Hogan Lovells

Market Access in Europe:

Navigating Pricing & Reimbursement Pathways

Introduction.

The regulation of pricing and reimbursement for medicinal products is only rudimentary at the European Union (EU) level. Pricing and reimbursement are still subject to the national policies of European Member States. The competence of the EU on pricing and reimbursement is limited. This is because the European Member States have retained the power to take decisions which affect their national budgets, and are reluctant to cede competence to the EU in this regard.

This article briefly outlines the few laws that were introduced at European level to at least slightly harmonise pricing and reimbursement in the EU Member States. Further, we will briefly explain reference pricing in Europe (*i.e.* how the reimbursement system of one EU country refers to the prices of other countries in order to determine local reimbursement prices). This reference pricing, and the local rules on when and how reimbursement for a product can be obtained right after launch, determine the usual launch sequence for medicinal products in Europe.

Pricing and reimbursement laws are essential to ensuring that medicinal products are accessible to patients, whilst also promoting innovation within the pharmaceutical industry. The EU has established a framework that tries, within the very limited competence of the EU, to harmonise regulations across all Member States, allowing for a more cohesive approach to drug pricing and reimbursement.

1. EU Legal framework

The EU's legal framework regarding regulatory aspects of medicinal products is mostly determined by the following two regulations:

- Directive 2001/83/EC: This directive provides a comprehensive regulatory framework for medicinal products in the EU. It outlines requirements for marketing authorisation, including safety, efficacy, quality standards, and labelling.
- Regulation (EC) No 726/2004: This regulation establishes procedures for the authorisation and supervision of medicinal products at EU level. It aims to ensure that all medicines available in the market meet high safety standards.

In addition to regulations governing medicinal products, there are specific regulatory frameworks applicable to medical devices and IVDs within the European Union:

- Regulation (EU) 2017/745 on Medical Devices (MDR): This regulation governs the placing on the market of medical devices across EU Member States.
- Regulation (EU) 2017/746 on In Vitro Diagnostic Medical Devices (IVDR): Similar to the MDR, this regulation focuses specifically on IVDs and regulatory aspects thereof.

However, the above legislative acts do not regulate the respective pricing and reimbursement of medicinal products or medical devices. With regard to pricing and reimbursement, there are mainly two acts to be mentioned:

- Council Directive 89/105/EEC ("Transparency Directive"), which specifically addresses transparency in pricing and reimbursement decisions made by Member States with regard to pharmaceutical products (medicinal products). It mandates that national authorities provide clear criteria for pricing decisions and ensure timely access to information regarding reimbursement.
- Regulation (EU) 2021/2282 on health technology assessment and amending Directive 2011/24/EU ("HTA Regulation"), which tries to provide an EU-wide scheme for joint clinical assessment of health technologies (mostly medicinal products, but also certain procedures performed by use of medical devices) for purposes of later reimbursement decisions.

Of course, there are various additional pieces of EU legislation dealing with patient access to health technologies, such as the right of EU citizens to receive treatment in a country other than their own country of residence. Such laws may have implications on the reimbursement of products, but these implications are limited in scope and effect.

Taking into account the above two pieces of legislation and the implications that each national reimbursement scheme may have on the reimbursement scheme of another nation, the following aspects are worth considering:

2. Price transparency under directive 89/105/EEC

Price transparency is a cornerstone of effective health care systems, as it fosters trust among stakeholders while facilitating informed decision-making by patients and providers alike. Under the Transparency Directive, it was previously defined Member States are required to disclose comprehensive information about prices for medicinal products prior to market entry, as well as ongoing updates related to any changes in pricing or reimbursement status. This includes making public the criteria used for determining prices – such as cost effectiveness analyses – and ensuring that patients have access to relevant information about which medicines are reimbursed under their national health systems.

By enhancing price transparency, the Transparency Directive aims not only to empower consumers, but also to encourage competition among pharmaceutical companies by providing them with insights into market dynamics across different countries within the EU. Ultimately, increased transparency can lead to better negotiation outcomes between payors (such as government health authorities) and manufacturers while supporting equitable access to necessary treatments.

With regard to pharmaceutical companies, the implications of the transparency directive are limited, since the Directive imposes obligations mostly on the Member States, and not really on pharmaceutical companies. However, given that the Transparency Directive aims at improving transparency of decision-making for drug reimbursement, there are situations where this Directive is a means of giving pharmaceutical companies certain rights or legal arguments in challenging the reimbursement law itself, or reimbursement decisions of Member States and their local payor organisations.

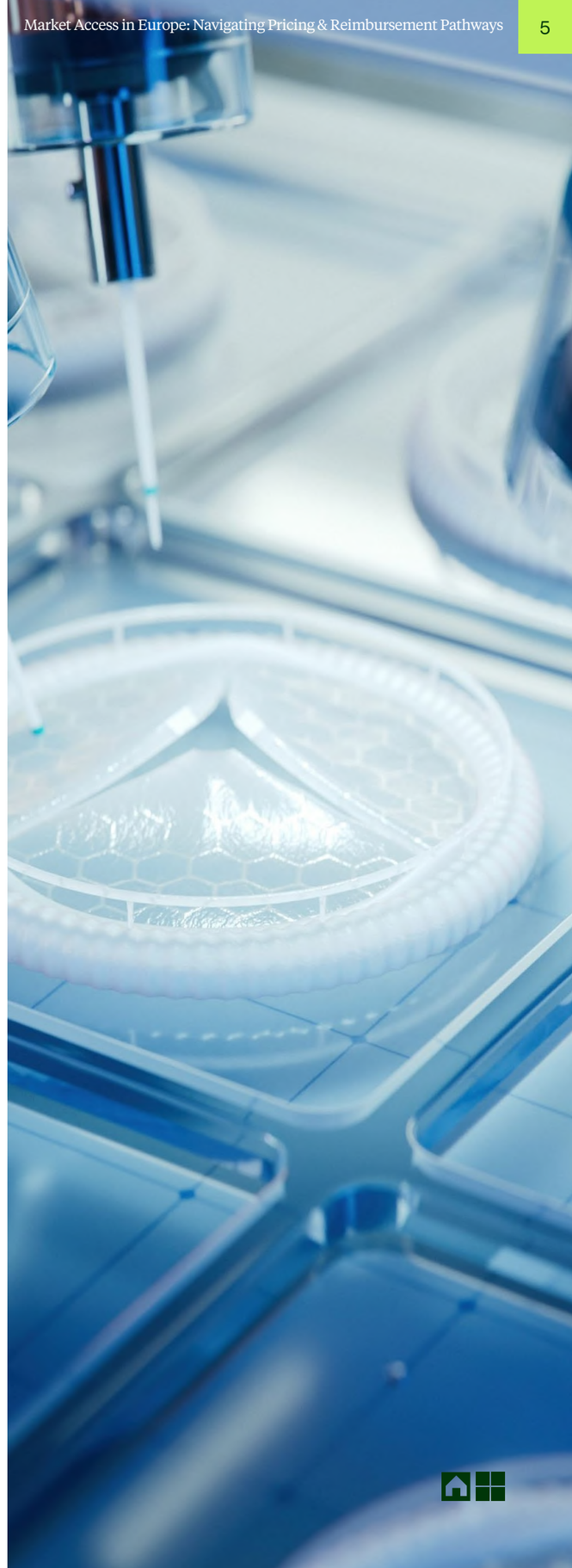
3. HTA regulation applying to certain medicinal products

A major development which is likely to affect all national health technology assessment and reimbursement procedures throughout the EU is Regulation (EU) 2021/2282 on health technology assessment and amending Directive 2011/24/EU ("HTA Regulation"). The HTA Regulation entered into force on 11 January 2022, and sets out rules for the joint clinical assessment ("JCA") of health technologies on EU-level, *i.e.* the "the scientific compilation and the description of a comparative analysis of the available clinical evidence on a health technology in comparison with one or more other health technologies or existing procedures."

The scope of the HTA Regulation comprises different types of technologies, including medicinal products and medical devices, as well as certain medical procedures for the treatment or diagnosis of diseases. With respect to medicinal products, the HTA Regulation will come into effect in a staggered manner as follows:

- From 12 January 2025: medicinal products which contain a new active substance for which the therapeutic indication is the treatment of cancer, and medicinal products which are regulated as ATMP under Regulation (EC) No 1394/2007.
- From 13 January 2028: medicinal products with orphan drug designation pursuant to Regulation (EC) No 141/2000.
- From 13 January 2030: all other medicinal products subject to a mandatory central authorisation procedure under Regulation (EC) No 726/2004 or voluntarily undergoing such central authorisation procedure.

Importantly, the reports resulting from such JCA shall not contain any judgement or conclusions on the clinical or other patient value added by a health technology. Rather, the reports shall be limited to a description of the scientific analysis of the relative effects of the assessed health technology and the degree of certainty of such effects.



Therefore, the EU JCA under the HTA Regulation will in no way replace the health technology assessment procedures in place in the respective EU Member States. The results of the JCA will just provide (if at all) a basis for such national health technology assessment procedures in each Member State, where specific conclusions as to the added value of a certain health technology will need to be drawn. Nevertheless, the JCA and its results will play an important role in national procedures. This is, firstly, due to the procedural rules which provide that all relevant data, analyses or other evidence shall be submitted by the developer of a health technology already in the EU HTA – and not in the national procedures following later. Secondly, the HTA Regulation requires the Member States to "give due consideration to the published joint clinical assessment reports …". While it is yet to be seen how this interplay between the EU JCA report and national health technology assessments will work out in practice, it is likely that an unfavourable EU JCA report will negatively affect national health technology assessment and reimbursement procedures. Therefore, health technology developers (*i.e.* pharmaceutical and medical device companies) will need to invest significant efforts into the EU HTA procedures, and thus cannot save efforts and resources for the later national procedures only.

In terms of the health technology assessment procedures on EU level, the developer of the health technology has to submit its dossier within 100 days from the date of notification of the first request by the Commission (cf. Art. 12(2) of Commission Implementing Regulation (EU) 2024/1381 of 23 May 2024). This is a tight deadline, which demonstrates that health technology developers need to make sure they are sufficiently prepared for the new procedures once they become applicable. Following submission of the dossier, the EU JCA will take place in parallel to the regulatory approval procedures. The final JCA reports shall normally be published within 30 + 10 (4) days from the granting of the central marketing authorisation by the European Commission. The final published report is basically the endpoint of the EU JCA, and shall then be taken into consideration by national reimbursement bodies during the national health technology assessments.

4. Reference pricing

One notable aspect of pricing regulation within the context of harmonisation is reference pricing: – a system whereby a country sets its drug prices based on prices established in other countries.

The way this usually works is as follows: certain national health authorities (in certain Member States) evaluate prices from selected countries (often those with similar economic conditions or health care systems) as benchmarks when determining reimbursement prices for medicinal products or when negotiating such prices with pharmaceutical companies.

For pharmaceutical companies, reference pricing may limit their ability to set higher prices based on local market conditions or innovative value, since their price may be influenced by lower-priced markets. Further, reference pricing determines the strategy of a pharmaceutical company as to in which sequence it may launch a product in certain EU Member States.

5. Typical launch sequence in European countries

Determined by the aforementioned reference pricing, as well as the specific aspects of the different local reimbursement systems, there is a typical sequence for pharmaceutical companies to launch a pharmaceutical product in Europe. Unless the therapy determines otherwise (*e.g.*, higher prevalence in specific countries), the launch sequence is usually as follows:

The focus of pharmaceutical companies is to first launch in the major European markets, *i.e.*, the big five, France, Germany, Italy, Spain and the UK, as well as the Benelux. Within these countries, pharmaceutical companies mostly launch first in Germany. This is because the German reimbursement system provides for instant reimbursement on the basis of the manufacturer-determined selling price; only six months after official launch does the negotiated, lower, reimbursement price take effect. The initial, higher, manufacturer-determined price is then referenced in other countries, which is a good starting point for negotiations. Thereafter, our clients mostly focus on Italy and Spain, as well as the UK. Italy and Spain have been seen to allow for revenue to still be generated for considerable periods of time after launch. Ultimately, the UK may develop into an even earlier market for launches, given that the UK recognises regulatory approval by certain other countries, and thus allows for early launches, even before market approval has been obtained; certainly, the process of obtaining NHS reimbursement then still has to be pursued. France used to be an early launch market as well, since it has the best early access scheme: it allows pharmaceutical companies to collect revenue for products being supplied in compassionate use situations; however the revenue is subject to later clawbacks.

Of course, launch sequences depend on the specificities of the product and the competitive market. In any case, launch sequences must be properly planned, and well ahead of the actual launch, in particular in countries that have imposed health technology assessment requirements as a prerequisite for reimbursement. The preparation of HTA dossiers can take up to nine months, and dossiers which are filed in different countries need to be aligned. Further, before a dossier is drafted, it is strongly recommended that a pharmaceutical company seek early advice from the respective HTA bodies as to their expectations for their respective dossier (*i.e.*, comparator product, scientific data, patient benefits data etc.).

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Contents.

Belgium.

1. Summary

- The Belgian health care system combines a statutory health care insurance and optional additional health care insurance:
  - Compulsory health insurance is organized through private, non-profit-making national associations of health insurance and a public national association of health care insurance funds;
  - The role of the health care insurance funds is to reimburse treatment received by patients.
- The majority of medicinal products in Belgium are reimbursed by the statutory health insurance funds.
- Key features of the pricing and reimbursement of medicinal products:
  - Pricing: determination of the maximum ex-factory price is made by the Minister of Economic Affairs;
  - Reimbursement: determination of the reimbursement status is made by Minister of Social Affairs and Public Health;
    - positive list of reimbursed medicinal products;
    - differential reimbursement depending on the "medico-therapeutic value" of the medicinal product and related reimbursement category: A, B, C, Cs, Cx or D;
    - reimbursement ranges from reimbursement of the complete cost of the product to only a certain percentage thereof, which will imply a specific co-payment rate for patients (in French the *ticket modérateur*).
- Various measures are in place or are being introduced by the government to cut back the costs of medicinal products:
  - maximum prices for medicinal products;
  - reference pricing groups;
  - differentiated reimbursement levels;
  - limitations of the pharmacists and wholesaler margins;
  - price decreases, i.e. where the authorities can apply measures to reduce the price and the reimbursement basis (ex-factory level) of medicinal products containing an active ingredient (or a combination of active ingredients) that has been reimbursable by health care insurance for 12 years.

