively, they may be weighted by the sales volumes of just the reference country, in which case the volumes are identical and the price differences, for this country, could be pinpointed.

[48] Or DDD: The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (WHO)

Lastly, exchange rates can influence the results of price referencing outside the eurozone, for example with the UK: variations in the EUR/GBP exchange rate must be ironed out.

II/ Main results listed

II 1/ Studies on original (branded) medicines

II 1 1/ Studies presented by national authorities

- **The NHS report to the British Parliament[49]:**

Bilateral comparisons of ex-manufacturer prices

Country	2004	2005	2006	2007	2008	2009	2010	2010 indices using five-year* average exchange rate
Australia	–	–	–	94	94	126	139	106
Austria	94	96	94	96	111	125	117	107
Belgium	90	95	97	101	122	132	122	112
Finland	96	101	96	99	119	113	105	96
France	84	96	89	92	108	115	104	95
Germany	106	108	105	113	142	169	155	142
Ireland	99	103	105	112	134	144	133	122
Italy	78	84	78	83	101	120	113	103
Netherlands	92	95	94	99	115	–	–	–
Spain	80	84	85	88	109	118	106	97
Sweden	–	–	103	105	116	126	130	114
UK	100	100	100	100	100	100	100	100
USA	176	198	188	183	252	249	281	254

This study compares the ex-manufacturer prices of the 250 top-selling community products in the UK and weights prices by sales volumes in this country. It concerns bilateral referencing, which means that the basket of product formats varies from one country to another.

The changes observed from one year to the next may stem from the changing basket of products selected, from price changes, from movements in exchange rate or from prescription rules that might affect sales volumes. The prices compared do not factor in any rebates negotiated by insurers. Moreover, because the product basket includes formats for which there is a reference reimbursement price in some countries, the price does not reflect real insurer spending.

- **Patented Medicine Prices Review Board-Canada report[50]**

Average Foreign-to-Canadian Price Ratios, Bilateral Comparisons, 2013

At Market Exchange Rates								
	Canada	**France**	**Italy**	**Germany**	**Sweden**	**Switzerland**	**United Kingdom**	**United States**
Average price ratio 2013	1	0.72	0.79	1.04	0.9	0.95	0.77	2.07
Average price ratio 2012	1	0.76	0.80	1.11	0.90	1.01	0.80	2.02
Average price ratio 2011	1	0.84	0.84	1.2	0.95	1.03	0.82	1.98
Average price ratio 2010	1	0.9	0.87	1.2	0.98	1.03	0.86	1.91
Number of patented drug products	1,306	760	772	919	903	847	913	1,088
Sales ($ millions)	13,676.49	11,062.06	10,704.40	11,832.60	11,575.50	11,446.00	11,596.30	12,811.50

[49] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215156/dh_132793.pdf
[50] http://www.pmprb-cepmb.gc.ca/francais/view.asp?x=1779&mid=1712

- **Santé suisse report (2010 and 2012)[51]**

Swiss health insurers compare the ex-manufacturer prices of 155 on-patent community products with the biggest turnovers in Switzerland.

Country, Switzerland index base 100	Switzerland	Germany	Denmark	Austria	Netherlands	France	United Kingdom
2010	100	117	113	88	86	79	72
2012	100	108	96	89	86	74	70

This study weighted prices by sales volumes in Switzerland. Swiss prices are 26% higher than in France due to the Swiss market composition, and do not factor in any rebates negotiated by the insurers.

II 1 2/ Academic studies

PRICE COMPARISON OF PHARMACEUTICAL PRODUCTS on the market since 2008 (same molecule, format and dosage): France, Germany, Italy, Spain and United Kingdom[52]

This study compares the ex-manufacturer prices of a basket of community products marketed since 2008 and 2012 in France and at least one other comparator country, and grouped according to the degree of improvement in medical benefit attributed by the Transparency Commission in France. 51 molecules have been marketed in five countries in the same format and dosage and can therefore be analysed on all of the markets in question. The table below presents the results with prices weighted by sales volumes for France, in standard intake units.

	Germany 2012	Italy 2012	Spain 2012	UK 2012
ASMR 1-2-3	1.21	1.37	1.14	0.77
n	4	4	4	4
ASMR 4	1.02	0.95	1.01	0.96
n	9	9	9	9
ASMR 5	1.41	1.05	1.13	1.07
n	38	38	38	38
All ASMR	1.32	1.07	1.11	1.02
n	51	51	51	51

NB: weighting with sales volumes in France; index>1: foreign price> French price; n: number of molecules considered
French prices appear low overall. The prices of "innovative" molecules appear lowest in the UK. German prices are the highest. Compared to 2007[53], the situation is exactly the same overall, except for an increase in differential with Germany (+22% in 2007, +32% in June 2012) and a reduction/disappearance in the differential with the UK (+29% in 2007 versus just +2% in June 2012).

[51] http://www.santesuisse.ch/datasheets/files/201302151800370.pdf
[52] Pharmaceuticals Direct and Indirect Price Regulation: A price comparison of recent pharmaceutical products in Europe, 2008-2012, Claude Le Pen, Nathalie Grandfils, Dana Vigier, currently being published
[53] International Comparison of Prices for New Drugs PY Geoffard, Lluis Sauri, 2008

II 2/ Studies on generic prices

II 2 1/ Studies presented by national authorities

- **Point de repère CNAMTs, 2011**[54]

Average cost of generics per standard unit for eight countries (in €), 2011

Country	France	Italy	Germany	Norway	Finland	Spain	United Kingdom	Netherlands
Cost by SU	0.15	0.14	0.12	0.12	0.12	0.11	0.07	0.07

The study weighted prices by quantities sold in each country. The cost differences can be explained by the different prices and market compositions between countries. The relative weight of these two determining factors in the cost differences has not been estimated.

II 2 2/ Academic studies

- **Study P. Février for GEMME, 2010**

Average cost of generics per standard unit for ten countries (in €), 2010

Country	Port.	Belg.	Austria	Ger.	Italy	RU	Fin.	Spain	France	Pol.
Cost by SU	0.27	0.27	0.26	0.24	0.20	0.20	0.18	0.18	0.18	0.11

The table shows the average price of a basket of generic medicines accounting for 50% of the top-selling molecules in France, with no weighting by volumes. Because no weighting has been carried out, each product is considered in exactly the same way, irrespective of its sales volumes. A low-selling product in France will count for just as much in the average as a high-selling product. This approach looking at the average of non-weighted prices thus only brings to light the level of prices.

Weighting mechanisms can be used to analyse the costs of products for health insurance schemes, by taking on board their actual weight in reimbursable spending.

Irrespective of the difference in scope between the two CNAMTS and GEMME studies, the first therefore probably reveals more economical consumption structures (higher consumption of cheaper generics) in the UK and Germany, compared with France.

[54] http://www.ameli.fr/fileadmin/user_upload/documents/Points_de_reperes_n_39_-_Cout_des_generiques_en_Europe.pdf

III/ CEPS studies

III 1/ Studies on generic medicines (statins, PPI, ACE inhibitors, sartans)

The study compares French prices of generic medicines in France compared to four other reference European country prices (Germany, Spain, Italy and UK). Three groups are studied: statins, PPI, ACE inhibitors and sartans. These account for EUR 735 million in turnover before tax (i.e. 22% of the generic market). The aim is to answer the following question: are the prices of these generic medicines in France higher or lower than the prices in the four reference European countries?

The study uses the following method:

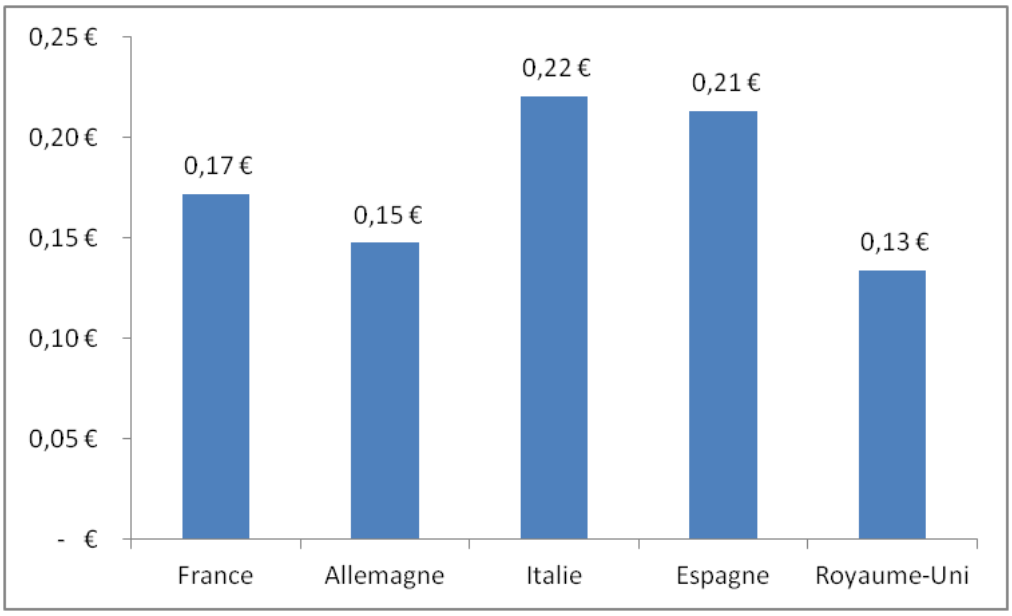
- The sample of generic medicines concerns generic medicines[55] marketed in the community sector.
- For the four reference countries, the 2014 data comes from the IMS MIDAS base (price data). For France, the data comes from the GERS 2014 base and CEPS price base (which factors in the reductions introduced in 2015).
- The prices are ex-manufacturer and the quantities are expressed in standard units[56][57].
- The price unit of measurement is the average ex-manufacturer price (in standard unit) in force in a country weighted by the French units so as to offset the market composition effects (French composition with foreign prices).

[55] Reference proprietary (original) products are not taken into account.
[56] One standard unit corresponds to the smallest possible unit (one tablet, one capsule, etc.).
[57] Exchange rate EUR 1.241 = GBP 1

The study results are as follows:

- **French prices are within the European average. By adding together all of the prices studied for the three product groups (statins, PPI, AEC inhibitors and sartans), an average price per standard unit of EUR 0.17 emerges for France.**

Figure 24: Average price per standard unit of the main generic groups (statins, PPI, ACE inhibitors and sartans)



- **French prices are within the European average for ACE inhibitors/Sartans, are low for PPI and are high for statins.**

- **Previous studies have estimated higher French prices of generics than average European prices. In 2014, French prices fall markedly within the European average. The 2011 CNAMTS study, which had used almost exactly the same method to this study, had found an average price per standard unit, for statins, of EUR 0.27 for France; in 2014 this price is EUR 0.18 (down by more than 30%). For PPI, the price per standard unit has dropped from EUR 0.27 to 0.19 (down by 30%).**

- The results were compared to the average prices weighted by volumes of each country, and the resulting figures are almost identical. The main source of difference is explained by the high consumption of low-cost molecules in the UK.