2. Overview of the health care system in Belgium

The Belgian health care system is funded from social security charges levied from salaries and social security contributions from self-employed individuals. Additional funds are collected from other sources, such as social security contributions collected from companies. The responsibility for health policy is shared between the federal state and the federated entities, including regions and communities.

2.1 Payors – Health care insurance funds

The Belgian health care system combines a statutory health care insurance and optional additional health care insurance. Compulsory health insurance is organized through private, non-profit-making national associations of health insurance, and a public national association of health care insurance funds. The role of the health care insurance funds is to reimburse treatment received by the patients. There are no differences in the tasks performed by the different types of insurance funds in relation to the reimbursement of costs for treatment of patients.

The National Institute for Health and Disability Insurance (hereafter the "NIHDI") is a public social security institution that reports to the Minister of Social Affairs and Public Health. NIHDI is responsible for the general organization and financial management of the compulsory health care insurance.

Medicinal products prescribed to patients are generally reimbursed but patients may be required to contribute to the cost of these medicinal products. The amount of the patients' co-payment is, however, limited by the law.

2.2 Prescribers – physicians and dentists

In Belgium, prescription-only medicinal products are prescribed to patients by physicians and dentists. Nurses are not permitted to prescribe medicinal products to patients.

2.3 Patients who are entitled to reimbursement of their medicinal products

Patients in Belgium are entitled to a (full or partial) reimbursement of almost all medicinal products. The categories of patients that are entitled to reimbursement include, among others:

- employees who are affiliated with a compulsory health insurance fund;
- employees who are not capable to work;
- unemployed individuals;
- employees on maternity or paternity leave;
- self-employed who are affiliated with a compulsory health insurance fund;
- individuals who are retired.

3. Pricing and reimbursement procedure for medicinal products

Only medicinal products that are authorised to be placed on the market in Belgium could be granted pricing and reimbursement status in the country. This includes medicinal products that were centrally authorised by the European Commission. It also includes medicinal products that were authorised by the Belgian Federal Agency for Medicinal Products and Health care Products ("FAMPHP") through the national, decentralised and mutual recognition marketing authorisation procedures.

3.1 Legal bases

The major Laws and Royal Decrees governing the pricing and reimbursement of medicinal products in Belgium include.

General framework:

- Law of 25 March 1964 on medicinal products;
- Royal Decree of 14 December 2006 on medicinal products for human and veterinary use;

Pricing legislation:

- Book V, Section 2 of the Belgian Code of Economic Law;
- Royal Decree of 10 April 2014 fixing the conditions of admissibility, deadlines and practical modalities of price fixing applications, price increase applications, price notifications and (price) communications for medicinal products and objects, devices and substances assimilated to medicinal products;
- Ministerial Decree of 17 June 2014 specifying the objects, devices and substances assimilated to medicinal products and setting the maximum prices and maximum margins of objects, devices and substances assimilated to medicinal products;

Reimbursement legislation:

- Law of 14 July 1994 on compulsory health care insurance and compensation ;
- Royal Decree of 1 February 2018 laying down the procedures, deadlines and conditions for the intervention of the compulsory health care and benefits insurance in the cost of pharmaceutical specialties.

3.2 Pricing of medicinal products

The maximum ex-factory price for the medicinal product is determined by the Minister of Economic Affairs. The ex-factory price will be determined on the basis of scientific and economic information submitted by the marketing authorisation holder to the Price Department of the Federal Public Service for Economic Affairs ("Price Department") as part of the pricing dossier. The pricing dossier is aimed at justifying the requested ex-factory price and must include, among other things:

- pharmaceutical form;
- indication and dosage of the product;
- therapeutic improvement of the product (if any);
- copy of the MA;
- cost structure, including production cost;
- copy of the company's annual accounts for the past three years;
- description of the market and the competition conditions (including a comparison with the prices of comparable products marketed in Belgium and prices applies in other EU Member States where applicable).

After completion of the pricing review process by the Pricing Department, the Minister of Economic Affairs will determine the maximum ex-factory price on the basis of this advice of the Price Department.

Determination of the maximum ex-factory price represents a key step in the pricing procedure as it forms part of the maximum price charged to patients, which is referred to in Belgium as the "maximum public price". The maximum public price is composed of the following:

- Ex-factory price
- Margin for wholesalers or pharmacists (which are maximum margins)
- Pharmacist fee for delivery of the reimbursement product (if reimbursable medicinal products are involved)
- VAT (currently 6%).

The Minister is required to adopt the decision within 90 days following the submission of the application by the marketing authorisation holder. This period is reduced to 45 days for medicinal products that are subject to parallel import into Belgium. If the Minister does not adopt a decision within these timelines, the marketing authorisation holder is permitted to use the maximum ex-factory price that was proposed in its application.

The responsibility of the Minister of Economic Affairs for price determination and regulation for medicinal products, includes also the approval of price increases and reductions. Any future price reduction of the ex-factory price must be communicated to the Price Department. Please note that a specific procedure is applicable for increases of the ex-factory price, which is similar to the initial procedure for obtaining the ex-factory price, as above described.

3.3 Reimbursement of medicinal products

The marketing authorisation holder that wishes to obtain a reimbursement status for its medicinal product is required to submit an application for the inclusion of this medicinal product in the list of reimbursed medicinal products. The application should be submitted to the Commission for Reimbursement of Medicinal Products ("CRM"). This application could be submitted at the same time as the submission of the pricing application to the Ministry of Economic Affairs.

The decision concerning grant or refusal of reimbursement status for a medicinal product is adopted by the Minister responsible for Social Affairs and Public Health. The Minister is required to provide the grounds supporting the decision.

The Minister adopts the decision for grant or refusal of reimbursement status for a medicinal product on the basis of a proposal by the CRM. The Minister is required to adopt this decision within **180 days** following the submission of the application for reimbursement by the marketing authorisation holder. Shorter timelines exist for some pharmaceutical specialties depending on the therapeutic class (or sub class) allocated (as further detailed below);

- for pharmaceutical specialties ranked in sub-classes 2C, 3B or 3C, reimbursement decision shall be adopted within **90 days**;
- for pharmaceutical specialties ranked in sub-classes 2A or 3A, there is a simplified and shortened procedure in which the CRM is not involved and the Minister of Social Affairs and Public Health adopts the reimbursement decision within **60 days**.

Should the decision not be adopted within the period of 180 days (or any reduced period where applicable, as indicated above), the reimbursement application shall be deemed approved by the Minister of Social Affairs and Public Health.

The elements taken into account by the CRM and the Minister in their assessment include:

- therapeutic value of the pharmaceutical specialty. Reference is made to "pharmaceutical specialties" by the NIHDI as medicinal products produced by a pharmaceutical company. This therapeutic value is expressed in one of the three following classes of added value:
  - class 1: pharmaceutical specialties with proven therapeutic added value compared to existing therapeutic alternatives;
  - class 2 (further divided in subclasses 2A, 2B and 2C): pharmaceutical specialties with no proven therapeutic added value compared to existing therapeutic alternatives, and which do not belong to class 3;
  - class 3 (further divided in subclasses 3A, 3B and 3C): pharmaceutical specialties which include generic medicinal products and "copy" medicinal products;

- price of the pharmaceutical specialty and the reimbursement basis proposed by the applicant;
- interest of the pharmaceutical specialty in medical practice according to therapeutic and social needs;
- budgetary impact for the compulsory health care insurance;
- relationship between the cost for the compulsory health care insurance and the therapeutic value.

(a) The CRM

The members of the CRM with voting rights include:

- seven representatives of Belgian academia;
- eight representatives of the Belgian health insurance funds;
- three representatives of the professional organisations of pharmacist;
- four representatives of the professional organisations of physicians.
- two representatives of the associations of pharmaceutical industry;
- one representative of the Minister of Social Affairs and Public Health;
- one representative of the Minister of Public Health;
- one representative of the Minister of Economic Affairs;
- one representative of the Medical Control Department of INAMI.

The tasks of the CRM include:

- draft proposals for grant or refusal of reimbursement status for a medicinal product;
- upon the request of the Minister responsible for Social Affairs and Public Health, prepare opinions concerning the policy for the reimbursement of medicinal products;
- draft proposals for guidance concerning the interpretation of the rules governing the reimbursement of medicinal products.

(b) List of reimbursed medicinal products

The list of reimbursed medicinal products is divided in various Chapters. The Chapters reflect the nature of the medicinal products and the therapeutic indications that are covered by reimbursement.

As a general principle, only medicinal products that are authorised to be placed on the market in Belgium are eligible for inclusion in the list of reimbursed medicinal products. Moreover, only the therapeutic indications that are covered by the marketing authorisation may be subject to reimbursement.

This list is available at: https://www.inami.fgov.be/fr/themes/cout-remboursement/par-mutualite/medicament-produits-sante/remboursement/specialites/Pages/default.aspx

The medicinal products included in Chapter I of the list of reimbursed medicinal products qualify for unrestricted reimbursement. These medicinal products are reimbursed when:

- the pharmacist receives a prescription written by a doctor (or dentist, midwife);
- the pharmacist delivers the pharmaceutical speciality.

Chapter II lists the classes of medicinal products for which there are widely used and generally known principles of good medical practice. Similarly to Chapter I, medicinal products included in Chapter II of the list of reimbursed medicinal products are subject to reimbursement when:

- the pharmacist receives a prescription written by a doctor (or dentist, midwife);
- the pharmacist delivers the pharmaceutical speciality.

Please note that for Chapter II pharmaceutical specialities, a posteriori control applies.

Chapter III includes infusion fluids, for instance blood substitutes and hydrating medium.

The pharmaceutical specialities in Chapter III are reimbursable when:

- the prescriber complies with the indications in the scientific information leaflet
- the pharmacist receives a prescription written by a doctor (or dentist, midwife)
- the pharmacist dispenses the pharmaceutical speciality.

The reimbursement of a pharmaceutical specialities listed in Chapter IV is subject to conditions imposed for medical and/or budgetary reasons. This means that reimbursement is limited in terms of the level of indications, target group, age, etc. These are the so-called “medicinal products with authorisation”.

These conditions are set out in the paragraph where the pharmaceutical speciality is registered.

In addition, reimbursement depends on prior authorisation by the examining doctor (in French *médecin conseil*) (a priori control).

In some exceptional cases, prior authorisation is not necessary and it is sufficient to indicate a specific mention on the prescription. This is then specified in the paragraph where the pharmaceutical speciality is listed.

Pharmaceutical specialties listed in Chapter IV are reimbursable when:

- the patient meets the conditions for reimbursement;
- the pharmacist receives a prescription written by a doctor;
- the pharmacist systematically checks to see if the patient’s prescription is eligible for reimbursement. The pharmacist sends the data on the authorisation to the pricing office. If the pharmacist finds that the data do not correspond to those on the “paper” authorisation in the patient’s possession, he or she will ask the patient to contact either his or her mutual insurance company or his or her doctor to find out about his or her situation or possibly to regularise it;
- the pharmacist delivers the pharmaceutical speciality.

Chapter IVbis includes the pharmaceutical specialties which are not registered in Belgium and which are therefore imported by the pharmacist. The pharmaceutical specialities in chapter IVbis are reimbursable when:

- the patient meets the conditions for reimbursement;
- the pharmacist receives a prescription written by a doctor;
- the pharmacist orders the pharmaceutical speciality from abroad;
- the pharmacist delivers the pharmaceutical speciality.

It should be noted that the pharmacist may only import a medicinal product from abroad in one of the following situations:

- the medicinal product is not registered in Belgium;
- the medicinal product is registered in Belgium but not placed on the market;
- the medicinal product is registered in Belgium but is no longer available on the market.

Chapter V lists the pharmaceutical specialities that are reimbursable by the health care insurance fund without the pharmaceutical company marketing it in Belgium having submitted a reimbursement application in Belgium. This is the case when the Commission for the Reimbursement of Medicines (CRM) or the Minister of Social Affairs and Public Health finds that patients are denied reimbursement for valid therapeutic means.

The registration of a speciality in Chapter V is automatically withdrawn if another identical speciality is reimbursable following an application for reimbursement.

Chapter VIII includes “personalised” medicinal products that are reimbursed only after the presence or absence of a molecular biomarker has been demonstrated. Chapter VIII is very similar to Chapter IV: reimbursement of a proprietary medicine is subject to the conditions set out in the paragraph in which the medicine is registered and authorisation must be sought from a medical officer. Authorisations for a medicinal product that has been transferred from Chapter IV to Chapter VIII cannot be extended to the former. Specific instructions are provided to this effect.

In addition to a list of proprietary medicinal products, Chapter VIII also contains a list with the corresponding “companion diagnostics” or “predictive biomarkers”.

(c) Categories of reimbursement

Each medicinal product that is included in the list of reimbursed medicinal products is attributed to a reimbursement category. The category corresponds to the percentage of the cost of the medicinal product that is reimbursed by the health insurance funds in Belgium. The categories are A, B, C, Cs, Cx, Fa and Fb.

The attribution of a medicinal product to a reimbursement category is made by the Ministry of Social Affairs and Public Health. The decision of the Ministry is based on a proposal by the CRM.

The medicinal products in categories A, B, C, Fa and Fb are considered to be "necessary" treatments. These medicinal products are classified in accordance with their "medicotherapeutic value". This value is determined by the CRM.

- Medicinal products in category A and Fa have vital importance. These medicinal products include treatments for diabetes and cancer. Medicinal products classified in these categories are reimbursed at 100% of their maximum reimbursement price. For the products in the other below categories, the percentage of reimbursement progressively decreases.
- Medicinal products that are considered important for the treatment of patients are classified in category B and Fb. Antibiotics are an example of such medicinal products.
- Medicinal products for symptomatic treatment, such as the treatment of chronic bronchitis, are classified in category C.
- Medicinal products in category Cs include for instance allergy medication.
- Medicinal products in category Cx include for instance contraceptive products.

It is important to note that the reimbursement levels for medicinal products in categories B, C, Cs, Cx and Fb depend on the maximum reimbursement price of the medicinal products. Medicinal products that cost less than €14.38 are reimbursed at lower rates.

Medicinal products that are not included in any of these seven categories of reimbursement are sometimes referred to as category D medicinal products. These are medicinal products for which no reimbursement is provided.

3.4 Reference reimbursement

Specific rules apply to the determination of the reimbursement level for medicinal products that are covered by reference pricing. The reference reimbursement system applies when a reimbursable generic alternative (cheaper and with the same active ingredient(s)) exists for an original speciality.

When using a "reference cluster", the price and the reimbursement basis of the original speciality decrease by a certain percentage:

- 51.52% decrease for reimbursable medicinal products in category A;
- 44.75% decrease for other reimbursable medicines.

This reduction applies to the ex-factory price.

Exceptions to the application of the reference reimbursement system are possible for

- injectable forms of original specialities;
- original specialities recognised as having significant added value in terms of form of administration, safety and/or efficacy;
- specialities with a complex active principle, i.e. non-biological specialities composed of one (or more) active principles with a chemical structure that may vary within the same batch or between different batches.

The price and reimbursement basis for these exceptions are reduced by only half the percentage reduction:

- 27.82% reduction for category A reimbursable medicines;
- 23.37% reduction for other reimbursable medicines.

For reference reimbursement, the Minister of Social Affairs and Public Health makes this recognition, on the advice of the CRM, on the basis of an exception request file submitted by the applicant.

3.5 Reimbursement of medicinal products administered to patients in hospitals

The costs of medicinal products administered to patients in hospitals are partly covered by a hospitalisation budget that is attributed to each patient. The amount of this budget is determined depending on the medical condition and therapeutic needs of the patient.

The remaining cost is reimbursed in accordance with the general reimbursement rules discussed in the previous Sections of this Document. The same applies to the cost of the medicinal products that exceed the limits of the patient budget.

In accordance with the applicable rules, hospitals in Belgium are required to organise public tenders for the purchase of medicinal products. These tenders should either be based on a single stage procedure where price is the only criterion or on a multiple stage procedure where a mix of quantitative and qualitative criteria is used.

This requirement applies to both public and private hospitals in Belgium.

It is also important to note that specific invoicing requirements apply in certain cases when hospitals invoice the health care insurance system for medicinal products administered to patients. Under the "**85% rule**" (or "85% pricing"), hospitals are only allowed to invoice 85% of the standard reimbursement amount for the following categories:

- contrast agents;
- biological medicinal products for which a reimbursable biosimilar is available;
- reimbursable pharmaceutical specialties when they belong to a cluster to which the reference reimbursement system applies.

This measure creates a **15% reimbursement gap**. Hospitals receive, therefore, less than the full reimbursement amount they would normally be entitled to under standard rules.

Hospitals are strictly prohibited from passing this 15% difference on to patients. Instead, it is expected that the pharmaceutical companies supplying the affected medicinal products absorb this cost, either directly or through negotiated discounts. The actual ex-factory price and reimbursement basis remain unchanged, but the hospital's real purchasing price is effectively reduced in practice.

3.6 Social Solidarity Fund

The Solidarity Fund established by the Belgian State provides funding for the treatment of patients with medicinal products that are:

- not reimbursed;
- expensive;
- intended to treat rare diseases.

Funding from the Solidarity Fund is provided to individual patients or identified groups of patients.

3.7 Prescription of medicinal products

Physicians are permitted to prescribe a number of medicinal products to a single patient in the course of the same medical visit. The validity of the prescriptions is, however, limited to three months.

The CRM has established Recommendations for Good Medical Practice. These Recommendations provide guidance for the physicians concerning the establishment of prescriptions for medicinal products. The Recommendations reflect the principles of "evidence based medicine".

The medicinal products falling in the Scope of Chapter IV cannot be reimbursed by the health insurance funds unless the physician who is appointed as a medical advisor by the health insurance fund authorises this reimbursement. The decision of the medical advisor is based on the medical history of the patient and his or her therapeutic needs.

3.8 Margins for pharmacists and wholesalers included in the price of medicinal products

The price of medicinal products in the pharmacies in Belgium includes a margin for the pharmacists and wholesalers. The margin for the pharmacists is different for non-reimbursable medicines and reimbursable medicines. It can be summarised as follows:

- remuneration for non-reimbursable medicines:

The distribution margins for non-reimbursable medicines are calculated on the selling price excluding VAT.

- Selling price including VAT ≤ 25,43 €: 31% of the selling price excluding VAT.
- Selling price including VAT > 25,43 €: 7,44 € per presentation.
- Remuneration for reimbursable medicines.

The distribution margins for reimbursable medicines are calculated on the ex-factory price excluding VAT.

- Ex-factory price excluding VAT ≤ 60 €: 6,42% of the ex-factory price excluding VAT;
- Ex-factory price excluding VAT > 60 €: 3,85 € + 2,12 of the ex-factory price excluding VAT.

4. Pricing and reimbursement of medical devices

The relevant legislation for medical devices can be summarised as follows:

- Law of 15 December 2013 on medical devices;
- Law of 22 December 2020 on medical devices and its implementing decrees;
- Royal Decree of 10 April 2014 fixing the conditions of admissibility, deadlines and practical modalities of price fixing applications, price increase applications, price notifications and (price) communications for medicinal products and objects, devices and substances assimilated to medicinal products;
- Ministerial Decree of 17 June 2014 specifying the objects, devices and substances assimilated to medicinal products and setting the maximum prices and maximum margins of objects, devices and substances assimilated to medicinal products;
- Law of 14 July 1994 on compulsory health insurance and compensation;
- Royal Decree of 24 June 2014 laying down the procedures, time limits and conditions for the intervention of compulsory health care insurance and compensation in the costs of implants and invasive medical devices.

Medical devices, such as implants and hearing aids are also subject to the above described pricing procedure. The pricing application to determine the ex-factory price must be submitted to the Price Department. Within 90 days, the Minister of Economic Affairs sets the maximum authorised price of the medical device in a ministerial decree.

Some devices (such as implants) can be recognised as reimbursable, while others can be covered by the general expenses of the hospitals where they are used. The conditions for reimbursement vary according to whether they are non-implantable medical devices, implants and invasive medical devices or certain services provided by bandagers.

Some medical devices, such as medical devices used for the diagnostics of a medical condition or the administration of a medicinal product, are included in the list of reimbursed medicinal products. These devices are classified in the reimbursement categories applicable to medicinal products. The reimbursement of the costs of the medicinal devices included in the reimbursement list is governed by the rules governing the reimbursement of medicinal products.

Certain medical mobile applications, also known as digital health applications, may be eligible for reimbursement under the Belgian health care insurance system. Since 2021, a regulatory framework has made it possible to assess and support the reimbursement of these digital tools that enhance health care delivery. A new procedure, effective as of 1 October 2023, now governs the reimbursement of such applications. These applications are evaluated based on their clinical and organisational added value and may receive either temporary or permanent reimbursement. The process involves several stages, including admissibility verification, scientific assessment, and the development of a reimbursement proposal. Various stakeholders in the health care sector, such as companies, hospitals, or professional associations, can submit a reimbursement request.

5. Coming changes

Belgium aligned its existing administrative and procedural frameworks with the requirements of HTA Regulation, primarily through the INAMI-RIZIV and the Belgian Health Care Knowledge Centre (KCE). These bodies updated their internal processes to incorporate joint clinical assessments and participate in EU-level coordination, ensuring that European outputs are integrated into national reimbursement and pricing decisions.

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France.

1. Summary

- In France, pharmaceutical products and medical devices ("*health care products*") may be reimbursed by public and/or private bodies:
  - The French public body is the *French National Health Insurance ("Assurance maladie")* which *will reimburse, in whole or in part, health care products registered under reimbursement lists, on the basis of a rate* set by the French National Union of Health Insurance Funds ("Union nationale des caisses d'assurance maladie" – *"UNCAM"), between 15% and 100% (cf. 6.3).*
  - Private bodies is *private insurance* which *will be reimbursed on the remaining cost of the health care products, in whole or in part, depending on the agreement* concluded by the insured person. Indeed, any person can subscribe to a health supplement on an individual basis, and possibly for the benefit of one or more members of their family. There are multiple private insurances in France with different terms and policies.
- *The price* of health care products is *either set freely* by the pharmaceutical company *or fixed by an interministerial body* placed under the joint authority of the Minister for Health, the Minister for Social Security and the Minister for Economy, depending on whether the health care product is subject to reimbursement by the French National Health Insurance:
  - *if the health care product is not reimbursed* by the French National Health Insurance, *the pharmaceutical company can freely set its price;* and
  - *if the health care product is reimbursed,* in whole or in part, *by the French National Health Insurance, its price will have to be negotiated with an interministerial body,* the Economic Committee for Health Products *("Comité économique des produits de santé" – "CEPS") (cf. 6.2).*
- Outside the common law framework, some health care products may also be reimbursed by the French National Health Insurance without being registered on one of the reimbursement lists, notably as part of the early access procedure for innovative pharmaceutical products (cf. 6.6). In those cases, *the price is set freely by the pharmaceutical company.*
- It must be noted that *pharmaceutical companies* marketing reimbursed health care products will have to *pay back a portion of their sales to the French National Health Insurance,* as part of schemes to regulate health care expenditure (safeguard clauses, contributions on sales, clawbacks, *etc.*).
- The players and procedures are similar for *pricing* and *reimbursement procedures* regarding *pharmaceutical products* and *medical devices*, although there are some *notable differences* that will be reviewed below.

2. Overview of the pricing and reimbursement for pharmaceutical products in France

In France, the reimbursement of a pharmaceutical product by the French National Health Insurance ("*Assurance maladie*") is subject to its registration by the Ministers for Health and Social Security on the list of pharmaceutical products reimbursable in pharmacies provided for in Article L.162-17 of the French Social Security Code ("*SSC*") (the "*liste des médicaments remboursables*") or on the list of pharmaceutical products reimbursable in health care establishments provided for in Article L.5123-2 of the French Public Health Code ("*PHC*") (the "*liste des spécialités agréées aux collectivités*"), and to the setting of its price by the Economic Committee for Health Products (*"Comité économique des produits de santé"* – "*CEPS*") (*cf.* diagram in *Annex*).

This registration involves various players at different stages of the procedure:

- the Transparency Committee (*"Commission de la transparence"* – "*CT*"), an independent scientific body of the French National Authority for Health ("Haute Autorité de santé" – "*HAS*"), which *assess the clinical value* of the pharmaceutical product;
- the Economic and Public Health Evaluation Committee (*"Commission d'évaluation économique et de santé publique*" – "*CEESP*"), another independent body of the HAS, which *assess the economic value* of the pharmaceutical product;
- the *CEPS* which *sets the price* of the pharmaceutical product;
- the French National Union of Health Insurance Funds *("Union nationale des caisses d'assurance maladie" – "UNCAM") which determine the reimbursement rate of a pharmaceutical product;* and
- the Ministers for Health and Social Security which *decide to register a pharmaceutical product* on the lists provided for in Article L.162-17 of the SSC and L.5123-2 of the PHC.

The application for registration must be submitted by the pharmaceutical company holding the marketing authorisation ("*MA*") or by the *exploitant*[1] and addressed to the Minister for Social Security who acknowledges receipt and informs the Minister in charge of Health. A copy is simultaneously addressed to the *CT* and to the *UNCAM*[2]. Each application has to be supported by a dossier containing the information required to assess the conditions for registration, as defined in Articles R.163-3 and R.163-5 of the SSC and described below.

Concurrently, the pharmaceutical company must suggest a price to the *CEPS* by means of an agreement.

Firstly, as a basis for pricing and reimbursement decisions, the *CT* performs (i) a clinical assessment while, if required, (ii) an economic assessment is performed by the *CEESP* (*cf. 6.1*). However, the clinical assessment is not required for generic and biosimilar pharmaceutical products, which are presumed to have the same clinical benefit as the reference pharmaceutical product[3].

Then, the *CEPS* will set the price of the pharmaceutical product while the *UNCAM* will determine its reimbursement rate, both with regard to the opinion of the *CT* and, where applicable, to the opinion of the *CEESP* (*cf. 6.2 and 6.3*).

Finally, the Ministers for Health and Social Security which decide whether the pharmaceutical product is registered on the *"liste des médicaments remboursables"* and/or the *"liste des spécialités agréées aux collectivités" (cf. 6.4)*.

However, other mechanisms exist in France allowing a pharmaceutical product to be reimbursed by the French National Health Insurance without being registered on the *"liste des médicaments remboursables"* or the "*liste des spécialités agréées aux collectivités" (cf. 6.6)*.

3. Pricing and reimbursement of pharmaceutical products in France

3.1 Assessment of the pharmaceutical product by the CT and, where applicable, by the CEEPS

(a) Clinical assessment by the CT

The *CT* is an independent scientific body of the *HAS*. One of the *CT*'s missions is to assess the appropriateness of a pharmaceutical product registration on the *"liste des médicaments remboursables"* and/or on the *"liste des spécialités agréées aux collectivités"*, indication by indication, by issuing a *clinical assessment of the pharmaceutical product in the light of its clinical benefit*.

The *clinical benefit ("CB")* of a pharmaceutical product in a given indication is assessed according to the following criteria[4]:

- the efficacy and adverse effects of the pharmaceutical product;
- the place in the therapeutic strategy of the pharmaceutical product, particularly with respect to the other therapies available;
- the seriousness of the disease targeted by the pharmaceutical product;
- the preventive, curative or symptomatic nature of the treatment; and
- the public health benefit of the pharmaceutical product.