III 1/1 Result: Statins[58]

Figure 25: Average price per standard unit of the genericised statin group

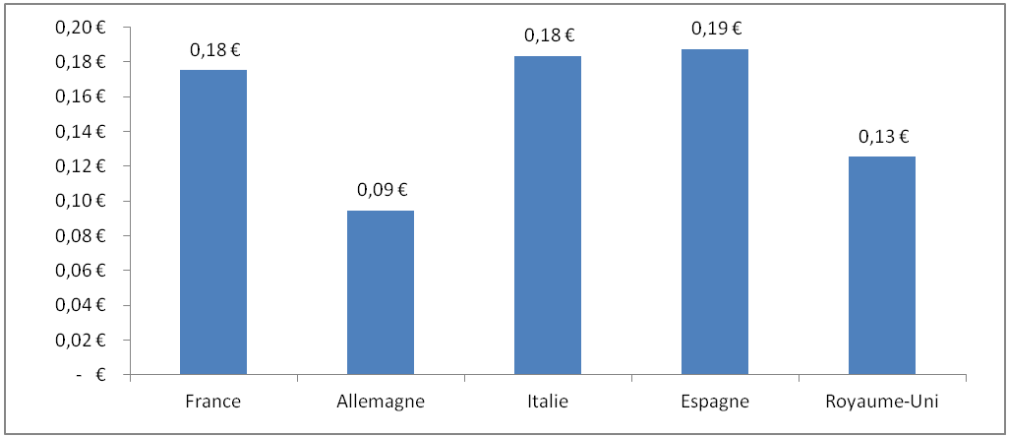
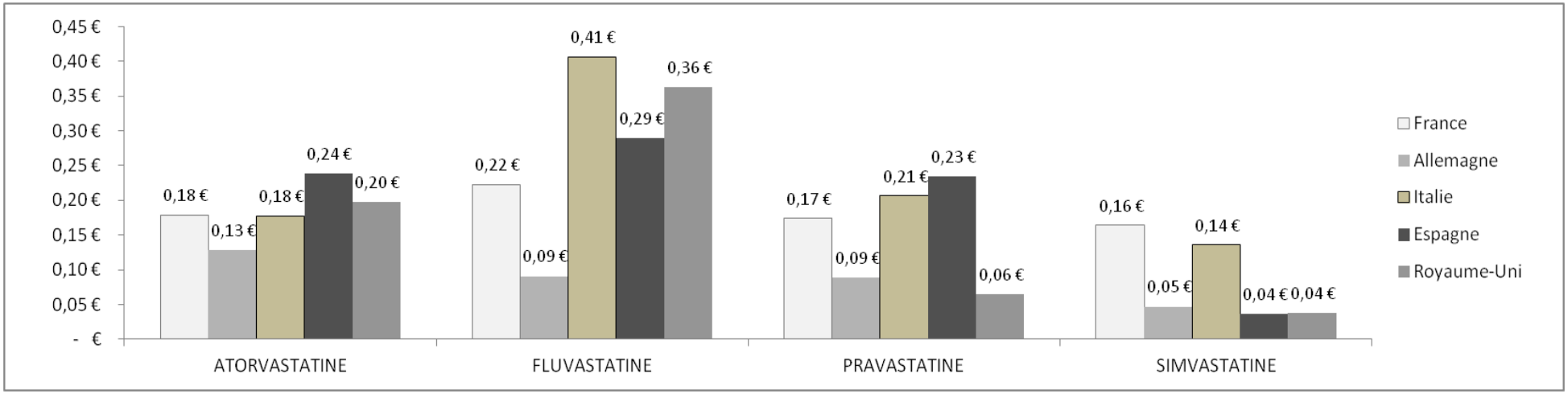


Figure 26: Average price per standard unit by genericised statin molecule



[58] Crestor® Rosuvastatin non-genericised (see study on on-patent high-turnover medicines)

III 1/2 Proton pump inhibitors (PPI)

Figure 27: Average price per standard unit of the genericised PPI group

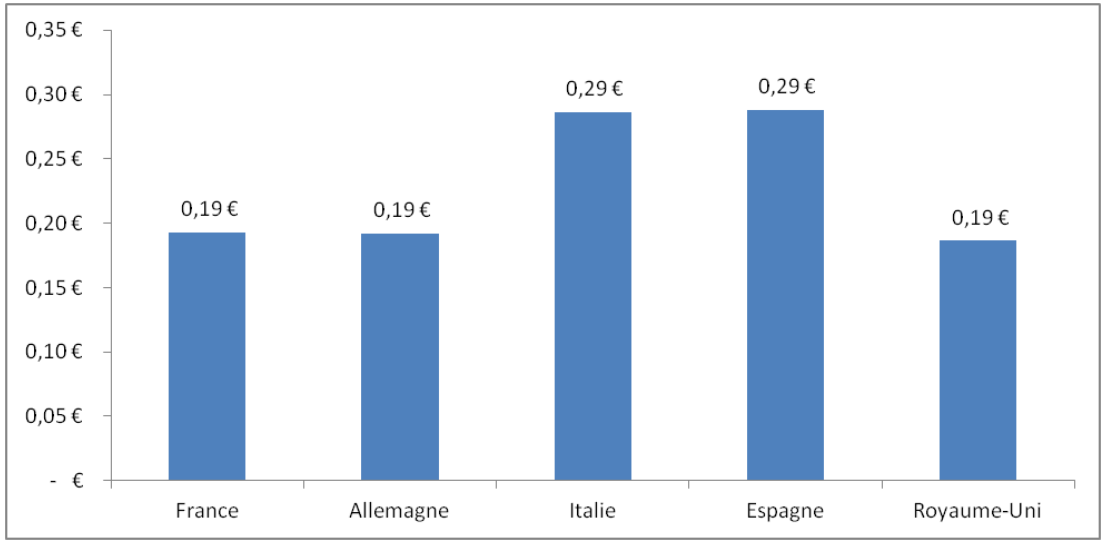
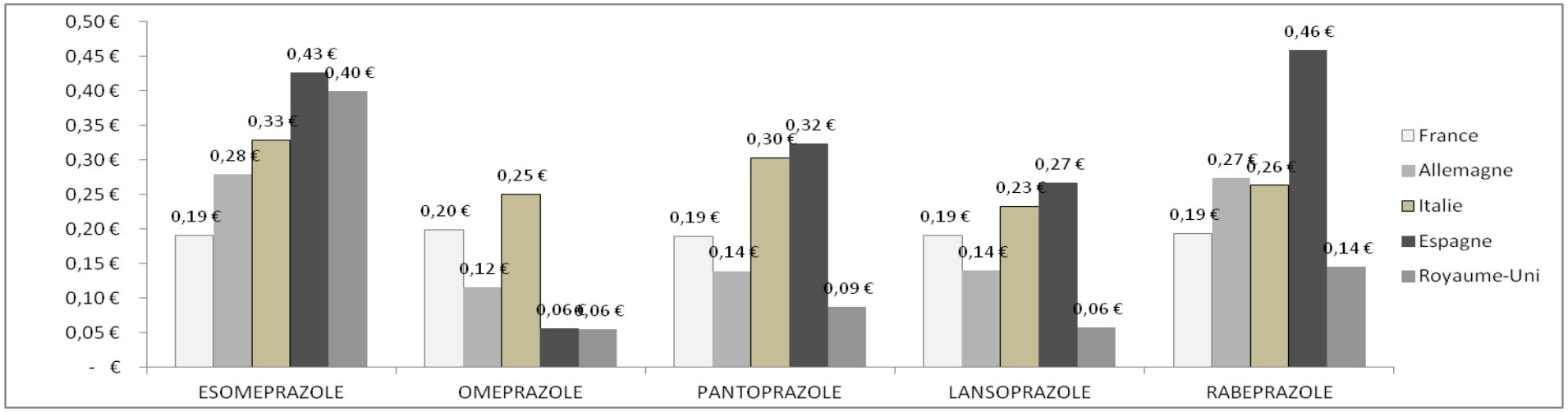


Figure 28: Average price per standard unit by genericised PPI molecule



III 1/2 Angiotensin-converting-enzyme (ACE) inhibitors and SARTAN

Figure 29: Average price per standard unit of the genericised ACE inhibitor/Sartans group

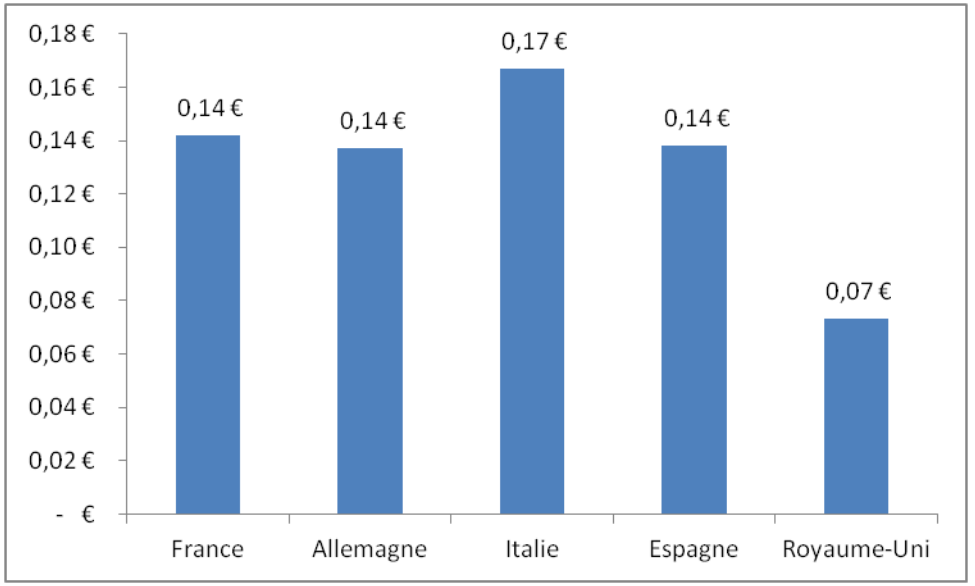
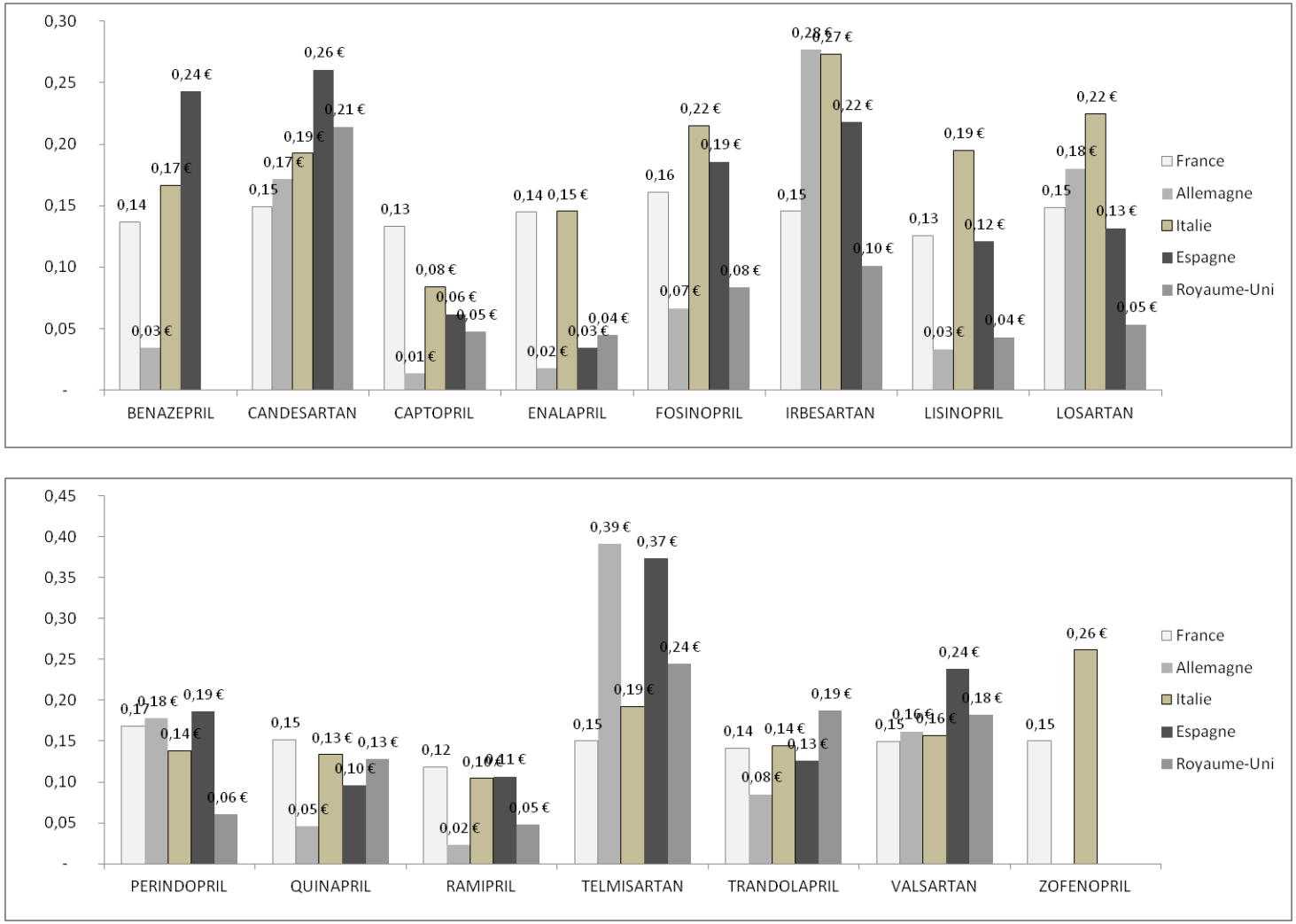


Figure 30: Average price per standard unit per genericised ACE inhibitor/Sartans molecule



III 2/1 Studies on on-patent high-turnover medicines in France

In order to compare the prices of reimbursed on-patent medicines[59] that achieve high turnovers in France in both the community and hospital sectors, with those in four comparator countries (Germany, UK, Spain and Italy), CEPS analysed the prices of molecule units with a turnover in France of over EUR 100 million in the community sector, or of over EUR 50 million in the hospital sector. Added together, these products represent EUR 6.4 billion worth of sales before tax, which is the equivalent of 25% of the whole reimbursable market. The community products studied account for 20% of this market. The hospital products studied account for 37% of all hospital purchases (on-top of GHS (DRG-based funding) list and outpatients list, including medicines with temporary authorisations/ATU) and represent 86% of the "on-top list" market.

The study used the following method:

IMS MIDAS data regarding volumes and IHS database (ex-manufacturer prices, July 2015) for the prices of the four comparator countries were used. Unlike the study on generics, the international prices obtained from the IHS database, which are more reliable than prices estimated from the IMS MIDAS base, were used. This was possible due to the low number of product formats per molecule and the fact that there was only one manufacturer on the market.

The volume data for France comes from the GERS community pharmacy sales data 2014 and hospital quarterly sales declarations and the prices come from the CEPS bases (July 2015).

The weighted average prices of the comparator countries have been calculated on the basis of volumes for France (France composition with the foreign price[6061]), thus providing an answer to the question: **are the prices of these products higher or lower than the prices observed in the comparator European countries?**

The study results are as follows:

In **20 out of 40 cases** (so for 50% of products) French prices are **lower than the lowest European price** and in **37 out of 40 cases** (so for 93% of products) they are **lower than the average** of the five countries.

These results are in line with the results of the international studies cited above.

This study has not taken into account the taxes on the turnover present in some countries, which might be compared to compulsory clawback payments (7% in Germany). That said, even if they were taken into account, the results would not change significantly.

The study does not factor in the specific product clawback payments that exist in each of these countries (since such data is confidential). France does, however, also collect sometimes considerable clawback amounts on a good number of these products.

[59] Sovaldi was registered for reimbursement at the end of the year and has not been included, see text box 1 for international price referencing.

[60] EUR 1.327 = GBP 1

[61]The results obtained by applying the volumes of each country to its own prices are almost the same. Variations are mainly observed as regards the formats with multiple dosages (e.g. Seretide and Kogenate) because of the consumption structure.

Table 35: Ratio of European prices of on-patent proprietary products registered for community reimbursement with over EUR 100 million in turnover in France (France index =1)

	France	Germany	Italy	Spain	United Kingdom	Comments
ABILIFY	1.00	2.36	1.07	0.68	1.42	French price cut by 20% as of 1 September 2015 (not taken into account)
ARANESP	1.00	1.53		1.38	1.57	No price in the IHS base for Italy
CRESTOR	1.00	2.08	1.08	1.02	1.49	
ENBREL	1.00	1.66	1.15	1.12	1.12	
EYLEA	1.00	1.21	0.94	1.04	1.33	French price cut by 16% as of 1 September 2015 (not taken into account)
EZETROL	1.00	1.35	0.97	1.08	1.00	
GILENYA	1.00	0.79	0.93	0.92	1.12	The 400mg is not marketed in Italy
GLIVEC	1.00	1.32		1.13	1.16	Comparison is not possible with Italy as a dosage marketed in France is not available there
HUMIRA	1.00	1.69	1.22	1.23	1.12	
INEGY	1.00	1.31	0.98	0.98	1.20	
INNOHEP	1.00	1.02				Different dosages in Italy, Spain and UK, which limits the comparison
LANTUS	1.00	1.08	0.97	0.99	1.10	
LOVENOX	1.00	0.93	1.11	1.71	0.77	Some German dosages which are not marketed in France have not been taken into account
LUCENTIS	1.00	1.53	1.26	1.15	1.52	
LYRICA	1.00	2.94	1.59	0.87	3.09	
NEULASTA	1.00		1.04	1.11	1.05	No IHS price for Germany
PREVNAR	1.00	1.24	1.45	1.13	1.48	
TRUVADA	1.00	1.49	1.01	1.01	1.10	Dual channel (community-hospital) in France
SERETIDE/SERETIDEDISKUS	1.00		1.19	1.37	1.26	Some product formats are not marketed in Germany, which limits the comparison
SYMBICORT	1.00	1.25	1.24		1.32	Different dosages in Italy, which limits the comparison
VICTOZA	1.00	1.00	0.95	1.00	1.18	
XARELTO	1.00	1.25	1.10	0.95	1.22	Recent reduction in the Spanish price (taken into account)
ZYTIGA	1.00	1.11	1.17	1.14	1.31	

Table 36: Ratio of European prices of on-patent proprietary products registered for hospital reimbursement ("on top" list) with over EUR 50 million in turnover in France (France index =1)

	France	Germany	Italy	Spain	UK	Comments
ADVATE	1.00		0.90	0.86		No price in the IHS base for Germany and the UK
ALIMTA	1.00	1.96	1.33	1.17	1.03	
AVASTIN	1.00	1.35	1.24	1.29	1.25	
CANCIDAS	1.00	1.09	0.91	1.02	0.99	
ERBITUX	1.00	1.40	1.09	1.17	1.43	
HERCEPTIN	1.00	1.27	1.14	1.11	1.01	
KOGENATE	1.00		1.02	0.86	1.16	
MABTHERA	1.00	1.23	1.00	0.95	0.88	
PRIVIGEN	1.00	2.17	1.21	1.09	1.54	
REMICADE	1.00	1.73	1.19	1.23	1.28	
REVLIMID	1.00	1.53	1.39	1.45	1.38	
SOLIRIS	1.00	1.09	0.95	1.02	0.96	
TRACLEER	1.00	1.34	1.15	1.13	1.01	
TYSABRI	1.00	0.99	0.94	0.95		No price in the IHS base for the UK
VELCADE	1.00	1.24	1.12	1.07	0.97	
VIDAZA	1.00	1.13	1.00	1.11	1.34	
YERVOY	1.00	0.91	1.10	1.21	1.42	Recent reduction in the German price (taken into account)

APPENDIX 9: PRICING OF NEW MEDICINES WITH AN ASMR V RATING ON THE COMMUNITY MARKET IN 2014

NOMCOURT	Date marketed	CIP code	CIP description	TC opinion date	Ex-manufacturer price	Pricing argument
FYCOMPA	May 2014	2677698	FYCOMPA 10MG CPR BT28	24 July 2013	98.00	The DTC varies from EUR 1.20 for the 2 mg dosage to EUR 3.50 for the 10 and 12 mg dosages The weighted average DTC is equal to EUR 2.395, which is 4.2% less than the reference product Zebinix (DTC = EUR 2.50)
		2677712	FYCOMPA 12MG CPR BT28		98.00	
		2684474	FYCOMPA 2MG CPR BT28		33.60	
		2677600	FYCOMPA 2MG CPR BT7		8.40	
		2677623	FYCOMPA 4MG CPR BT28		68.60	
		2677652	FYCOMPA 6MG CPR BT28		68.60	
		2677675	FYCOMPA 8MG CPR BT28		79.80	
TAFINLAR	July 2014	2754967	TAFINLAR 50MG GELU FL120	7 May 2014	4572.43	Price based on a DTC of EUR 222.53 (according to the weighting between the DTC for the 75 mg dosage = EUR 228.62 and the DTC for the 50 mg dosage = EUR 152.41), a 25% markdown compared to Zelboraf
		2754973	TAFINLAR 75MG GELU FL120		6858.65	
GIOTRIF	August 2014	2756564	GIOTRIF 20MGC PRBT 28D.U	19 February 2014	1794.52	DTC of EUR 64.09 corresponding to the price of the reference product Tarceva, 5% markdown
		2756570	GIOTRIF 30 MGC PRBT 28D.U		1794.52	
		2756587	GIOTRIF 40 MGC PRBT 28D.U		1794.52	
		2756593	GIOTRIF 50 MGC PRBT 28D.U		1794.52	
AUBAGIO	October 2014	2749989	AUBAGIO 14MGC PRPELLIC BT28	5 March 2014	€728.77	Price based on a DTC of EUR 26.03, a 3% markdown compared with the weighted DTCs (EUR 26.90) of the reference products (Rebif, Avonex, Copaxone, Extavia, Betaferon)

Comments: the price of Giotrif was reduced on 1 August 2015, making the DTC 10% lower than that of Tarceva

APPENDIX 10: DOOR-TO-DOOR OR CANVASSING INFORMATION CHARTER AIMED AT PROMOTING MEDICINES

The aim of this charter is determine the conditions for providing information, in any place, about proprietary pharmaceuticals via door-to-door or canvassing methods aimed at promotion.