1 French notion referring to *"the company or organization exploiting pharmaceutical products other than investigational pharmaceutical products, generators, kits and precursors. Exploitation includes wholesaling or free distribution, advertising, medical information, pharmacovigilance, batch monitoring and, where applicable, batch recall. as well as, where applicable, corresponding storage operations."* (Article R.5124-2 3° of the PHC).
2 Article R.163-8 of the SSC.
3 Articles R.163-3 (II) and R.163-4 of the SSC.

> For pharmaceutical products with a new action mechanism that have "demonstrated, with a high level of evidence, its superiority, combined with a clinically relevant effect in terms of mortality and morbidity, compared to a clinically relevant comparator, in a context of an inadequately met medical need for a serious disease."[6]

The *clinical added value ("CAV")* is an assessment of the therapeutic progress provided by a pharmaceutical product – notably in terms of efficacy or safety – compared with existing alternatives identified by the *CT*, which can be registered or not on a reimbursable list. In its doctrine, the *CT* outlines that particular attention is paid to the following criteria, in view of the medical need, to assess the CAV:

- the quality of the demonstration, which includes the comparison and the choice of comparator(s), the methodological quality of the study, the appropriateness of the population included for the indication, the relevance of the clinical endpoint and its significance, etc.;
- the effect size in terms of clinical efficacy, quality of life and safety in view of the robustness of the demonstration; and
- the clinical relevance of this effect compared to clinically relevant comparators[5].

The CAV can be rated as:

- *CAV I: major therapeutic progress*

  For pharmaceutical products with a new action mechanism that have *"demonstrated, with a high level of evidence, its superiority, combined with a clinically relevant effect in terms of mortality and morbidity, compared to a clinically relevant comparator, in a context of an inadequately met medical need for a serious disease."*[6]

4 Article R.163-3 of the SSC.
5 Doctrine of the CT, December 2, 2020, page 6.
6 Doctrine of the CT, December 2, 2020, page 10.

- *CAV II and III: substantial and moderate therapeutic progress*

  For pharmaceutical products that have *"demonstrated superiority combined with clinical efficacy in terms of mortality and morbidity, in a context of an inadequately met medical need. The evaluation of this efficacy may be positively adjusted by a substantial improvement in quality of life and/or safety."*

- *CAV IV: minor therapeutic progress*

  For pharmaceutical products that have a *"progress that is small compared to existing therapies it reflects a non-optimal demonstration and/or effect size (efficacy, quality of life and safety) in view of the medical context."*

- *CAV V: no improvement*

  For pharmaceutical products for which the demonstration was *"founded on a noninferiority trial"* or where *"a generic medicine, a biosimilar or a range supplement."*

The *CT* opinion must also include the following information[7]:

- an assessment, indication by indication, of the conditions of use of the pharmaceutical product, and in particular the duration of treatment, dosage and other indications useful for the correct prescription of the pharmaceutical product;
- an estimation of the target population based on available epidemiological data concerning the disease and the effects of existing treatments;
- for inclusion on the *"liste des médicaments remboursables"*, the classification of the pharmaceutical products with regard to the contribution of insured persons to the acquisition costs in three categories determined according to whether the CB is either major or substantial, moderate or minor; the *CT* also specifies, where applicable, whether the pharmaceutical product is to be considered irreplaceable; and
- an assessment of the appropriateness of the prescription conditions according to the indication, the dosage and the treatment duration.

The *CT* may also request additional data and post-registration studies (observational studies, early access data) for subsequent reassessment of the CB or the CAV which will have to be submitted by a date stipulated by the *CT*.

The opinion's project of the *CT* is communicated to the pharmaceutical company requesting the registration of its pharmaceutical product, which can submit written observation to the *CT* or request a hearing, ten (10) days following the reception of the opinion's project. This hearing must be held withing a maximum of forty-five (45) days of receipt of the request (reduced to one (1) month if requested by the Ministers for Health or Social Security)[8].

The *CT's* final opinion is communicated to the pharmaceutical company, with a copy to the *CEPS* and the *UNCAM*, and published on the *HAS* website.

Alongside the clinical assessment by the CT, the CEESP may carry out an economic assessment of the pharmaceutical product when several conditions are met.

(b) Economic assessment by the CEESP

The *CEESP* is an independent economic body of the HAS. One of the *CEEPS'* missions is to assess the appropriateness of a pharmaceutical product registration on the *"liste des médicaments remboursables" and/or on the "liste des spécialités agréées aux collectivités"*, indication by indication, by issuing an *economic assessment of the pharmaceutical product.*

This assessment will only be required *when the following two conditions are met*[9]*:*

- the pharmaceutical company requests recognition or confirmation of a major, substantial or moderate CAV; and
- the product or technology has or is likely to have a significant impact on health insurance expenditure, given its impact on the organisation of care, professional practices or patient care conditions and, where applicable, its price.

If these two conditions are met, the pharmaceutical company must submit, at the same time as it applies for registration, any medico-economic studies relating to the pharmaceutical product concerned, and the medico-economic models or data required for the CEESP' assessment. Simultaneously, the pharmaceutical company must send a copy of these elements to the *CEPS* electronically.

The *CEESP* may request additional data and specify the deadline for the pharmaceutical company to submit this information. The *CEESP* may also grant a hearing to the pharmaceutical company.

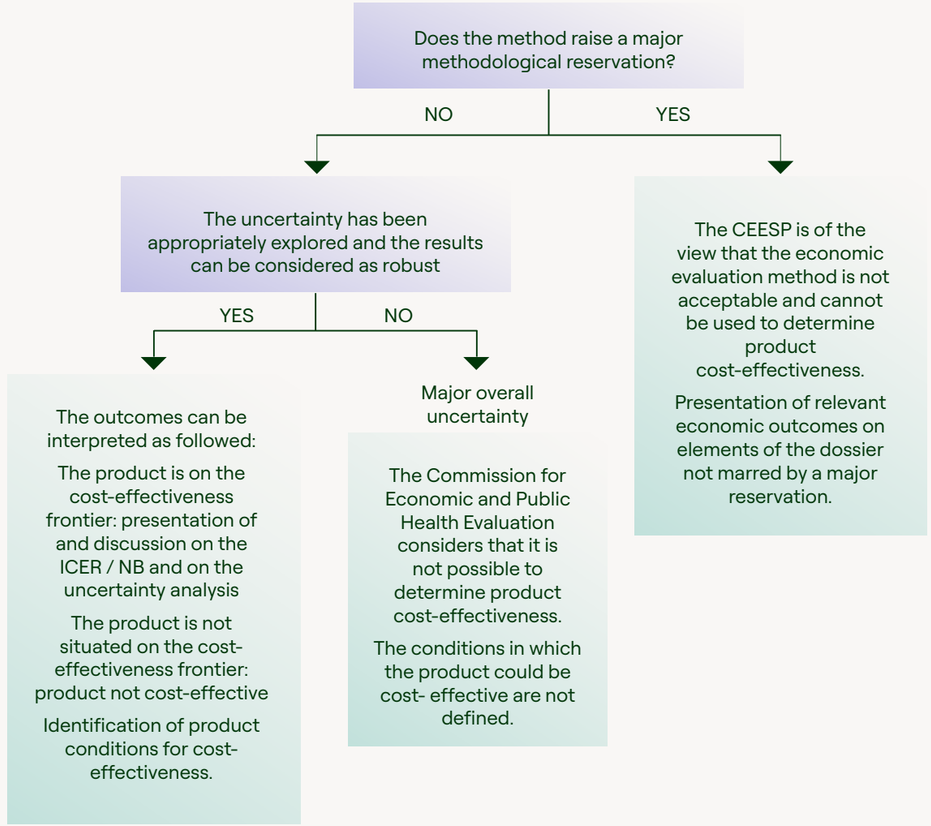
Once the dossier is complete, the *CEESP* will issue an opinion on the foreseeable or observed cost-effectiveness of the pharmaceutical product reimbursement, based on a comparative analysis, between the different medically relevant therapeutic alternatives, of the ratio between the costs incurred and the expected or observed benefits for the health and quality of life of the patients.

7 Article R.163-8 6° of the SSC.
8 Article R.163-16 (III) of the SSC.
9 Article R.161-71-3 of the SSC.

The *CEESP* may express reservations on the methodology used to generate the data involved in the economic evaluation (e.g. efficacy, safety, utility score or costs) or on the methodological choices used in the mode[10]:

- *minor reservation:* item deemed to fail to comply with the current recommendations, but which is justified or which has a negligible expected impact on the findings;
- *important reservation:* item deemed to fail to comply with the current recommendations, which can be justified, with a significant expected impact on the findings (particularly in terms of uncertainty). An important reservation does not call into question the validity of the economic evaluation but challenges the robustness of the quantitative outcomes set out on their proposed interpretation; and
- *major reservation:* item deemed to fail to comply with the current recommendations which invalidates all or part of the economic evaluation. The arguments associated with this item are not necessarily sufficient: a major shortcoming, even if it is justified, means that the analysis is no longer valid or informative.

The diagram below summarizes the main stages of *CEESP* analyses and findings[11].



The opinion's project is communicated to the *exploitant*, which may, within ten (10) days of receiving the opinion, request to be heard by the *CEESP* or submit written observations. The *CEESP* may modify its opinion in light of the observations submitted.

The final opinion is then communicated to the pharmaceutical company, with a copy to the *CEPS*, and is immediately published on the *HAS* website.

Once the CT, and where applicable the CEESP, have issued their opinions, negotiations on the price of the pharmaceutical product begins with the CEPS. At the same time, the Director General of the UNCAM decides on the reimbursement rate of the pharmaceutical product.

3.2 Pricing of the pharmaceutical product by the CEPS

The *CEPS* is an interministerial body placed under the joint authority of the Minister for Health, the Minister for Social Security and the Minister for Economy, which is involved in drawing up the economic policy for pharmaceutical products, and implements the guidelines it receives from the relevant ministers, in application of the Social Security Financing Laws.

The opinion's project is communicated to the exploitant, which may, within ten (10) days of receiving the opinion, request to be heard by the CEESP or submit written observations.

These ministerial guidance letters *("Lettres d'orientations ministérielles" – "LOM")* cover, in particular, ways of ensuring compliance with the National Health Insurance Expenditure Target (*"Objectif national de dépenses d'assurance maladie" "ONDAM"*).

One of the *CEPS* main missions is to set the facial price (price published in the Official Gazette) and the net price (facial price *less any clawbacks* agreed with the CEPS) of reimbursed pharmaceutical products in collaboration with the *exploitant*, according to various criteria (*cf.6.2.a*), which are different for generics and biosimilar pharmaceutical products (*cf. 6.2.d*).

Indeed, *in France, the price of reimbursable pharmaceutical products is set by an agreement between the exploitant and the CEPS or, if such negotiations fail, by a unilateral decision of the CEPS*, unless there is joint opposition from the ministers concerned, who then set the price within fifteen (15) days of the *CEPS'* decision[12].

Firstly, *within two (2) weeks* following receipt of the assessment from the *CT* and, where applicable, the *CEESP*, *the pharmaceutical companies wishing to enter into negotiations* concerning the pricing of their pharmaceutical product *must submit the relevant economic interest note* (*"note d'intérêt économique"* – "*NIE*") to the *CEPS*[13]. The *NIE* must contain the pharmaceutical company's initial price proposal and sales forecasts[14].

10 Doctrine of the CEESP, 6 July 2021, page 6.
11 Doctrine of the CEESP, 6 July 2021, page 10.
12 Article L.162-16-4 of the SSC.
13 Article R.163-8 of the SSC.
14 CEPS, Annual report 2023, December 2024, page 13.

Then, within four (4) weeks following receipt of the complete documentation, the *CEPS* must make a price counter-proposal to the pharmaceutical company. Once the *CEPS* has submitted its counter-proposal, negotiations with the pharmaceutical company begin.

Finally, if the negotiations between the *CEPS* and the pharmaceutical company s*ucceed, the pricing will be set in an agreement* between those entities. However, *if the negotiations fail*, the *CEPS will set the price unilaterally*. In both cases, the pricing decision is a regulatory decision that can be challenged before the administrative jurisdictions[15].

It should be noted that the final price may be subject to modification during the marketing of the pharmaceutical product *(cf. 6.2.e)*.

(a) Price-setting rules

The Article L.162-16-4 of the SSC sets a non-exhaustive list of the legal criteria taken into account by the *CEPS* to determine the facial price of pharmaceutical products:

- the CAV of the pharmaceutical product assessed by the *CT*;
- the prices of pharmaceutical products with the same therapeutic purpose;
- forecast or actual sales volumes;
- the foreseeable and actual conditions of use of the pharmaceutical product;
- the results of medico-economic evaluations; and
- supply security.

Also, other criteria, conventional and doctrinal criteria, have a major impact on the price-setting procedure:

- *conventional criteria:* a framework agreement concluded between the *CEPS* and the professional organisation representing pharmaceutical companies (the "*LEEM*") on 3 March 2021 (the "*Framework Agreement*" – "*Accord-cadre*") defines the price-setting rules and procedure, in particular how negotiations with the *CEPS* are to be conducted[16]; and
- *CEPS' doctrinal criteria:* finally, the price-setting rules and procedure are governed by the *CEPS'* doctrine which is a set of considerations and practices resulting from negotiations already carried out by the *CEPS, LOM,* and the consistent positions of the majority of its members in certain situations. The *CEPS'* doctrine is supposed to be published every year as an Activity Report for the past year[17].

According to all those criteria, the price of the pharmaceutical product will mostly be defined by the CAV level. However, the *CEPS* is not constrained by the *CT's* assessment of the CAV. When the setting of the pharmaceutical product's price is based on an assessment of the CAV different from that of the *CT*, the *CEPS* informs the *CT* of the reasons for its assessment [18].

(b) Pricing of pharmaceutical products with major, substantial, moderate or minor CAV (I, II, III or IV)

The Framework Agreement provides a European price guarantee for pharmaceutical products with major, substantial or moderate CAV (I, II or III) if the main manufacturing phases are carried out in France[19]. A European price guarantee means that the *facial price excluding taxes cannot be lower than the lowest price on the four European reference countries,* which are the United Kingdom, Germany, Spain and Italy[20].