The charter scope includes all forms of information, irrespective of the format, by door-to-door, canvassing or incentive-raising methods aimed at promoting the prescription, dispensing or use of proprietary pharmaceuticals by any professional authorised to prescribe, dispense and use such medicines.

Under the law, this charter sets out to improve the quality of information aimed at promoting medicines to ensure their responsible use by healthcare stakeholders.

The purpose of the information provided, based on regulated, validated scientific information, is to promote medicines among healthcare professionals. To that end it must encourage medical treatment of a high standard so as to avoid medicine misuse and unnecessary spending and to help to inform healthcare professionals.

I RESPONSIBILITIES OF PEOPLE PROVIDING INFORMATION VIA DOOR-TO-DOOR OR CANVASSING METHODS AIMED AT PROMOTION

1- A person who is providing information via door-to-door or canvassing methods shall present the proprietary pharmaceuticals to healthcare professionals in keeping with legislation, this charter and the policy of the company s/he is representing. This promotional work involves providing high-quality medical information on the medicine, presented in strict compliance with the MA, and ensuring its responsible use among healthcare professionals.

This information shall explain the role that the medicine plays in the recommended therapeutic strategy, for treating the illness in question, as validated by the Transparency Commission and in line with the recommendations of the French National Authority for Health (HAS), French National Healthcare and Medicines Safety Agency (ANSM) and French National Institute for Cancer as well as with the consensus conferences validated by HAS. This role must take responsible use campaigns and public health programmes into account. The information provided also includes facts relating to safety and monitoring of the medicine. A person who is providing information via door-to-door or canvassing methods presents and offers to hand out all of the documents on minimising the risks stipulated in the risk management plans or risk minimisation plans.

No information may be provided via door-to-door or canvassing methods aimed at promoting a medicine whose risk/benefit report is undergoing reassessment following an adverse event report, until this procedure has been concluded.

2- Providing information via door-to-door or canvassing methods involves informing healthcare professionals about all the regulatory, pharmacotherapeutic and medico-economic aspects of the medicine in question:

- therapeutic indications of the marketing authorisation,

- posologies (particularly paediatric posologies if these exist),

- treatment durations,

- undesirable effects,

- contraindications,

- interaction with other medicines and monitoring information,
- prescribing conditions,

- price and reimbursement (indications reimbursed to social insurers and reimbursement rates),

- registration on the lists of expensive medicines excluding ‘standard hospital stay groups’ (similar to diagnosis-related groups) (GHS) for medicines for internal use and medicines that are dispensed by hospital pharmacies to outpatients.

Pursuant to the regulations, information should not be provided via door-to-door or canvassing methods aimed at promoting medicines with a temporary authorisation for use (ATU).

Furthermore, information on whether or not a medicine is covered by a temporary recommendation for off-label use (RTU) and any associated updates can be presented provided that it is not part of any promotional communication, that it is validated by the ANSM and that documents are handed out at the same time for the systematic collection of data on this RTU.

3- Pursuant to current legislation (particularly Art. L162-17-4-1 of the Social Security Code), if prescriptions at odds with the MA are observed, the administrative authority may ask the company concerned to communicate to healthcare professionals, for the purposes of reminding them of the prescription framework defined by the MA and, where applicable, of recommending any worthwhile corrective action. Such specific information measures by the company or group of companies for the attention of prescribers may be carried out by people whose job it is to provide information by door-to-door or canvassing methods. CEPS may request communication thereof.

These people thus help to limit any off-label use made of medicines that is not in line with the recommendations of the competent health authorities.

If a company does find that prescriptions at odds with a medicine's responsible use have been made, it can ask people whose job it is to provide information by door-to-door or canvassing methods aimed at promotion to pass on the appropriate information measures to the healthcare professionals concerned and to notify the ANSM immediately.

These people shall report to the company all information concerning the use of the medicines that they advertise, particularly as regards any undesirable effects and off-label uses that are brought to their attention.

4- The organisation (recruitment and financial relations with professionals authorised to prescribe, dispense and use medicines) of pharmacoeconomic analyses, clinical trials – including phase IV trials – and observational studies is not one of the responsibilities of people who provide promotional information by door-to-door or canvassing methods. They may provide monitoring in these instances, however.

5- Information on apprenticeship programmes presented by people providing information via door-to-door or canvassing methods must be kept separate from any promotional communication concerning the programme's medicine.

II QUALITY OF THE INFORMATION PROVIDED

1- Preparation of the material by the company

a) Preparation of documentation and training material

Promotional documents made available to people whose job it is to provide information via door-to-door or canvassing methods must be prepared in accordance with the Public Health Code and recommendations of the ANSM. These documents shall bear the date on which the information was produced or updated, as well as a valid, official ANSM stamp or signature.
Information about a medicine's use, and particularly undesirable effects, precautions for use and contraindications, shall be clearly mentioned so that their connection with the indication and the benefit claimed is clear.

b) *Updating of promotional material*

The company shall see to the scientific, medical and regulatory updating of promotional information documents.

c) *Post-marketing studies*

The kind of studies that can be used are those that are published in a peer-reviewed journal and have been conducted under the medicine's conditions for use as defined by the MA and other existing references (opinion from the Transparency Commission, good practice recommendations). Moreover, to ensure the recipient receives complete information in line with the ANSM's recommendations on the advertising of medicines, the advertising must specify whether the publication concerns a study adopted from the transparency application and/or MA application.

When the company makes use of such studies, it shall present them in full and impartially.

d) *Comparative advertising*

Information provided on a proprietary product and on rival products providing the same treatment and forming part of the therapeutic strategy defined by the Transparency Commission must meet the defined criteria for comparative advertising as follows:

Any advertising which compares medicines by implicitly or explicitly identifying medicines marketed by a competitor may only be carried out if:

1º It is not misleading or likely to lead to error;

2º It concerns medicines that meet the same needs or have the same therapeutic indication;

3º It objectively compares one or more essential, relevant and verifiable characteristics that are representative of these medicines, one such example being the price.

Comparative advertising may not:

1º Take undue advantage of the reputation attached to a brand, commercial name or other distinctive signs of a competitor;
2º Discredit or undermine the brands, commercial names, other distinctive signs or situation of a competitor;

3º Sow confusion between the advertiser and a competitor, or between the brands, commercial names or other distinctive signs of the advertiser and those of a competitor;
4º Subject to the provisions on generic products, present medicines as an imitation or reproduction of another medicine that is protected by a brand or commercial name.

2- **Training of a person who provides information via door-to-door or canvassing methods aimed at promotion**

a) *Initial training*

Pursuant to the legal, regulatory and contractual provisions, people who provide information via door-to-door or canvassing methods aimed at promotion must have sufficient initial training, certified by a degree, qualification or certificate, particularly as regards validation of learning through experience or the equivalent acquired in terms of validation of learning through experience as provided for by Article L.335-5 of the Education Code.

b) *Continuing professional development*

Beyond the new-to-the-job training administered to each new recruit, the company shall systematically administer the necessary training for updating regulatory and scientific knowledge and for maintaining and developing professional skills, including preparation for oral presentations.
Training on regulatory knowledge addresses the following themes:

a. The medicine: medicine groups, prescribing and dispensing rules, responsible medicine use;
b. Reimbursement of the medicine;
c. Pharmacovigilance and "product" complaints;
d. Code of conduct: DMOS (anti-benefits) law and disclosure of links;
e. Advertising;
f. The Charter and certification;
g. Organisation of the healthcare system.

The training administered must enable a person who provides information via door-to-door or canvassing methods to become familiar with and follow the regulations on medicines so as to inform and answer the questions of healthcare professionals. There are training objectives attached to each training theme which determine the training contents.

Training on scientific knowledge addresses:

a. The specialisation and/or one of the illnesses concerned by the medicine being presented
b. The therapeutic strategy regarding the specialisation and/or illness concerned, or current best practice

For each training scheme taken by a person who provides information via door-to-door or canvassing methods, the company shall conduct an annual assessment to attest that the employee possesses the knowledge corresponding to the quality of information s/he provides. The company shall define the assessment period and procedure. This assessment is performed systematically before any meetings with professionals for any new indication or product. It also provides for the thresholds for validating the training so that the required standard and corrective actions in the event of non-validation are defined. The assessment procedure must abide by the following principles:

- The knowledge tested corresponds to the contents of the training administered;
- The company shall demonstrate the random nature of the assessment carried out and its traceability;
- The company shall ensure that it keeps a sufficient database of assessment items to comply with the random principle of the assessment.

c) *Certification of initial training and continuing professional development by business card*

People who provide information via door-to-door or canvassing methods aimed at promoting are given a business card by LEEM, through the *Association de Gestion de la Visite Médicale* (Medical Visit Management Association/AGVM). This card guarantees that the employee's level of regulatory and scientific knowledge meets the requirements of Article L.5122-11 of the Public Health Code and the above-mentioned continuing professional development obligation.

In this context, every year the company shall send an individual statement of training schemes administered and the overall assessment results to the AGVM. The AGVM may ask the company for additional information concerning assessment.
This data shall be kept available to the certifying authorities.

See Chapter III Code of conduct

3 Documents used by the person who provides information via door-to-door or canvassing methods aimed at promotion

These documents are also subject to a priori inspection by the ANSM, and must therefore bear a valid official stamp or signature.

The person who provides information via door-to-door or canvassing methods shall carry out his/her assignment solely by means of the dated documents that the company has supplied, approved by the lead pharmacist (name and signature) and for which the ANSM has granted an advertising stamp. When the company updates a particular document, only the most recent version can be used.

The documents listed below must still be handed out in the event that audio, video or interactive material is used as well.

Pursuant to Article R.5122-11 of the Public Health Code, healthcare professionals must be supplied with:

- The Summary of Product Characteristics mentioned in Article R.5121-21 of the Public Health Code;

- The medicine's classification in terms of prescription and dispensing, mentioned in the marketing authorisation;

- The maximum purchase price public, accountability tariff or prescription fee when such a price or tariff is set pursuant to the current laws and regulations, together, in this case, with the daily treatment cost;

- The medicine's situation in terms of reimbursement by the health insurance bodies or the approval for public authorities as stipulated in Article L. 5123-2;

- The opinion issued pursuant to Article R. 163-4 of the Social Security Code by the Transparency Commission mentioned in Article R. 163-15 of said Code and most recently published in the conditions stipulated in the last paragraph of III of Article R. 163-16 of said Code (when several opinions have been issued on the medicine because of extended therapeutic indications, the notion of "opinion" encompasses all of the opinions assessing the medical benefit provided in each of the therapeutic indications for the medicine in question);

- the ruling(s) concerning registration on the "on top" list and/or outpatients medicines list, where applicable.

In addition, the healthcare professional must also be given any document that HAS, ANSM, National Institute for Cancer or CEPS deems necessary.

These documents must be entirely legible and bear the date on which they were written or last revised.

The documents below must be presented and may be handed out by the person providing information via door-to-door or canvassing methods:
- responsible use factsheets,
- therapeutic factsheets,
- good practice recommendations,
- consensus conferences,
- the opinions of the French High Council for Public Health (technical vaccinations committee),
- or other reference documents issued or approved by HAS, ANSM or the National Institute for Cancer.
- as well as risk minimisation documents stipulated by risk management plans or risk minimisation plans.

III CODE OF CONDUCT

1- As regards patients

The person who provides information via door-to-door or canvassing methods aimed at promotion is bound by professional secrecy and must not reveal anything of what s/he might have seen or heard in the places s/he conducts the assignment.

S/he must behave discreetly in waiting areas and not hamper the delivery of care (limit conversations between professionals, using a mobile phone, dressing appropriately).

2- As regards the healthcare professionals met with

The supervisors of people who provide information via door-to-door or canvassing methods ensure that the visits are organised as effectively as possible and oversee their planning and frequency.

In terms of conduct, the person who provides information via door-to-door or canvassing methods must not use incentives to obtain appointments, nor offer any compensation or remuneration to this end.

a) *Organising the visits*

α- In any healthcare professionals' workplaces

The person who provides information via door-to-door or canvassing methods aimed at promotion shall do his/her utmost not to disrupt the smooth running of the surgery or healthcare establishment s/he is visiting. To this end s/he must abide by the following organisational principles:

- S/he must ensure that the person s/he is meeting with knows exactly who s/he is, what his/her role is, the name of the company and/or network represented and, where applicable the holder's name of the MA for the medicine being presented.

- S/he must stick to the times, conditions regarding access and movement around the various premises where the meeting is being held and the place and duration specified by the healthcare professional or healthcare establishment.

The healthcare professionals being visited must agree to any accompanied visits (for example with the company or network regional director). The accompanying professional must state who they are and what their role is.

β- In healthcare establishments

In healthcare establishments, in addition to the general rules stipulated in this Charter, the person who provides information via door-to-door or canvassing methods aimed at promotion shall follow the practical organisation rules specific to the establishment, particularly:

- by wearing a professional badge (e.g.: visitor's pass worn as a badge);

- the conditions for accessing the establishment, internal areas and healthcare professionals, whatever their role within the establishment;

- the identification and movement rules within the establishment as defined in its Rules for Procedure;

- the group or one-on-one nature of the visit.

In all cases, when in healthcare establishments,

- Access to restricted areas (operating theatres, sterile areas, intensive care, etc.) is prohibited without prior agreement, for each visit, from the heads of the structures in question.

- The appointment must have been organised beforehand.

- The person who provides information via door-to-door or canvassing methods shall only meet with trainee staff if the lead supervisor or head of the structure has given his/her prior agreement.

- The person who provides information via door-to-door or canvassing methods shall only meet with interns in the presence of or with prior agreement from their supervising practitioner.

- The person who provides information via door-to-door or canvassing methods shall not seek specific information (consumption, cost, etc.) specific to the internal structures or prescribers.

b) *Collecting information and complying with the French Data Protection Act*

Information concerning professionals authorised to prescribe, dispense and use medicines collected by the person whose job it is to provide information via door-to-door or canvassing methods is done so pursuant to the French Data Protection Act (no. 78-17 of 6 January 1978).

This information is collected for the purposes of understanding these professionals' expectations more clearly as regards the medicine and its use or as regards the therapeutic group concerned, of providing them with customised information and of enabling the person who provides promotional information via door-to-door or canvassing methods to carry out his/her job more effectively.

The information listed in compiled databases must therefore only bear upon professional and factual data, rather than judgements of value or data of a subjective nature.

The database in which such information is compiled shall be declared to the French Data Protection Authority (CNIL). Pursuant to the law, professionals authorised to prescribe, dispense and use medicines are informed that digital data concerning them is being collected. The person who provides promotional information via door-to-door or canvassing methods must inform the professionals authorised to prescribe, dispense and use medicines about the data obtained concerning them during individual or department-based dispensing or prescribing surveys and which is available to them.

The person who provides information via door-to-door or canvassing methods can send the personal information concerning any healthcare professional who makes such a request in writing.

c) *Professional relations – congresses*

Invitations to scientific congresses and/or promotional events, as well as participation in research or scientific assessment activities must be covered by an agreement that has been forwarded to the professional association concerned beforehand. These agreements may contain provisions concerning healthcare professionals receiving the benefits mentioned in Article L. 4113-6 of the Public Health Code. Said benefits must, moreover, be disclosed publicly by the companies granting them pursuant to Article L. 1453-1 of the Public Health Code and according to the procedure stipulated in Articles D. 1453-1 and R. 1453-2 et seq. of the Public Health Code.

d) *Samples*

People who provide information via door-to-door or canvassing methods are prohibited from handing out samples of proprietary pharmaceuticals.

They are also prohibited from handing out samples of cosmetics, food supplements or medical devices when presenting a proprietary pharmaceutical, subject to application of Paragraph 4 of Article L5122-10 of the Public Health Code.

Samples of medical devices may nevertheless be used during demonstrations, subject to the provisions of Chapter III, Code 1, Book II, Part 5 of the Public Health Code.

e) *Gifts*

The person who provides information via door-to-door or canvassing methods must not offer healthcare professionals gifts in kind or cash whether or not covered by an agreement, or respond to any such requests.

Neither may s/he offer or facilitate the granting of a benefit covered by the exemptions stipulated in Paragraph 2 of Article L. 4113-6 of the Public Health Code.

f) *Meals*

Meals offered by people who provide information via door-to-door or canvassing methods to healthcare professionals are likely to be construed as benefits in the meaning of the provisions of Article L. 4113-6 of the Public Health Code.

In all cases, so as not to give rise to an agreement, they must not have been planned and must be taken as part of the visit to the healthcare professional. Where applicable, they shall be published as stipulated in the provisions of Point II, Article L. 1453-1 and Articles D. 1453-1 and R. 1453-2 et seq. of said Code.

3- As regards rival companies

The information that the person providing such information via door-to-door or canvassing methods delivers on the medicine s/he is promoting and on the rival products that provide the same treatment and featuring in the therapeutic strategy defined by the Transparency Commission must not be undermining in any way and be based primarily on the opinions of the Transparency Commission. The ASMR level set by HAS is presented loyally.

The person who provides information via door-to-door or canvassing methods shall abstain from undermining the products of rival companies, including generics and biosimilars.

4- As regards his/her company

Pursuant to the law, the person who provides information via door-to-door or canvassing methods shall immediately bring to the attention of the lead pharmacist or his/her pharmacovigilance department any information collected from healthcare professionals concerning an adverse event and/or irresponsible use of the medicine.

5 As regards the French health insurance system

The person who provides information via door-to-door or canvassing methods shall specify which indications are reimbursable and which are not for the products s/he presents.

S/he shall present diverse pack formats in terms of their cost for l'*Assurance Maladie* (French health insurance system) and, in particular, for treatments for chronic conditions, the most suitable formats for the patient and the most economical, particularly in terms of practitioners whose prescriptions are intended to be carried out in community pharmacies.

S/he shall specify whether the product s/he is presenting is subject to a fixed accountability tariff.

IV- MONITORING THE WORK OF PEOPLE WHO PROVIDE INFORMATION VIA DOOR-TO-DOOR OR CANVASSING METHODS AIMED AT PROMOTION

1- Responsibility of the Lead Pharmacist

a) *On content*

The lead pharmacist shall set up a quality control system which ensures that the scientific and economic content of the promotional material used to provide information via door-to-door or

canvassing methods is appropriate and, in general, ensures compliance with II-1 of this charter. S/he shall approve said material.

The lead pharmacist shall keep up-to-date the lists of materials that can and must be supplied by the person who provides information via door-to-door or canvassing methods.

S/he shall be responsible for the contents of the messages delivered by the person who provides information via door-to-door or canvassing methods.

b) *On training*

The lead pharmacist ensures that the person who provides information via door-to-door or canvassing methods has the necessary knowledge for the job and that s/he embarks on continuing professional development at regular intervals to update his/her knowledge and prepare for promotional campaigns.

c) *On procedures*

The lead pharmacist ensures the development and application of information-related procedures within the company.

2- Procedures

a) *Document traceability*

The lead pharmacist ensures that the documents used for the medical visit are, at all times, those and only those whose scientific, medical and economic quality s/he has guaranteed by signing and dating them.

b) *Feedback*

The healthcare professionals visited are given regular opportunities, for no charge, to share their views with the company of the scientific quality of the information, how objective it is and its conformity to the laws and regulations and this charter.

Any views forwarded to the company by healthcare professionals are recorded and analysed by the lead pharmacist.

The company shall also ensure that it is able to assess its contribution to responsible use and to detecting prescriptions that are at odds with such use as well as measures aimed at correcting such prescriptions (L5121-14-3 Public Health Code)**.**

c) *Monitoring contacts*

The company shall ensure that it is able to assess at regular intervals its role in providing information via door-to-door or canvassing methods.

Such data shall be made available to the joint monitoring committee mentioned in V of this Charter, which may ask to see it should the quality of promotional information identified by the observer deteriorate, and/or if there is a warning from the ANSM or HAS.

3- Certification and audits

Pursuant to Article L. 162-17-4 of the Social Security Code, a certification standard guaranteeing the certified companies' compliance with the provisions of this charter shall be drawn up.

This standard also provides for the procedures according to which compliance with the charter shall be ensured by each of the company's directors, the supervisors of people who provide information via door-to-door or canvassing methods and such people themselves.

When a company calls on a service provider or another pharmaceutical company to provide information via door-to-door or canvassing methods aimed at promoting its medicines, it shall be responsible for the conformity to the charter of the practices used by said service provider or pharmaceutical company.