The European price guarantee can also be granted to pharmaceutical products with a minor CAV (IV) that meet one of the following conditions[21]:

- the CAV has been assessed in relation to a clinically relevant comparator with a major, substantial or moderate CAV (I, II or III) assessed less than five (5) years ago;
- the pharmaceutical product is dominant in terms of efficiency, as demonstrated by the economic assessment of the *CEESP*, in the absence of major reservation or major overall uncertainty;
- it fulfills a medical need or a public health need given the insufficient number of comparators available;
- it is an antibiotic pharmaceutical product with a new active substance;
- it is an orphan pharmaceutical product; or
- it is a new pharmaceutical product associated with a combo-therapy.

15 CE, December 30, 2015, Mylan, no. 375777 and CE, December 30, 2003, Serono France, no. 243954.
16 Articles 9 and 11 of the Framework Agreement.
17 Article D.162-2-4 of the SSC.
18 Article L.162-16-4 of the SSC.
19 Article 11 of the Framework Agreement.

However, the facial price of pharmaceutical products with a minor CAV (IV) that do not meet any of the conditions listed above is set according to the price of the relevant comparators under intellectual property rights, and will have to be lower than the price of the product in the European reference countries.

After setting the facial price of the pharmaceutical product, *the pharmaceutical company negotiates the net price with the CEPS via the use of clawbacks, which can be of seven different types*[22]: (i) volume clawbacks at the first box; (ii) price-volume clawbacks; (iii) daily treatment cost clawbacks; (iv) proper-use clawbacks; (v) capping clawbacks; (vi) performance-based clawbacks and (vii) compassionate access or early access clawbacks.

(i) Volume clawback at the first box

From the first unit and for every unit sold, the pharmaceutical company pays to the French National Health Insurance the difference between the facial price and the net price for each unit. These clawbacks are intended to be converted into price reductions[23].

(ii) Price-volume clawbacks

Price-volume clawbacks are designed to take account of sales volumes, or to ensure that the indication population or a sub-population is not exceeded. If actual sales exceed a certain amount, which is set during negotiations with the *CEPS*, the pharmaceutical company must pay a certain amount to the French National Health Insurance[24].

(iii) Daily treatment cost clawbacks

The purpose of these clawbacks is to ensure the stability of the negotiated net cost of treatment with regard to the diversity of clinical situations and the unpredictability of prescribers' behavior. Such clawbacks are not intended to be triggered if the reference situation is indeed an average reflection of real life and are harder to implement, as they require additional data beyond just the number of units sold and, at the very least, the number of patients treated or initiating treatment[25].

(iv) Proper-use clawbacks

Proper-use clawbacks are designed to secure the product's budgetary impact strictly within the perimeter covered at the time of registration. They may be based either on an annual expenditure threshold, beyond which the company reimburses additional units sold in full, or on the collection of specific information relating to the indication or patient treated[26].

(v) Capping clawbacks

Capping clawbacks refer to the payment of 100% of sales in excess of an amount set out in the price agreement, corresponding to a negotiated lump sum, notably under Article 15.a of the Framework Agreement for orphan pharmaceutical products, in return for the granting of a price in line with international practice.

In some cases, the *CEPS* may wish to associate a caping clause with other products if there is a risk of prescribing outside the reimbursed indication, or if prescribers are likely to anticipate a forthcoming extension of the indication before the terms of reimbursement and pricing have been established[27].

(vi) Performance-based clawbacks

Performance-based clawbacks are based on individual clinical results, and assume reliable data collection. In the event of poor results, the pharmaceutical company will be required to pay an amount confidentially negotiated with the *CEPS* to the French National Health Insurance.

Nevertheless, the *CEPS* has observed a high degree of stability in performance results, and concludes that performance-based clawbacks are not sufficiently useful to justify their complexity and cost. As a result, no performance-based clawbacks were signed in 2022[28].

20 Article D.162-2-9 of the SSC.
21 Article 11 of the Framework Agreement.
22 Article 23 of the Framework Agreement and CEPS, Annual report 2023, December 2024, pages 15 to 19.
23 Article 19 of the Framework Agreement.
24 Article 23 of the Framework Agreement.
25 CEPS, Annual report 2023, December 2024, page 17.
26 CEPS, Annual report 2023, December 2024, page 18.
27 CEPS, Annual report 2023, December 2024, page 18.
28 Article 16 of the Framework Agreement.

(vii) Compassionate access or early access clawbacks

Pharmaceutical products under compassionate access or early access schemes are subject to specific clawbacks negotiated with the *CEPS (cf. 6.2.b)*.

(c) Pricing of pharmaceutical products with no CAV (V)

The facial price of pharmaceutical products with no CAV (V) is equivalent to the net price. In other terms, there are no clawbacks negotiated between the pharmaceutical company and the CEPS for pharmaceutical products with no clinical added value (V).

CEPS, however, points out a few situations in which the facial price is different from the net price:

- either it is an orphan pharmaceutical product subject to lump-sum financing under Article 15.a) of the Framework Agreement, in compliance with Article R.163-5 of the SSC; and
- or the CAV (V) has been assessed in relation to a very recent and innovative comparator, whose facial price is itself decorrelated from the net price. In such cases, the CEPS may accept the use of a temporary, low-amplitude clawback for a pharmaceutical product with no CAV (V)[29].

(d) Pricing of generic and biosimilar pharmaceutical products

The procedure described above does not apply to generic and biosimilar pharmaceutical products because *their price will be based on the price of the reference pharmaceutical product.*

Indeed, the Framework Agreement stipulates that the price of the *generics* is to be 60% of the price of the reference pharmaceutical product. Moreover, the Framework Agreement also provided for a 20% price reduction for the reference pharmaceutical product when the generic is actually marketed, and a second price decrease after 18 months (12,5% for the reference pharmaceutical product and 7% for the generic)[30].

The Framework Agreement also stipulates that the price of the *biosimilars* is set on the basis of the reference pharmaceutical product to which a price reduction is applied, fixed by agreement between the pharmaceutical company and the *CEPS*. Moreover, the Framework Agreement also provided for a 20% to 40% price decrease for the reference pharmaceutical product when the biosimilar is actually marketed, and various additional price reductions to the reference pharmaceutical product after twenty four (24) months of marketing of the biosimilar[31].

(e) Price variations

Price variations may be (i) stipulated by agreement or (ii) requested by the company or (iii) the public bodies.

For pharmaceutical products with major, substantial or moderate CAV (I, II or III) that benefit from the European price guarantee and have been economically assessed by the *CEESP*, the price cannot be modified before a five (5) year period from the marketing date. For all other pharmaceutical products, the period during which the price cannot be modified is three (3) years[32].

(i) Conventional price variations

Variations of the price of a pharmaceutical product may be provided for by an agreement[33]. The price of a pharmaceutical product may be modified by an agreement between the pharmaceutical company and the *CEPS*[34], such contractual revisions may take place in the event of a change in the initial data for inclusion of the pharmaceutical product on a reimbursement list[35] or in the event of a new ministerial guideline and/or the *ONDAM*[36].

When the change in the selling price of a pharmaceutical product has been provided for in the agreement, the company sends the necessary information to the *CEPS*, at least forty (40) days before the date on which the new price is to be applied. The *CEPS* ensures that the conditions for price changes laid down in the agreement have been met, and informs the company before this date. If so, the new price is published in the Official Gazette before the said date.

In particular, the *CEPS* may agree to adjust the price of a pharmaceutical product according to the overall sales volume of all pharmaceutical products in the product's therapeutic class[37].

29 CEPS, Annual report 2023, December 2024, page 21.
30 Article 24 of the Framework Agreement.
31 Article 25 of the Framework Agreement.
32 Article 17 of the Framework Agreement.

The request for a price modification can be made by the pharmaceutical company, which sends its request to the CEPS, with a copy to the Minister for Social Security.

(ii) Price variations at the company's request

The request for a price modification can be made by the pharmaceutical company, which sends its request to the *CEPS*, with a copy to the Minister for Social Security. The *CEPS* renders its decision within ninety (90) days (one hundred and fifty (150) days in the case of high activity[38].

If the information provided by the pharmaceutical company marketing the pharmaceutical product or ensuring its parallel importation or distribution is insufficient, in particular for the negotiation of the agreement, the *CEPS* will immediately notify the pharmaceutical company of the list of additional information it must provide. In this case, the deadline is suspended from the date of receipt of the notification until the date of receipt of the additional information requested.

The absence of a response within those deadlines is deemed to be an implicit decision to accept the price modification which will be published in the Official Gazette[39].

Decisions to refuse all or part of a price modification is communicated to the pharmaceutical company, together with the reasons for the decision and the applicable appeal procedures and deadlines[40].

The Council of State – the French administrative supreme court – *("Conseil d'Etat")* has annulled a refusal to increase the price of a pharmaceutical product on the grounds of insufficient justification. On this occasion, the Council of State emphasized that, while the *CEPS* may base its estimate of the CAV on the information contained in the opinion issued by the *CT* when the pharmaceutical product was included on the list of reimbursable pharmaceutical products, it is up to the *CEPS* itself to assess all the factors leading to the setting the price of the pharmaceutical products, and in particular to verify that this price is justified in relation to the prices of products with the same therapeutic purpose, taking into account the difference in CAV provided by this product[41].

33 Article R.162-20-1 of the SSC.
34 Article R.163-11 (I) of the SSC.
35 Article R.163-12 of the SSC.
36 Articles L.162-17-4 and R.162-20-2 of the SSC.
37 CE, 1st and 6th ss-sect, October 20, 2004, Bayer Pharma, no. 256899.
38 Article R.163-11 (II) of the SSC.
39 Article R.163-11 (II) of the SSC.
40 Article R.163-14 of the SSC.
41 CE, October 23, 2002, Mayoly Spindler, no. 237875.

(iii) Price variations at the request of the public bodies

When the request for a price modification is made by the Minister for Social Security, the Minister for Health and the Minister for Economy, or by the *CEPS*, the pharmaceutical company is informed and may submit written observations or ask to be heard by the *CEPS* within one (1) month of receipt. In this case, the hearing takes place on a date set by the *CEPS*, no later than forty-five (45) days after receipt of the request[42].

In addition, when the agreements concluded are no longer compatible with the ministerial guidelines received by the *CEPS*, or when the trend in pharmaceutical products expenditure is clearly not compatible with the *ONDAM* or when the scientific and epidemiological data taken into account in concluding the agreements have changed significantly, the *CEPS* asks the pharmaceutical company to conclude an amendment to adapt the agreement to this situation, indicating the reasons for this proposal[43].

If the pharmaceutical company refuses to enter into the said amendment within two (2) months of the same date, the *CEPS* may terminate the agreement or some of its provisions and set the price of the pharmaceutical product by a unilateral decision taken by way of application in Article L.162-16-4 of the SSC[44].

3.3 Determination of the reimbursement rate by the UNCAM

The level of reimbursement for pharmaceutical products is determined by the Director General of the *UNCAM*, *who sets the rate of contribution for insured persons on the basis of the opinion of the CT*. Indeed, as previously outlined (*cf. 6.1*), the *CT* must classify the pharmaceutical product in one of the three (3) categories determined *on the basis of the level of CB*[45].

42 Article R.163-14 (III) of the SSC.
43 Article R.162-20-2 of the SSC.
44 Article L.162-17-4 of the SSC.
45 Article R.163-8 6° of the SSC.
46 Article R.165-8 of the SSC.51 Article R.163-10-1 paragraph 1 of the SSC.

The *CT's* opinion therefore classifies the pharmaceutical product according to the following scale:

- *15%:* for pharmaceutical products with a minor CB (usually as part of a reassessment);
- *30%:* for pharmaceutical products with a moderate CB, homeopathic pharmaceutical products and certain magistral preparations;
- *65%:* for pharmaceutical products with a major or important CB; and
- *100%:* for pharmaceutical products deemed irreplaceable and costly.

With regards to these scales, the rate of contribution for insured persons is set by the Director General of *UNCAM* within the following limits:

- *0%:* pharmaceutical products deemed irreplaceable and costly[46];
- *between 80% and 90%:* pharmaceutical products with a minor CB in all of their indications[47];
- *between 70% and 75%:* pharmaceutical products intended primarily for the treatment of disorders or diseases which are not usually serious, and for pharmaceutical products with a moderate CB[48]; and
- *between 30 and 40%:* all other pharmaceutical products[49].

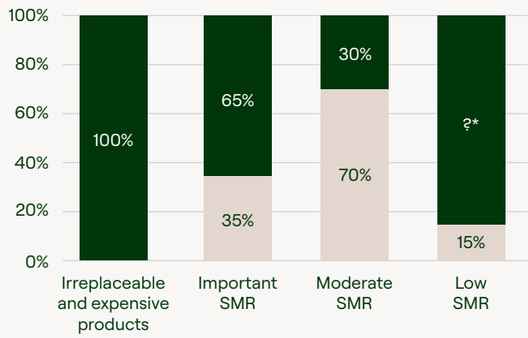
Therefore, the Director General of the UNCAM has limited powers to determine the reimbursement rate, since it is based on the level of CB determined by the CT. The Council of State has confirmed that the Director General of the *UNCAM* has a margin of appreciation that is limited to the possible adjustment of the rate within a range of the scale determined by the *CT* in its opinion[50].

Furthermore, the *UNCAM*'s decision is only effective if the pharmaceutical product is registered on the *"liste des médicaments remboursables"* by the Ministers for Health and Social Security[51].

47 Article R.160-5 14° of the SSC.
48 Article R.160-5 6° of the SSC.
49 Article R.160-5 11° of the SSC.
50 CE, October 4, 2013, Laboratoires Servier, no. 355097.
51 Article R.163-10-1 paragraph 1 of the SSC.