4- **Implementation of Articles L162-17-4 and L162-17-8 of the Social Security Code**

The company gives precedence to the contents of visits made by people who provide information via door-to-door or canvassing methods, rather than to their frequency, so that the information provided is as complete and objective as possible, and particularly to ensure that enough time is given over to informing healthcare professionals on the medicine's responsible use.

In this context, CEPS and LEEM have decided to set up a national promotional information observatory. The purpose of this observatory will be to assess the quality of promotional practices on the basis of objective, verifiable and transparent criteria.

A non-exclusive reference tool for signatories to this charter, this observatory will be useful for obtaining shared information between the parties to this charter. Once a year, the pharmaceutical companies falling within the scope of this charter shall send a survey to healthcare professionals to assess the quality of their promotional practices on their most promoted medicine as well as any other medicine at CEPS' justified request, up to three products maximum. The survey criteria and method applicable to all companies are defined jointly by CEPS and LEEM. They are appended to this charter.

Once gathered, this information is forwarded to a trusted third party for data aggregation and analysis. An annual report will then be drawn up on the basis of all this and sent to the signatories to this charter. Furthermore, said trusted third party must also be able to warn the signatories to this charter of any quality practices that do not meet the requirements herein. Said trusted third party is chosen jointly by CEPS and LEEM.

A joint CEPS/LEEM monitoring committee shall be set up, and meet at either party's instigation. This shall particularly analyse the information forwarded by the observatory that demonstrates there has been a deterioration in the quality of promotional information, and any other relevant information (warning from the health authorities, information at CEPS' disposal, etc.). This committee shall meet at least once a year to examine the observatory's annual report drawn up by the trusted third party. On this occasion, it shall draw up its own annual report, the advertising for which it shall carry out. It represents a forum where manufacturers can come together to discuss and explain their promotional practices and, where applicable, provide CEPs and/or the health authorities with answers.

CEPS can set annual target figures concerning promotional practice trends, where applicable for certain pharmaco-therapeutic groups or certain products pursuant to Article L.162-17-8 of

the Social Security Code. For that, it shall refer to a set of facts which may indicate any commercial and promotional practices that may undermine care quality.

In view of the information gathered, if CEPS wishes to set quantified objectives, it shall meet with the companies concerned. Following these discussions and any additional information that companies may provide, CEPS can set said annual target figures concerning promotional practice trends by agreement, or if no consent is given within two months, unilaterally.

In the event these targets are not met, once the company has been given the opportunity to present its comments CEPS shall pronounce a financial penalty against said company.

V - JOINT MONITORING OF THE CHARTER

The parties shall agree to set up a joint monitoring committee concerning application of this charter and achievement of its objectives. Said monitoring committee shall consult the professional associations concerned as necessary regarding the code for conduct, as well as the ANSM and HAS. It shall meet at either party's instigation, and particularly once a year when the observatory's annual report is submitted**.** It shall examine the items put forward on the agenda by both parties.

VI- TERM AND TERMINATION

This agreement shall come into force as soon as it is signed.
It shall be renewed by tacit agreement once a year and may be amended by a rider.
It may be terminated by either party, in which case its termination shall take effect 12 months after the party has notified the other, which gives enough time for the appropriate regulatory measures to be taken.

Signed in Paris, on 15 October 2014, in two copies

For CEPS

Mr Dominique Giorgi
Chairman

For LEEM

Mr Patrick Errard
Chairman

APPENDIX TO THE CHARTER CONCERNING INFORMATION VIA DOOR-TO-DOOR OR CANVASSING METHODS AIMED AT PROMOTING MEDICINES

SETUP AND RUNNING OF THE NATIONAL PROMOTIONAL INFORMATION OBSERVATORY

1) **General framework**

Under the charter concerning information on medicines via door-to-door and canvassing methods aimed at promotion, CEPS and LEEM have decided to set up an observatory to assess the quality of promotional practices on the basis of objective, verifiable and transparent criteria.

Data that pharmaceutical companies gather from healthcare professionals and which falls within the scope of the charter shall be forwarded to this observatory every year. Once a year, these pharmaceutical companies shall send a survey to healthcare professionals to assess the quality of their promotional practices on their most promoted medicine as well as any other medicine at CEPS' justified request, up to three products maximum.

Once gathered, this information is forwarded to a trusted third party for data aggregation and analysis. If significant deviations regarding practices are identified, said trusted third party shall inform LEEM and CEPS thereof.

The trusted third party shall be chosen jointly by CEPS and LEEM after a competitive tendering procedure. The cost of the trusted third party's service shall be borne equally by CEPS and LEEM.

The signatories to this charter shall draw up the specifications for choosing the service provider within one month following the charter's signature as well as a grading grid for selection. Their answers must be sent separately to CEPS and LEEM within two months of the specifications being dispatched.

The signatories to this charter shall meet within the following two weeks to examine the applicant's submissions. They may also decide to interview the applicants during this meeting.

2) **Survey method**

The surveys that the companies send out are in the form of a digital questionnaire for healthcare professionals to complete. The panellist criteria – identical for all companies – are determined by the trusted third party.

Each questionnaire includes questions written by the trusted third party, according to the following four themes:

Identification of the healthcare professional

- Specialisation
- Workplace
- Welcome of the MV
- Visit frequency

Description of the visit

- Identification of the MV and/or his/her supervisor
- Compliance with the visiting rules laid down by the healthcare professionals
- Visit venue
- Handing out of samples (MD)
- Number of products presented

Contents of the information provided for the products presented

Therapeutic indications

- Clinical particulars on the medicine's benefit
- The medicine's role in the patient's treatment
- Responsible use: undesirable effects – contraindications
- Adverse event report or RMP (risk management or minimisation plan)
- Official recommendations (HAS, etc.)
- Supply of the SPC
- Supply of the Transparency Commission's opinion
- Pricing aspects (reimbursable and non-reimbursable indications, fixed accountability rate, pack format, etc.)

Satisfaction of healthcare professionals

- Objectiveness of information
- Usefulness of visit
- Visits carried out at suitable intervals

The questions written by trusted third parties will be approved beforehand by the charter signatories during a dedicated work group session.

The answers to the questions on the four above-mentioned themes shall be sent to the trusted third party within one month of the survey being completed and, in all cases, at the end of every year.

This survey was sent out for the first time for 2014.

APPENDIX 11: COMMITTEE AND SECRETARIAT MEMBERS

1. Members of CEPS

Dominique GIORGI, Chairman

1.1. Medicines section

Jean-Yves FAGON, Vice-Chairman

Representatives of the Director for Social Security – Ministry for Social Affairs, Health and Women's Rights:

Thomas WANECQ, Deputy Head, Healthcare Finance Department
Claire BIOT, Head, Healthcare Products Office
Anne-Aurélie EPIS de FLEURIAN, Deputy Head, Healthcare Products Office
Aurélie OLIVIER, Healthcare Products Office
Florent DROMZEE, Healthcare Products Office
Guillaume DEDET, Healthcare Products Office

Representatives of the Director for Health – Ministry for Social Affairs, Health and Women's Rights:

Catherine CHOMA, Deputy Head, Healthcare Products Policy Department
Nadine DAVID, Head, Medicines Office
Arlette MEYER, Medicines Office
Gaëlle GERNIGON, Medicines Office
Bertrand PARADIS, Medicines Office

Representatives of the Director for Care Provision – Ministry for Social Affairs, Health and Women's Rights:

Yannick LE GUEN, Deputy Head, Department for Care Provision Stakeholders Performance Coordination
Benoît MOURLAT, Policy Officer, Care Quality and Safety Office

Representatives of the Director for Competition, Consumer Affairs and Fraud Control – Ministry for the Economy, Finance and the Digital Sector:

Axel THONIER, Deputy Head, Health, Industry and Commerce Department
Alain BOULANGER, Head, Health Office
Makram LARGUEM, Health Economist, Health Office

Representatives of the Director for Enterprise – Ministry for the Economy, Finance and the Digital Sector:

Pierre ANGOT, Head, Department of Industry and Life Sciences, Chemistry and Materials Technology, then Benjamin LEPERCHEY, Head, Department of Health Industries and Consumer Goods
Gaëtan PONCELIN de RAUCOURT, Head, Department of Food Processing and Health Industries
Aristide SUN, Policy Officer, Medicines Industry, Department of Industry and Life Sciences, Chemistry and Materials Technology, then Alain-Yves BREGENT, Deputy Head, Food Processing and Health Industries
François LHOSTE, Financial Services Officer, Department of Industry and Life Sciences, Chemistry and Materials Technology (until April 2015)

Representatives of national health insurance bodies appointed by the Director General of National Health Insurance Fund for Salaried Workers (CNAMTS):

Mathilde LIGNOT-LELOUP, Head of Care Organisation and Management
Christelle RATIGNIER-CARBONNEIL, Deputy Director, Head of the Healthcare Products Department
Thierry DEMERENS, Medical Examiner, Deputy Head, Healthcare Products Department
Martine PIGEON, Deputy Director, Healthcare Products Department
Laurence ROBBA, Senior Consulting Pharmacist, Healthcare Products Department

Representatives of national health insurance bodies appointed jointly by the Director of CNAMTS and Director of the National Health Insurance Fund for Agricultural Workers:

Hélène BOURDEL, Senior Consulting Pharmacist, Self-employed workers' health insurance plan (RSI) (until July 2015)

Representatives of the National Union of Top-Up Health Insurance Bodies:

Sébastien TRINQUARD, Health Economist
Martine STERN, Policy Officer (until May 2014)

Representative of the Minister for Research:

Jocelyne BERILLE, Policy Officer at the Biology and Health Unit, Directorate General for Research and Innovation

1.2. Medical devices section

André TANTI, Vice-Chairman

Representatives of the Director for Social Security – Ministry for Social Affairs, Health and Women's Rights:

Thomas WANECQ, Deputy Head, Healthcare Finance Department
Claire BIOT, Head, Healthcare Products Office
Anne-Aurélie EPIS de FLEURIAN, Deputy Head, Healthcare Products Office
Sandrine FARÉ, Healthcare Products Office
Olivier VERNEY, Healthcare Products Office

Representatives of the Director for Health – Ministry for Social affairs, Health and Women's Rights:

Catherine CHOMA, Deputy Head, Healthcare Products Policy Department
Catherine BONNARD-LANN, Medical Devices and Other Healthcare Products Office
Patricia DESCAMPS-MANDINE, Medical Devices and Other Healthcare Products Office

Representatives of the Director for Care Provision – Ministry for Social Affairs, Health and Women's Rights:

Yannick LE GUEN, Deputy Head, Department for Care Provision Stakeholders Performance Coordination
Anne L'HOSTIS, Chief Public Health Medical Examiner, Policy Officer, Care Quality and Safety Office
Cédric CARBONNEIL, Innovation and Clinical Research Office

Representatives of the Director for Competition, Consumer Affairs and Fraud Control – Ministry for the Economy, Finance and the Digital Sector:

Axel THONIER, Deputy Head, Health, Industry and Commerce Department
Alain BOULANGER, Head, Health Office
Makram LARGUEM, Health Economist, Health Office

Representatives of the Director for Enterprise – Ministry for the Economy, Finance and the Digital Sector:

Pierre ANGOT, Head, Department of Industry and Life Sciences, Chemistry and Materials Technology, then Benjamin LEPERCHEY, Head, Department of Health Industries and Consumer Goods,
Gaëtan PONCELIN de RAUCOURT, Head, Department of Food Processing and Health Industries
Claire COQUEBLIN, Policy Officer, Department of Industry and Life Sciences, Chemistry and Materials Technology

Representatives of national health insurance bodies appointed by the Director General of National Health Insurance Fund for Salaried Workers (CNAMTS):

Philippe ULMANN, Director of Care Provision
Christelle RATIGNIER-CARBONNEIL, Deputy Director, Head of the Healthcare Products Department
Olivier ALLAIRE, Dental Surgeon Examiner, Healthcare Products Department,
Marc MASURE, Health Economy Officer, Healthcare Products Department
Bénédicte BELLERI, Policy Officer, Healthcare Products Department

Representatives of national health insurance bodies appointed jointly by the Director of CNAMTS and Director of the National Health Insurance Fund for Agricultural Workers:

Isabelle CHEINEY, National Health Insurance Fund for Agricultural Workers

Representatives of the National Union of Top-Up Health Insurance Bodies:

Sébastien TRINQUARD, Health Economist
Martine STERN, Policy Officer (until May 2014)

Representative of the Minister for Research:

(pending appointment)

Representative of the Independent Living Fund:

Bernadette MOREAU, Director for Disability Support

Representative of the Directorate General for Social Action:

Céline PERRUCHON, Head, Disability Aids and Rights Office

2. Committee rapporteurs

Mr Henri BENECH
Ms Diane KARSENTY,
Mr Philippe LALANDE,
Ms Régine LEMEE-PECQUEUR,
Ms Marie-Odile PROY,
Mr Bruno STALLA.

3. Contact details for Committee secretariat members[62]

Fax: 01 40 56 71 79

Name	Duties	Telephone	email
Hélène Bourdel	Hospital medicines	01 40 56 69 51	helene.bourdel@sante.gouv.fr
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Jean-Philippe Cicurel	General Secretary	01 40 56 46 95	jean-philippe.cicurel@sante.gouv.fr
Marie-Dominique Furet	Legal and dispute-related matters / Observatory – CSEVR – Price increases	01 40 56 41 57	marie-dominique.furet@sante.gouv.fr
Catherine Guiock	Recording price and reimbursement applications, drafting and publishing decisions, rulings and notices in the *Journal Officiel* - medicines section	01 40 56 44 27	catherine.guiock@sante.gouv.fr
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Manuela Lenormand	Following up price and reimbursement applications, medical devices section	01 40 56 57 55	manuela.lenormand@sante.gouv.fr
Sylvie Marteau	Recording price and reimbursement applications, drafting and publishing decisions, rulings and notices in the *Journal Officiel* - medicines section	01 40 56 53 70	sylvie.marteau@sante.gouv.fr
Mylène Niquet	Following up price and reimbursement applications, medical devices section	01 40 56 71 27	mylene.niquet@sante.gouv.fr
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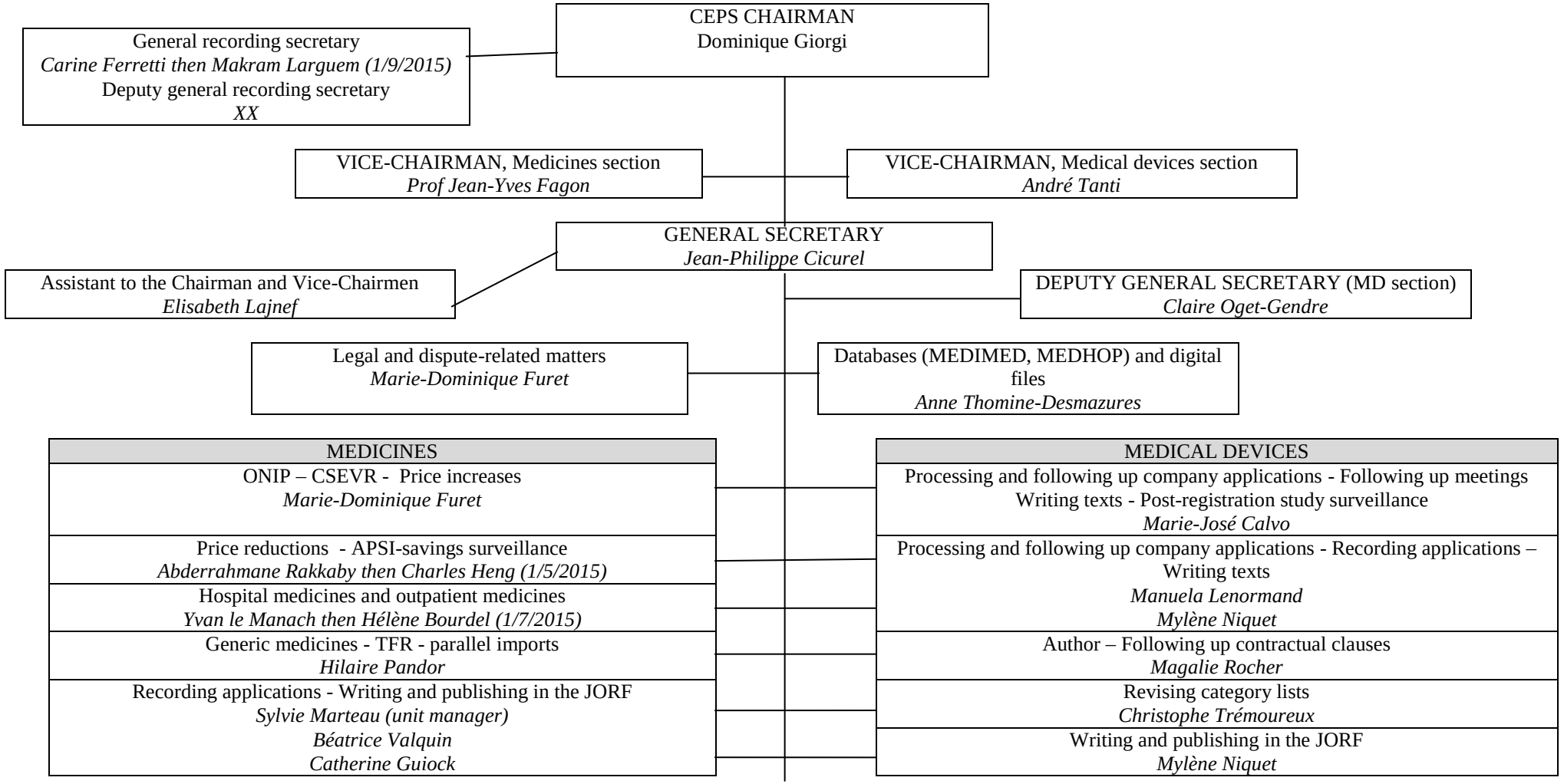
Magalie Rocher	Assessment supervisor for medical device costs and tariffs	01 40 56 61 73	magalie.rocher@sante.gouv.fr
Anne Thomine-Desmazures	Database and office automation manager	01 40 56 53 46	anne.thomine-desmazures@sante.gouv.fr
Christophe Trémoureux	Author, medical devices section	01.40.56.71.63	christophe.tremoureux@sante.gouv.fr
Béatrice Valquin	Recording price and reimbursement applications, drafting and publishing decisions, rulings and notices in the *Journal Officiel* - medicines section	01 40 56 46 84	beatrice.valquin2@sante.gouv.fr

[62]Updated in September 2015

ORGANISATION CHART FOR THE GENERAL CABINET OFFICE OF THE FRENCH HEALTHCARE PRODUCTS PRICING COMMITTEE



4. Declarations of interest, year 2014

The table below gives a summary of the contents of declarations at the end of 2014, without seeking to provide complete publication information on PDIs. These are made publicly available by CEPS on www.sante.gouv.fr

	Nature of interest			
Name (section)	***Main duties***	***Secondary duties whether or not paid and supervised duties that have been financed***	***Financial stake in any company capital***	***Other declared interests***
Committee members and participants in committee meetings				
Healthcare Products Pricing Committee (CEPS)				
Dominique Giorgi	none	Unpaid participation solely concerning CEPS' responsibilities and work	none	none
Jean-Yves FAGON (M)	Professor of Medicine at Université Paris Descartes. Head of the Medical Intensive Care Department at the Hôpital Européen Georges Pompidou.	Unpaid participation in French and international medical congresses; institutional, academic and industrial promotional research with no direct remuneration.	none	unpaid participation solely concerning CEPS' responsibilities and work, in several meetings (IFIS, IMS, API, Ateliers de Giens, etc.) and in academic teaching, usually in faculties (of pharmacy, ESSEC, DU and DIU on therapies, etc.)
André TANTI (MD)	none	unpaid participation and training solely concerning CEPS' responsibilities and work	none	none
Jean-Philippe CICUREL	none	none	none	none
Carine FERRETTI	none	none	none	none
Claire OGET-GENDRE (MD)	none	none	none	none
Christophe TREMOUREUX (MD)	none	none	none	none
Magalie ROCHER (MD)	none	none	none	none
Marie-Dominique FURET	none	none	none	none
Yvan LE MANACH (M)	none	none	none	none
Hilaire PANDOR (M)	none	none	none	none
Abderrahmane RAKKABY (M)	none	2009-2013: Sanofi, Pfizer, Novartis and Cephalon internships	none	none
Charles HENG	none	2010-2013: Roche internship	none	none
Directorate for Social Security				
Thomas WANECQ	none	none	none	none
Claire BIOT	none	08/2008 to 06/2012: Institut Pasteur immunology PhD and co-inventor of the European patent application no. EP 12305086.6: no remuneration Participation: API, Ateliers de Giens, IFIS, EGA, China Health Economic Association	none	Close relative of Guerbet Board Member who also headed up the firm JNB Développement. Close relative working within the LFB Group
Aurélie OLIVIER (M)	none	none	none	none
Guillaume DEDET (M)	none	none	none	none
Anne-Aurélie EPIS de FLEURIAN (MD)	none	none	none	none
Sandrine FARÉ (MD)	none	2010: paid participation in a Sorin pharmacists thinktank	none	none
Olivier VERNEY (MD)	none	none	none	none
Directorate General for Health (DGS)				