In France, the public health reimbursement rate set by the *UNCAM* is usually complemented by private health insurances as follows:

Level of reimbursement depending on SMR



*Complementary private health insurances generally not reimburse low SMRs

3.4 Registration of the pharmaceutical product by the Ministers for Health and Social Security

Finally, once the *CEPS* has set the price and the *UNCAM* has determined the reimbursement rate of the pharmaceutical product, *the Ministers for Health and Social Security issue a joint Ministerial Order, published in the Official Gazette, registering the pharmaceutical product on the "liste des médicaments remboursables" and/or on the "liste des spécialités agréées aux collectivités".*

The Ministerial Order specifies the only therapeutic indications for which the pharmaceutical product is eligible for reimbursement[52]. Each extension of indication must be subject to another Ministerial Order issued by the Ministers for Health and Social Security[53].

The Ministers for Health and Social Security can refuse to register a pharmaceutical product. The Social Security Code sets out *legal criteria* for refusing to register a pharmaceutical product on the *"liste des médicaments remboursables" or on the "liste des spécialités agréées aux collectivités"*[54]:

- Pharmaceutical products whose packaging, labelling, package leaflet or advertising to health care professionals refer to non-therapeutic or non-diagnostic use.
- Pharmaceutical products that neither improve the clinical added value (CAV V) nor reduce the cost of treatment.
- Pharmaceutical products likely to lead to higher consumption or unjustified expenditure.
- Pharmaceutical products for which the price proposed by the pharmaceutical company is not justified in view of the CAV, where applicable of the results of any medico-economic assessment, of the prices of pharmaceutical products with the same therapeutic purpose, of forecast or actual sales volumes and of the foreseeable and actual conditions of use of the pharmaceutical product.
- Pharmaceutical products whose form, dosage or presentation are not justified by their therapeutic or diagnostic use.
- Pharmaceutical products which have been advertised to the public.

When the pharmaceutical products do not meet any of the legal criteria justifying refusal of registration, the Ministers for Health and Social Security will base their decision on the assessment of the CB, indication by indication, to decide whether to include these pharmaceutical products on the *"liste des médicaments remboursables" and/or on the "liste des spécialités agréées aux collectivités"*.

However, they are not bound by the opinion of the CT, unlike the *UNCAM*, and may depart from it to reach their decision.

Should a decision be taken to refuse to register a pharmaceutical product (in whole or in part), the Ministers for Health and Social Security must inform the pharmaceutical company of the *reasons for the refusal, based on objective and verifiable criteria, and the applicable appeal procedures and deadlines*[55].

The pharmaceutical company then *has two (2) months* from receipt of notification of the decision by the Ministers for Health and Social Security *to contest the refusal* of registration before the Council of State.

It should be noted that, as the above mentioned *opinion of the CT* is considered to be a preparatory act for a regulatory decision, it *cannot be contested before the courts*[56]. The Council of State recently confirmed that *the doctrine of the CT is not enforceable against the Ministers*, considering that it *"does not have the character of a prescription which is binding on the ministers"*[57].

Should a decision be taken to accept to register a pharmaceutical product, *the decision must be published in the Official Gazette, at the same time as the price decision and the reimbursement rate decision*.

52 Article L.162-17 of the SSC.
53 CE, May 28, 2003, Syndicat national de l'industrie pharmaceutique, no. 240795.
54 Article R.163-5 of the SSC.
55 Article R.163-14 of the SSC and CE, December 30, 2021, Syndicat Les Entreprises du médicament, no. 450193.
56 CE, June 12, 2002, Janssen-Cilag, no. 231314.
57 CE, July 17, 2024, Incyte Biosciences, no. 470665.
58 Article L.162-17-2 of the SSC.
59 Article R.163-9 of the SSC and Article 6 of the Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems.
60 Article R.163-9 of the SSC.
61 Article R.163-9 of the SSC.

It should also be noted that when a pharmaceutical company requested registration on the *"liste des médicaments remboursables"* and on the *"liste des spécialités agréées aux collectivités"*, the decision to register a pharmaceutical product on the *"liste des médicaments remboursables"* shall constitute a decision to register on the *"liste des spécialités agréées aux collectivités"*[58].

3.5 Registration procedure deadlines

The registration procedure must be completed within *one hundred and eighty (180) days* of receipt of the registration dossier application by the Ministers for Health and Social Security [59]. If the pharmaceutical company has applied for registration of its pharmaceutical product only on the *"liste des spécialités agréées aux collectivités"*, the decision of the Minister for Social Security alone must be published in the Official Gazette and notified to the pharmaceutical company within ninety (90) days of receipt of the application[60].

Furthermore, if the information provided by the pharmaceutical company is insufficient, these deadlines are suspended from the date of receipt of notification of the request for additional information by the Ministers for Health or Social Security, the *CEPS* or the *CT*[61].

The absence of a response within those deadlines is deemed to be an *implicit decision to reject the registration*[62].

However, this *one hundred and eighty (180) days* deadline is not sanctioned and is generally not respected, France being well known as the "worst country" in Europe in terms of market access timelines.

In 2022, the *average processing time for the "liste des médicaments remboursables" registration of non-generic pharmaceutical products* was *two hundred and eighteen (218) days* (one hundred and ten (110) days for generic) . *The average time to market* – from the date of the marketing authorisation to the date of the pharmaceutical product's registration – is *five hundred and twenty seven (527) days*. However, if the early access procedures are not included, the *average time to market* is *four hundred and twenty four (424) days*[64].

Within these theoretical *one hundred and eighty (180) days,* each player is subject to specific deadlines:

- For the *CT*: the *median processing time for applications for registration and extension of indication was one hundred and three (103) days in 2023,* with eighty nine (89) days for registration alone[65].
- For the *CEPS*: *the average instruction time was thirty nine (39) days* and the *average negotiation time was seventy (70) days for non-generic pharmaceutical products in 2022*[66].
- For the *UNCAM*: the decision setting the rate of the insured person's contribution must be communicated to the Ministers for Health and Social Security within a *maximum period of fifteen (15) days* following the date of receipt by the *UNCAM* of the final opinion of the *CT*[67].

3.6 Early access program

Outside the common law framework described above, some pharmaceutical products may also be reimbursed by the French National Health Insurance without being registered on the *"liste des médicaments remboursables"* or the *"liste des spécialités agréées aux collectivités",* notably as part of the early access procedure provided for in Article L.5121-12 of the PHC.

Early access authorisation is an exceptional derogation based scheme enabling the early availability and reimbursement in health care establishments for one or more indication(s) of a pharmaceutical product indicated for a severe, rare or incapacitating disease, when all the following conditions provided for in Article L.5121-12 of the PHC are met:

- there is no appropriate treatment;
- the initiation of the treatment cannot be deferred;
- the efficacy and safety of the medicinal product is strongly presumed based on the results of clinical trials;
- this medicinal product is presumed to be innovative, notably compared with a clinically relevant comparator.

62 CE, June 12, 2002, Janssen-Cillag, no. 231314; CE, March 26, 2004, Mayoly-Spindler, no. 246619.
63 CEPS, Activity Report 2022, January 2024, page 50.
64 IQVIA, EFPIA Patients W.A.I.T. Indicator 2023 Survey, June 2024, page 15.
65 CT, Activity Report 2023, page 12.
66 CEPS, Activity Report 2022, January 2024, page 54.
67 Article R.163-10-1 paragraph 2 of the SSC.

There are two distinct types of early access schemes:

- *pre-MA early access:* this refers to a pharmaceutical product which does not have a MA in the indication, and for which the pharmaceutical company has submitted, or has undertaken to submit, an application for such marketing authorisation within a timeframe set by the *HAS,* which may not exceed a limit set by decree at two years; and
- *post-MA early access:* this refers to a pharmaceutical product which has been granted a MA in the indication, but which is not registered on the *"liste des médicaments remboursables"* or the *"liste des spécialités agréées aux collectivités"* for that same indication, and for which the pharmaceutical company has submitted, or has undertaken to submit, an application for registration on one of these lists, within one month of obtaining its MA

Regardless of the situation involved, the decision to grant early access will be taken by the *HAS*, for each indication, for a maximum period of one (1) year, with several possible annual renewals[68]. In the case of a pre-MA early access decision, the *HAS* decision must be preceded by an approval from the *ANSM*, attesting to the strong presumption of efficacy and safety of the pharmaceutical product in each indication.

The application is sent by the MA holder, or its representative, by electronic means, to the *HAS* and to the Ministers for Health and Social Security, and, where applicable, to the *ANSM*. It must be supplemented by a dossier, including, in particular, the proposed summary of product characteristics, labelling and packaging leaflet [69].

The early access authorisation decision must be communicated to the pharmaceutical company within three (3) months from acknowledgement of receipt of the complete application dossier. The silence kept by the *HAS* constitutes acceptance in the case of post-MA early access and in the case of pre-MA early access if the *ANSM* has given its approval within this period[70].

Reimbursement under the early access scheme ends when the pharmaceutical product is registered on the *"liste des médicaments remboursables"* or *"liste des spécialités agréées aux collectivités"* for the indication.

Reimbursement under the early access scheme also ends in the following cases:

- in the case of withdrawal or suspension of the early access authorisation;
- in the event of a refusal to register the indication on the *"liste des médicaments remboursables"* or the *"liste des spécialités agréées aux collectivités"*; and
- in the event of a withdrawal of the MA application or a withdrawal of the application for registration on the *"liste des médicaments remboursables"* or the "*liste des spécialités agréées aux collectivités"*.

The price of early access pharmaceutical products is set freely by the pharmaceutical company, which declares the maximum compensation it claims to the *CEPS*.

On 15 February of each year, the pharmaceutical company informs the *CEPS* of its turnover for the pharmaceutical product under early access and the number of units sold, for each of the indications, for the previous calendar year.

Although the price is freely set by the pharmaceutical company, the French legislator has introduced clawback mechanisms designed to regulate expenditure of early access pharmaceutical products.

Firstly, the pharmaceutical company must pay *annual clawbacks* calculated on the basis of the turnover, excluding taxes charged to health care establishments. The rates of these clawbacks are defined according to a progressive scale by turnover tranches, set by ministerial decree as follows[71]:

- Between €0 and €1,000,000.00: 10%.
- Between €1,000,000.01 and €5,000,000.00: 25%.
- Between €5,000,000.01 and €20,000,000.00: 35%.
- Between €20,000,000.01 and €50,000,000.00: 50%.
- Between €50,000,000.01 and €100,000,000.00: 60%.
- Over €100,000,000: 70%.

68 Article D.5121-69-3 of the PHC.
69 Article R.5121-68 of the PHC.
70 Article R.5121-69 of the PHC.
71 Ministerial Order of July 1st, 2021, NOR SSAS2118381A.

The amount of these clawbacks may be increased for one of the following reasons:

- in the absence of a MA application or reimbursement registration within the deadline;
- in the absence of an agreement signed with the *CEPS* within one hundred and eighty (180) days of the application for registration on the *"liste des médicaments remboursables"* or the *"liste des spécialités agréées aux collectivités"*;
- in the event of registration for reimbursement of another pharmaceutical product identified by the *HAS* as covering the therapeutic need in the indication; and
- when the indication is the subject of the *HAS* assessment, at the time of application for registration on the *"liste des médicaments remboursables"* or on the *"liste des spécialités agréées aux collectivités"*, which challenges the presumption of innovation of the pharmaceutical product in question.

Secondly, the pharmaceutical company will be required to pay a second clawback when the pharmaceutical product is registered in one of the lists under its MA, which includes all or part of the indication concerned by the early access scheme. The amount of the clawback will be set by agreement or by unilateral decision of the *CEPS*, in accordance with the following modalities:

- the turnover that would have resulted from the valuation of units sold for the indication, reimbursed under early access and, where applicable, compassionate access, at the net reference price over the entire reimbursement period; and
- the turnover charged to health care establishments, after deduction of annual clawbacks, for the indication and for the calendar year for which the clawback was paid, over the entire reimbursement period.

If the first amount is lower than the second amount, the pharmaceutical company has to pay an additional clawback equal to the difference between these two amounts. If this is not the case, the difference between these two amounts is reimbursed to the pharmaceutical company, up to the limit of the annual clawback paid for the indication over the entire period of reimbursement under the early access scheme[72].

72 Article L.162-16-5-1-1 of the SSC.

The clawback must be paid in a single payment, for the year in which the indication is registered in the reimbursement list, unless the pharmaceutical company signs an agreement with the *CEPS* before 1 May of the year following the calendar year in which the registration in the reimbursement list occurred.

4. Overview of the pricing and reimbursement for medical devices in France

In France, the reimbursement of a medical device ("*MD*" or "*MDs*") by the National Health Insurance is contingent upon its registration on the *list of reimbursable products and services* (*"liste des produits et prestations remboursables"* – "*LPPR*") or through *diagnosis-related groups* (*"groupes homogènes de séjour"* – *"GHS") (cf. 8.1)*.

This process involves multiple key players at various stages:

- The *Ministers for Health and Social Security* that ultimately decides whether a medical device is registered on the *LPPR (cf. 8.1)*.
- The Committee for the Evaluation of Medical Devices and Health Technologies *("Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé"* – "*CNEDiMTS*") an independent scientific body of the HAS that assesses the clinical value and effectiveness of the medical device *(cf. 8.2)*, as does the *CT* for pharmaceutical products *(cf. 6.1.a)*.
- The *CEPS* is responsible for setting key factors regarding the price of the medical device, considering clinical evaluations and economic factors *(cf. 8.3)*.

To initiate registration, the manufacturer must submit an application to the *Ministers for Health and Social Security*, who acknowledge receipt and forward it to *CNEDiMTS* for clinical evaluation. If necessary, an additional economic assessment may be conducted.

The registration process can proceed in one of two ways *(cf. 8.1)*:

- *Generic registration:* the device is registered under a generic description in the *LPPR*, which specifies the technical requirements that the product must meet.
- *Trademark registration:* notably for innovative devices or those that require special monitoring, the registration is made under a trademark or brand name.

Based on *CNEDiMTS'* clinical assessment and, if applicable, the economic evaluation, the *CEPS* can impose a *responsibility tariff* and a *sale price limit*. The responsibility tariff is the amount used as base for reimbursement, the sale price limit is the maximum price that can be charged to patients *(cf. 8.3)*.