	Nature of interest			
Name (section)	***Main duties***	***Secondary duties whether or not paid and supervised duties that have been financed***	***Financial stake in any company capital***	***Other declared interests***
Catherine CHOMA	none	Administrator representing the DGS on the Board of ANSM, EFS, ABM, INTS – no remuneration- Representative of the DGS on the Hospitalisation Council – no remuneration- Unpaid participation: IFIS, SNITEM, SIDIV, SYFFOC, Ateliers de Giens, AFIPA, USPO	none	none
Nadine DAVID	none	none	none	none
Arlette MEYER (M)	none	none	none	none
Gaëlle GERNIGON (M)	none	2009: Ateliers de Giens	none	none
Bertrand PARADIS (M)	none	none	none	none
Catherine BONNARD-LANN (MD)	none	none	none	none
Patricia DESCAMPS-MANDINE (MD)	none	none	none	none
Directorate General for Care Provision				
Yannick LE GUEN	none	none	none	none
Anne L'HOSTIS (MD)	none	none	none	none
Benoît MOURLAT (M)	none	none	none	none
Directorate General for Competition, Consumer Affairs and Fraud Control				
Axel THONIER	none	none	none	none
Alain BOULANGER	none	Participation in IFIS, unpaid	none	none
Makram LARGUEM	none	none	none	none
Directorate General for Enterprise (DGE)				
Pierre ANGOT	none	Administrator representing the DGE on the Board of: ANSM, EFS, ANSES, INSERM, LNE and LFB- no remuneration-	none	none
Benjamin LEPERCHEY	none	Board Member of the National Reference Centre "Health and Independence at Home"- no remuneration-	none	none
Gaëtan PONCELIN de RAUCOURT	none	Administrator representing the DGE on the Board of: EFS, INSERM- no remuneration-	none	none
Alain-Yves BREGENT	none	none	none	none
François LHOSTE (M)	none	University teaching at Paris V Descartes and ESSEC Université	none	none
Aristide SUN (M)	none	none	none	none
Claire COQUEBLIN (MD)	none	none	none	Participation with transport expenses covered for Medtech and Ateliers de Giens
Directorate General for Research and Innovation				
Jocelyn BERILLE	none	2012-2013: Scientific Consultant for World Innovative Network (WIN)	none	none
Compulsory Health Insurance				
Mathilde LIGNOT-LELOUP	none	none	none	none
Christelle RATIGNIER-CARBONNEIL (M)	none	none	none	none
Thierry DEMERENS(M)	none	Unpaid participation	none	none

	Nature of interest			
Name (section)	***Main duties***	***Secondary duties whether or not paid and supervised duties that have been financed***	***Financial stake in any company capital***	***Other declared interests***
Martine PIGEON (M)	none	none	none	none
Laurence ROBBA (M)	none	none	none	none
Olivier ALLAIRE	none	Participation in SFBC, unpaid	none	none
Marc MASURE	none	none	none	none
Hélène BOURDEL (M)	none	none	none	none
Bénédicte BELLERI	none	none	none	none
Isabelle CHEINEY (MD)	none	none	none	none
Union of top-up insurance bodies				
Martine STERN	none	none	none	none
Sébastien TRINQUARD	none	none	none	none
Rapporteurs with CEPS				
Henri BENECH	none	Participation, consulting: Onexo, CEFIRA	none	none
Diane KARSENTY	none	none	none	none
Philippe LALANDE	none	none	none	none
Régine LEMEE-PECQUEUR	none	none	none	none
Marie-Odile PROY	none	none	none	none
Bruno STALLA	none	none	none	none

APPENDIX 12: PARTICIPANTS IN THE REAL-WORLD STUDY SURVEILLANCE COMMITTEE

Organisation	First name	Last name	Department and/or duties
CEPS	Dominique	GIORGI	CEPS Chairman
	Jean-Yves	FAGON	CEPS Vice-Chairman / Chairman of the Real-World Study Surveillance Committee
	Jean-Philippe	CICUREL	CEPS General Secretary
	Marie-Dominique	FURET	CEPS General Secretary - Coordinator of the Real-World Study Surveillance Committee
	Hélène	BOURDEL	CEPS General Secretary
	Charles	HENG	CEPS General Secretary
HAS	Loïc	GUILLEVIN	Chairman of the HAS Transparency Commission
	Jean-Patrick	SALES	Director of Public Health, Pricing and Medical Evaluation
	Catherine	RUMEAU-PICHON	Deputy Director of Public Health, Pricing and Medical Evaluation Head, Public Health and Pricing Evaluation Department
	Anne	d'ANDON	Head, Medicines Evaluation Department - Coordinator and contact for the Real-World Study Surveillance Committee
	Marion	PINET	Medicines Evaluation Department
	Emmanuelle	COHN	
	Laura	ZANETTI	
CNAMTS	Martine	PIGEON	Head of Care Organisation and Management – Healthcare Products Department
	Geneviève	MOTYKA	
	Stéphanie	DUBOIS	
DGCCRF	Makram	LARGUEM	Healthcare Services and Products Office
DGE	Alain-Henri	BREGENT	Office Deputy Head
	Marie	THORN	Division Deputy Head
DGS	Nadine	DAVID	Head, Medicines Office
	Mickaëla	RUSNAC	Medicines Office
DGOS	Benoit	MOURLAT	Care Quality and Safety Office
DSS	Sophie	KELLEY	Healthcare Products Office – Medical Advisor
	Florent	DROMZEE	Healthcare Products Office
DGRI	Jocelyne	BERILLE	Innovation and Research Strategy Department – Biology and Health Sector - Policy Officer "Healthcare Policy Surveillance"
RSI	Alain	MASCLAUX	Director of Health and Health Insurance and Deputy Director, Department for Risk Management and Social Action (DGRAS)
	Antoinette	SALAMA	DGRAS - Medical Examiner
	Chantal	DAISE	DGRAS
UNOCAM	Sébastien	TRINQUARD	Economist

APPENDIX 13: GLOSSARY OF ACRONYMS AND ABBREVIATIONS

ALD: *Affection de longue durée* - Chronic condition
AMO: *Assurance maladie obligatoire* - compulsory health insurance
ANSM: *Agence nationale de sécurité du médicament et des produits de santé* - French National Healthcare and Medicines Safety Agency (formerly AFSSAPS: *Agence française de sécurité sanitaire des produits de santé* - France's regulatory agency for healthcare products)
APSI: *Allergènes préparés pour un seul individu* - Allergens prepared for a specific person only
ASA: *Amélioration du service attendu* - Improvement in expected service
ASMR: *Amélioration du service médical rendu* - additional medical benefit: price rate bands for medicines, based on the added medical benefit compared to existing treatments for the same condition
ASR: *Amélioration du service rendu* - Improvement in service: price rate bands for medical devices, based on their added benefit compared to the existing products on offer
ATIH: *Agence technique de l'information sur l'hospitalisation* - Technical Agency for Hospitalisation Information
ATU: *Autorisation temporaire d'utilisation* - temporary authorisation for use granted under special circumstances to medicines that do not yet have marketing authorisation

CEESP: *Commission évaluation économique et de santé publique* - Public Health and Pricing Evaluation Department
CEPP: *Commission d'évaluation des produits et prestations* - Products and Services Assessment Committee
CEPS: *Comité économique des produits de santé* - Healthcare Products Pricing Committee
CNAMTS: *Caisse nationale d'assurance maladie des travailleurs salariés* - national health insurance fund for employed workers
CNEDiMTS: *Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé* - national medical device and health technologies assessment committee (formerly CEPP: *Decree no. 2009-1088 of 02 September 2009*)
CSIS: *Conseil stratégique des industries de santé* - Health Industries Strategic Council
CSEVR: *Comité de suivi des études en vie réelle* - Real-World Study Surveillance Committee
CSP: *Code de la Santé publique* - Public Health Code
CSS: *Code de la Sécurité sociale* - Social Security Code

DAAs: Direct-Acting Antivirals
DGCCRF: *Direction générale de la concurrence, de la consommation et de la répression des fraudes* - Directorate General for Competition, Consumer Affairs and Fraud Control
DGCIS: *Direction générale de la compétitivité de l'industrie et des services* - Directorate General for Competititveness in Industry and Services
DGOS: *Direction générale de l'offre de soins* - Directorate-General for Care Provision
DGS: *Direction générale de la santé* - Directorate General for Health
DSS: Direction de la sécurité sociale - Directorate for Social Security

EHPAD: *établissements hébergeant des personnes âgées dépendantes* - care homes for dependent elderly people

GAO: *Grand appareillage orthopédique* - Large orthotic and prosthetic devices
GERS: *Groupement pour l'élaboration et la réalisation de statistiques* - an economic interest group of pharmaceutical companies, which products market statistics
GHS: *Groupe homogène de séjours* - standard hospital stay group (similar to diagnosis-related group)

HAS: *Haute Autorité de Santé* - National Authority for Health
HCV: Hepatitis C virus

LEEM: *Les entreprises du médicament* - the pharmaceutical companies' representative body
LFSS: *Loi de financement de la Sécurité sociale* - annual Social Security Financing Act
LPPR: *Liste des produits et des prestations remboursables* - reimbursable medical device and services list

MA: Marketing Authorisation

MD: Medical device
MIGAC: *Mission d'intérêt général d'aide à la contractualisation* - funding for work 'in the general interest' and for implementing contracts with regional health agencies
MINEFI: *Ministère de l'Economie, des Finances et de l'Industrie* - Ministry for the Economy, Finance and Industry
MSA: *Mutualité sociale agricole* - a mutual health insurance fund for agricultural workers

ONDAM: *Objectif National Dépenses de l'Assurance Maladie* - the target annual national health insurance budget
ONIP: *Observatoire national de l'information promotionnelle* - national promotional information observatory

PDI: Public declaration of interest
PUI: *Pharmacie à usage intérieur* - Hospital pharmacy

RSI: *Régime Social des Indépendants* - self-employed workers' health insurance plan

SMR: *Service médical rendu* - Medical service provided (used in assessment of medical devices and services)
SNITEM: *Syndicat national de l'industrie des technologies médicales* - national medical technologies industry trade association

TAA-T2A: *Tarification à l'activité* - service-based pricing: state funding based on the services provided by the healthcare establishment, as opposed to a blanket grant
TFR: *Tarif forfaitaire de responsabilité* - fixed accountability tariff

UCD: *Unité commune de dispensation* - common dispensing unit
UFAT: *Union des fabricants d'aides techniques* - medical aid manufacturers' union
UFOP: *Union française des orthoprothésistes* - French orthotic and prosthetic device manufacturers' associations
UNCAM: *Union nationale des caisses d'assurance maladie* - national association of health insurance funds (CNAMTS, MSA and RSI)
UNOCAM: *Union nationale des organismes d'assurance maladie complémentaire* - national association of top-up health insurance organisations
URSSAF: *Union de recouvrement des cotisations de Sécurité sociale et d'allocations familiales* - family benefits and social security contributions collecting body

VPH: *Véhicules pour personnes handicapées* - disability-adapted vehicles (and other mobility equipment)