Furthermore, as the requirements for inclusion on the *LPPR* were not always adapted to digital remote monitoring medical devices, a new registration list for medical telemonitoring activities has been implemented by the Social Security Financing Law ("*SSFL*") for 2022: the *List of Medical Telemonitoring Activities* (*"liste des activités de télésurveillance médicale"* – "*LATM*")[73].

As for the *LPPR*, registration under the LATM can be made under a *generic description or under a brand name*. Moreover, the registration is made for a *maximum period of five (5) years*.

The registration on the LATM is subject to:

- the obtention of a certificate of compliance with the interoperability and security reference framework drawn up by the French Digital Health Agency ("*Agence du numérique en santé*" – "*ANS*"); and
- a favourable opinion from the *CNEDiMTS*, for registration under a brand name which attests to the existence of an improvement in the medical service provided by the remote medical monitoring activity with regard to the reference frameworks registered in the indication concerned, where they exist, or, failing that, with regard to the same treatment without remote monitoring.

Other reimbursement schemes also exist, such as the *Innovation Funding* ("*Forfait Innovation*"), which allows temporary reimbursement for innovative MDs, or the *transitional coverage* scheme, which offers reimbursement for devices pending standard registration on the *LPPR (cf. 8.4)*. Both systems facilitate access to innovative technologies under specific conditions while clinical and economic evaluations are conducted.

As for digital MDs, the early reimbursement for digital MDs scheme ("*prise en charge anticipée des dispositifs médicaux numériques*" – "*PECAN*") allows early reimbursement for *digital MDs used for therapeutic purposes or for remote monitoring.*

5. Pricing and reimbursement of medical devices in France

5.1 Registration of a medical device for reimbursement

In France, the reimbursement of a MD that is not intended to be used in health care organisations is subject to its *registration* on the *LPPR* set out under Article L.165-1 of the SSC.

As for MDs used in *health care establishments*, they are mainly reimbursed through *GHS*[74], with the exception of certain MDs reimbursed *outside of GHS*. These devices are *included in the LPPR* separately from hospital services, commonly referred to as the "*additional list*" ("*liste en sus*")[75].

The *application for registration* on the LPPR must be submitted to the *Ministers for Health and Social Security*. Registration is carried out either by means of *a generic description of all or part of the product concerned*, or in the form of a *trademark or brand name*. In practice, this means that the registration can be made in the form of a *generic description, under a generic line*. Those generic lines *are already registered* under the *LPPR* and set out *technical specifications* that the medical device *must meet* in order to be registered under it[76].

The registration of a MD by means of a *generic description* has a validity period of *ten (10) years renewable* and of *five (5) years renewable* for registration in the form of a *trademark or tradename*[76].

Where the medical device *cannot be included in one of the two classifications of the generic line* described above, the registration can be made in the form of a *trademark or brand name* for i*nnovative devices*, or when the *impact on health insurance expenditure*, *public health requirements* or the control of *minimum technical specifications* requires *special monitoring of the product*. In that case, a *medico-technical assessment* by the *CNEDiMTS (cf. 7.2)* is *mandatory*.

5.2 Medico-technical assessment of the MD

In the cases of *an initial application for registration on the LPPR*, a request to have the *conditions of registration modified* or an application for *registration renewal*, the *CNEDiMTS*, an independent scientific body of the *HAS*, assesses the *actual clinical benefit* ("*service attendu*" – "*SA*" for initial applications), ("*service rendu*" – "*SR*" for registration renewal requests) and, if it is sufficient, the clinical added value ("*amélioration du service attendu*" – "*ASA*" for initial applications), ("amélioration du service rendu" – "*ASR*" for registration renewal requests), that can be *absent, minor, moderate, important* or *major*.

The SA is used to determine whether a MD is to be *reimbursed or not* (sufficient or insufficient). The ASA is used during the *price fixation procedure (cf. 8.3)*.

The opinion of the *CNEDiMTS* is then sent to the *CEPS* for the price fixation procedure. Ultimately, the decision on reimbursement rests with the Ministers for Health and Social Security.

5.3 Price fixation and reimbursement procedures

The manufacturer can *freely set the price* of its MD whether it is registered for reimbursement or not.

However, if the MD is *reimbursed*, the *CEPS* can set a "*responsibility tariff*" ("tarif de responsabilité" – "*TR*") and a *sale price limit* ("prix limite de vente" – "*PLV*").

The *TR* is the amount on which the *reimbursement* is based. The *TR* can be *negotiated* with the *CEPS* or *unilaterally set* by it[77].

The *PLV* is the *maximum price* that the public can be charged for a MD. The *PLV* is indeed imposed on distributors (pharmacies, medical equipment suppliers, etc.)[78].

Thus, the difference between the *PLV* and the *TR* falls under the private insurance bodies.

In most cases, the *TR* and *PLV* are *identical*, therefore patients without supplemental private health insurance have no additional costs to cover[79].

73 Article L.162-52 of the SSC.
74 Article L.165-11 of the SSC.
75 Article L.162-22-7 of the SSC.
76 Article R.165-3 of the SSC.
77 Article L.165-2 of the SSC.
78 Article L.165-3 of the SSC.
79 HAS' Guide " Pathway of medical devices in France" – page 34.

Both the *TR* and *PLV* are determined mostly on the basis of[80]:

- the *ASA* or *ASR*;
- if applicable, the results of the medico-economic assessment of tariffs of comparable products or services;
- planned or observed sale volumes;
- planned or observed amounts reimbursed by the compulsory French National Health Insurance scheme; and
- anticipated and actual conditions of use.

For a registration by means of a *generic description (cf. 8.1)* a *TR* and a *PLV* are set in the *LPPR* for *each product category* and are applicable to *all MDs* meeting the *generic description*[81].

5.4 Specific procedure regarding pricing and reimbursement

(a) The Innovation Funding

The national *Innovation Funding* mechanism ("*Forfait Innovation*") allows *exceptional* and *temporary reimbursement* with the aim of facilitating access to *innovative technologies*[82].

This derogatory reimbursement is subject to the completion of clinical or medico-economic studies, the project for which must be presented when the application is submitted (pay to see principle)[84].

To be considered as innovative, a MD must meet *several criteria*[83]:

- the MD presents a character of *novelty* other than a simple technical evolution in relation to the health technologies used in the claimed indications;
- it is in an *early phase of diffusion*, does not justify a sufficient *SA* based on available clinical or medico-economic data, is not and has never been publicly reimbursed in the claimed indications;
- the *risks to the patient* and, where applicable, to the operator associated with the use of the health product or procedure which have been characterised in advance, as evidenced by available clinical studies; and
- clinical or medico-economic studies must establish that the use of the MD is likely to either (i) bring significant clinical benefit in terms of therapeutic, diagnostic or prognostic effect, making it possible to satisfy an unmet or inadequately met medical need or (ii) reduce health care expenditure.

This derogatory reimbursement is subject to the completion of *clinical or medico-economic studies*, the project for which must be presented when the application is submitted (*pay to see* principle)[84].

The request of reimbursement under temporary coverage must be sent to the *HAS*.

If the *HAS* issues a favourable opinion, a decree is issued by the Ministers for Health and Social Security, *specifying the amount to be reimbursed per patient*, the *duration* and *number of eligible patients*, as well as the *product's conditions of use* and the *studies to be carried out*.

(b) The transitional coverage scheme

Transitional coverage (*"prise en charge transitoire" – "PECT"*) is a *reimbursement scheme* for health products considered *innovative* and aimed at *therapeutic purposes* or *disability compensation*, that are falling under the *LPPR*. It allows these products to be reimbursed for *one year* while awaiting standard reimbursement through the *LPPR*[85].

The reimbursement under the temporary coverage scheme is subject to *cumulative criteria* set out in Article R.165-90 of the SSC.

To benefit from the temporary coverage scheme, MDs must be *likely to be innovative*, designed to treat *serious or rare diseases*, for which there is *no relevant comparator* and whose implementation *cannot be deferred* at the risk of compromising patients' lives.

Furthermore, the MD for which early reimbursement is envisaged must be *subject to an application for registration* on the *LPPR*. If such an application is not submitted within *12 months* after the request of temporary coverage, reimbursement will be *suspended*.

Regarding the pricing of a MD under the temporary coverage scheme, the manufacturer must send the Ministers for Health and Social Security the maximum "compensation" (price) it is requesting. In case of refusal by the Ministers for Health and Social Security, they send a *new price proposal* to the manufacturer. If it refuses, the price proposition from the Ministers for Health and Social Security, the request for temporary coverage is deemed *abandoned*[86].

Once the MD has been registered on the *LPPR*, if the reference price set by the *CEPS* is lower than the price requested from the establishments, the manufacturer must pay the *Urssaf* the "overpayment", i.e. the *difference* between the sales received under the *temporary coverage* and the sales that would have resulted if the *reference price had been applied* over the temporary coverage period.

(c) Early reimbursement for digital MDs ("PECAN")

The early reimbursement scheme for digital MDs was implemented by the SSFL in 2022 and allows early reimbursement for *digital medical devices used for therapeutic purposes or for remote monitoring*.

The early reimbursement can only concern a *specific indication* and is for a limited *non-renewable period of one (1) year*. It is decided by joint order by the *Ministers for Health and Social Security*, after the opinion of the *CNEDiMTS*, if the following conditions are met[87]:

- the digital MD is *presumed to be innovative*;
- the digital MD is *CE marked for the concerned indication*;
- the digital MD *exploitant*[88] guarantees *compliance with personal data* protection rules and applicable *interoperability and security standards*; and
- the digital MD enables *processed data* to be exported in *interoperable formats* and *nomenclature*.

Furthermore, the reimbursement *is conditional on the manufacturer submitting an application for registration on the LPPR or LATM within six (6) and nine (9) months respectively of the decision granting early reimbursement*.

The EU HTA Regulation has not yet implemented in the national HTA process in France. So, there may be changes to the national HTA process in the near future.

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80 Articles L.165-2 and R.165-14 of the SSC.
81 HAS' Guide "Pathway of medical devices in France" – page 35.
82 Article L.165-1-1 of the SSC.
83 Article R.165-63 of the SSC.
84 Article R.165-64 of the SSC.
85 Article L.165-1-5 of the SSC.
86 Article R.165-91 of the SSC.
87Article L.162-1-23 (II) of the SSC.
In the medical device sector, the concept of *exploitant* is different from that in the pharmaceutical sector.
It refers to the manufacturer or its authorised representative or, failing that, a distributor who operates the MD and obtains supplies directly from the manufacturer or its authorised representative. (Article L.165-1-1-1 of the SSC).

Germany.

1. Summary

Health care Insurance in Germany

- The health care system in Germany comprises two elements of health insurance:
  - A statutory system of health care provision funded by income-related contributions and tax financing. Approximately 90% of the population are mandatorily insured within the statutory system (Statutory Health Insurance – "SHI"), through 95 SHI funds (2024).
  - Approximately 10% of the population are exclusively privately insured. This group comprises mostly self-employed or individuals with high incomes. Private insurance companies offer insurance coverage based on individually concluded policies mostly reflecting the individual risk and scope of services insured. Private insurances also offer supplementary insurance in special areas for generally SHI insured individuals (e.g. in case of hospitalisation).
  - Physicians, hospitals and other health care professionals offer treatment to patients in both groups.
- The German legislator has regulated the health care system in the Social Security Act V (*Sozialgesetzbuch V*). This law covers the key rules for the health care services rendered to publicly insured patients, as said around 90% of the population, and hereby also determines to a large extent the treatment landscape for privately insured patients. While the legislator sporadically changes the key aspects of the statutory health system, many important decisions are still taken on the basis of the law by a quasi-governmental body, the Joint Federal Committee (*Gemeinsamer Bundesausschuss* – "G-BA") and the Federal Association of Public SHI Funds (*GKV-Spitzenverband*). Further, self-governing bodies (associations) of physicians, pharmacies, hospitals, etc. agree on or regulate the details of health care provisions and certain aspects of reimbursement.

Pharmaceuticals (medicinal product) & reimbursement

- There are a number of statutory cost-cutting instruments in force, including e.g. mandatory rebates, quotas for generics and imported medicinal products, fixed reimbursement caps (reference pricing) and – most importantly for innovative pharma and device manufacturers – health technology assessments (HTA).
- Unlike in any other European jurisdiction, innovative medicinal products are reimbursed and paid for right upon launch – based on the free pricing of the manufacturer[1]. This renders Germany a particularly attractive country for pharmaceutical companies to first launch their products in Europe. In the course of the first 12 months following launch, an HTA will be conducted and price negotiations with the Federal Association of SHI Funds held – based on the outcome of the HTA. The then negotiated price will become the unilateral reimbursement price in Germany; it retrospectively applies as of the 7th month after launch, so that the first 6 months after launch allow the manufacturer to collect revenues from its initially freely set price. The entire process is called the AMNOG process, according to the abbreviation of the law which introduced this concept. This process applies for all pharmaceutical medicinal products which contain a "new active substance", i.e. are innovative. It also applies to advanced medicinal products (ATMP), namely cell therapies and gene therapies.
- There is no positive list of reimbursable medicinal products in Germany. However, some pharmaceuticals are excluded from reimbursement by law (non-Rx products and lifestyle drugs) or decree (pharmaceuticals generally deemed inefficient). In addition, prescription restrictions and prescription guidelines may be applicable for individual products.

1 For the purpose of this article, "manufacturer" shall mean the pharmaceutical company that holds the market authorisation that markets medicinal products under its own name in Germany.

- The distribution chain for pharmaceuticals is rigidly regulated, whereas it is quite liberal for medical devices. In particular, medicinal products can only be distributed to patients through pharma wholesalers and (hospital) pharmacies – or exceptionally by other routes when directly administered at hospitals/ by physicians. Discounts and rebates for medicinal products are, as a rule, generally not permissible throughout the distribution chain, but may be granted to health insurance funds (for out-patient care) and hospitals (for in-patient care). Medicinal products for which manufacturers conclude rebate agreements with SHI funds are dispensed on a preferential basis.

Medical devices & reimbursement of devices and related procedures in hospitals and private practices

- For medical aids (*Hilfsmittel*) used or prescribed to patients, there is a medical aid reimbursement list for out-patient care. Although non-binding, reimbursement of medical devices is facilitated by the medical device being listed.
- Medical devices used by treatment providers in the scope of treatment are sold directly to such treatment providers (e.g. to hospitals for in-patient care, or, for out-patient care, e.g. to physicians). Their costs are covered and have to be refinanced via the reimbursements for treatment that treatment providers receive from public or private health insurance funds. In in-patient care, the treatment remuneration is paid on the basis of diagnosis-related group (DRG) lump sums; for out-patient care, a different tariff applies: for SHI patients it is the so-called EBM, for privately insured patients the so-called GOÄ. If a new innovative medical device is used in an established treatment, the already-established lump sum would need to refinance the, sometimes additional, costs of that medical device. Where the established lump sum is not sufficient, an amendment to the lump sum amount can be applied for and obtained.
- Completely innovative treatment measures/ procedures (which may be facilitated by new medical devices or not) can be performed in hospitals (in in-patient settings) without any prior approval. In out-patient SHI care, new procedures require general prior approval from the reimbursement body G-BA. Certain very innovative and high class medical devices need to undergo an HTA before reimbursement. Certain medical device digital treatment tools may be reimbursable after they have undergone a respective HTA reimbursement procedure.

2. German health care system: Overview

Germany is the largest market for pharmaceuticals and medical devices in Europe and the fourth largest market in the world. The annual sales of pharmaceuticals in Germany reached €54 billion in 2021.

In order to distribute pharmaceuticals to patients out in the field, manufacturers conclude sales contracts with regional or national wholesalers, and also sell directly to pharmacists and hospitals. Products used in hospitals are usually sold by manufacturers directly to hospital pharmacies. As mentioned above, the price of innovative medicinal products can initially be freely set but is subject to the so-called AMNOG process. This is the German HTA procedure by which the patient value of the product is rated by the G-BA and then a reimbursement price is negotiated with the Federal Association of SHI Funds.

End-user medical devices are usually sold by manufacturers to wholesalers or directly to pharmacies, to medical supply stores or to home care service providers which use or apply the respective devices. Medical equipment (e.g. bandaging material or a magnetic resonance tomograph) are bought by health care service providers and hospitals directly from manufacturers or, as the case may be, from wholesalers. Health care service providers and hospitals refinance their purchasing costs by use of the products and collection of treatment fees/ DRG lump sums from public or private funds.

2.1. Major legislation

The law governing pharmaceutical products and medical devices is laid down in a variety of laws, both on the regulatory side and on the reimbursement side:

Firstly, the *regulatory side:* On the European level, there are overarching regulatory laws like the European Community Code on medicinal products (Directive 2001/83/EC), the Regulation on centrally authorised medicinal products (Regulation (EC) 726/2004) or the Regulation on advanced medicinal products like cell or gene therapies (Regulation (EC) No 1394/2007). With regard to medical devices, European law provides for the Medical Device Regulation (Regulation (EC) 2017/745) and the IVD Regulation (Regulation (EC) 2017/745). These European laws are either directly applicable in Germany (e.g. the 'Regulations mentioned above), or need implementation in national laws.

Like European laws, German national laws differentiate between pharmaceutical products (medicinal products) and medical devices: The Medicinal Products Act (*Arzneimittelgesetz* – "AMG")[2] and the Medical Device Law Implementation Act (*Medizinprodukterecht-Durchführungsgesetz* – "MPDG"). In connection with European laws, they contain key provisions on clinical trials, early access, marketing requirements, product safety and vigilance, information requirements, importation, liability and distribution. The Health care Advertising Act (*Heilmittelwerbegesetz* – "HWG") regulates – and restricts – the advertising and promotion of medicinal products and medical devices as well as health care services.

Secondly, the *reimbursement side*: Reimbursement-related laws at European level are scarce: Firstly, there are some obligations for European countries to make their reimbursement restrictions transparent, so that the implications on markets and manufacturers can be determined (so-called Transparency Directive 2004/109/EC); further, there are basic rules on EU HTA (HTA Regulation 2021/2283). Please refer to our introduction on EU Reimbursement. In Germany, the key law regulating reimbursement is Social Security Code V (*Sozialgesetzbuch V* – "SGB V")[3]. It regulates prescription at payor's expense and reimbursement of medicinal products and medical devices for the 90% of the German population which are insured by SHI funds.

The SGB V is accompanied by a variety of amendment acts and ordinances as well as binding contracts and decisions of the major players:

Most notable for *medicinal products* is the Act on Reorganisation of the Pharmaceutical Market (*Arzneimittelmarktneuordnungsgesetz* - AMNOG) which entered into force in 2011 and was incorporated in the SGB V. It introduced health technology assessments in Germany for innovative medicinal products. The AMNOG was changed (mostly to the detriment of innovative manufacturers in 2022); then certain cost-curbing guardrails where introduced to enable negotiation of the reimbursement prices under the AMNOG procedure.

With the EU HTA Regulation coming into force on 12 January 2025, the German legislator took a first step to integrate the key changes outlined in the Regulation into the German AMNOG procedure. Therefore, the German Medicinal Products Benefit Assessment Ordinance ("AMNutzenV") has been adapted: the basic procedural steps of the AMNOG procedure remain in place, in particular, the set time periods for submitting a national dossier. The EU HTA results will be introduced either at the outset of the German AMNOG procedure - if available at that time - or later in the hearing period. Further, it lays with the pharmaceutical company to indicate "whether and which" evidence from the European dossier shall form the basis for the German benefit assessment. However, the amended AMNutzenV does not provide clarification regarding the notion of "due consideration" as set out in the EU HTA Regulation. It is therefore likely that the German HTA body must consider the EU HTA results via the documentation during the benefit assessment procedure as stated in the recitals of the EU HTA Regulation. The German legislator will monitor developments in the procedure on EU and national level and may adjust the national legislation if necessary.

2 For an English version see the homepage of the national regulator BfArM at www.bfarm.de.
3 For the latest major reform act of April 2007 see Schulz S, The Regulatory Affairs Journal – Pharma, 2007, 18(4), 225-227.

For *medical devices*, the abovementioned Social Security Code V likewise regulates the key reimbursement requirements. It regulates which medical devices are reimbursable upon prescription. It also regulates the reimbursement of medical procedures which are performed by use of medical devices and which determine the refinancing and thus the manufacturer prices. In 2015, a law was introduced which requires innovative medical devices which are the core of a new treatment method to undergo a mandatory HTA procedure. This applies to medical devices which are 'invasive' products with a high risk class (IIb or III) and form the core of a new treatment measure. Further, for medical device health apps, so-called digital health applications (*Digitale Gesundheitsanwendungen* – "DiGA"), reimbursement was introduced in December 2019. The reimbursement of DiGAs requires the prior assessment of the digital application by the government body BfArM. Subsequently, negotiations on the reimbursement price with the Federal SHI Association are held; during the first year on the market, the freely selected price of the app applies.

2.2. Payors – insurance funds

Pharmaceuticals and medical devices are paid for by private or public (SHI) insurance funds. Nearly 90% of the population are insured by one of the 95 SHI funds and around 10% are insured by private insurance companies. The biggest SHI funds are AOK, a cluster of eleven funds with approximately twenty seven million members, Barmer GEK and Techniker Krankenkasse, which each insure more than 8.5 million members. All SHI funds are represented by a single national head organisation, the Federal Association of SHI Funds (GKV-*Spitzenverband* – "GKV-SV"). Patients insured with the SHI pay income-dependent contributions which are collected by a central health insurance fund (*Gesundheitsfonds*). The fund then allocates payments to individual SHI funds based on a calculation which factors in the number of insured patients, the risk structure of the respective patients and social aspects.

This article mainly features the rules regarding prescription and reimbursement for *patients insured in SHI funds* (as said, 90% of the population). Private insurance companies reimburse their *privately insured patients* for medical procedures, medicinal products and medical devices on the basis of individual insurance contracts which differ widely. Basic contracts cap reimbursement to the level of SHI funds, whereas prime contracts guarantee reimbursement of any reasonable treatment costs. The featured reimbursement system for publicly insured patients also determines to a wide extent the treatment and reimbursement landscape for privately insured patients.

2.3. Prescribers and health care providers – physicians and hospitals

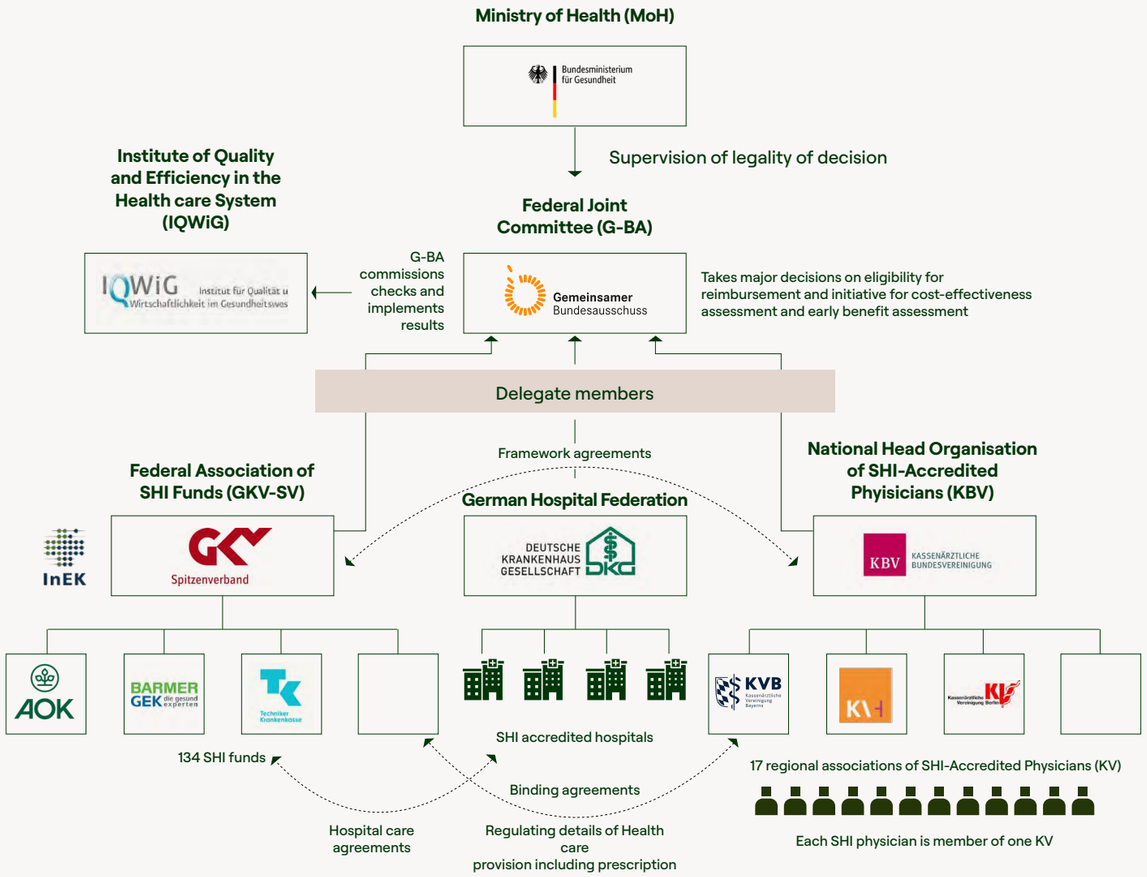
Prescription only ("Rx") medicinal products can only be prescribed (to SHI insured patients) by SHI accredited physicians or accredited general practitioners. In out-patient care, these SHI accredited physicians and practitioners are mandatorily organised in and represented by regional and federal Associations of SHI-accredited Physicians (*Kassenärztliche Vereinigung* – "KV"). The regional and federal Associations conclude agreements with SHI funds or their associations regulating, and limiting, the amount of overall fees for SHI accredited physicians and practitioners, and set up budgets for pharmaceuticals. They implement statutory cost-cutting tools and establish personal sanctions for physicians who do not comply with these regulations and the statutory stipulations in the social security laws. The abovementioned agreements are binding for each physician and directly affect reimbursement. In other instances, influence is wielded in a softer manner by agreements which offer additional bonuses for physicians if certain prescription quotas are reached (i.e. quota for prescribing many low-cost generics, so-called me-too-products, etc).

Major rules for prescribing medicinal products and medical devices are described below more specifically.

2.4. Decision-makers in German health care

The head organisations of SHI funds, SHI-accredited physicians and hospitals form the Federal Joint Committee (*Gemeinsamer Bundesausschuss*, G-BA). This public body is legally vested with power to, among other things, permit or foreclose the prescription of individual or groups of pharmaceuticals and medical devices and treatments, initiate checks of their benefits and cost-effectiveness and take other major decisions which apply nationwide. The G-BA also imposes the rules for physicians on prescribing products; this dictates which products can or cannot be prescribed and which are eventually reimbursed.

The G-BA is assisted by the Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen* – "IQWiG"). Similar to the British NICE, the IQWiG collects data on methods of medical treatment, pharmaceuticals and medical devices, and verifies their cost-effectiveness on behalf of the G-BA. Its medical and scientific assessments are not binding, but are often adopted and implemented by the G-BA.



The second key player in decision-making is the Federal Association of SHI Funds (GKV-*Spitzenverband*, GKV-SV). It is the federal association of all German SHI funds, i.e. it is basically the SHI payors' organisation. It is responsible for many decisions which involve reimbursement for products, in particular relating to the level of reimbursement and reimbursement prices. Inter alia, it determines or negotiates – partially together with other bodies – reimbursement tariffs for physicians and other health care providers; it determines the reimbursement amounts for pharmaceuticals and prescribed medical devices and negotiates the AMNOG reimbursement prices with manufacturers. It also determines the rules for dispensing products by pharmacies, which have a profound effect on which products are used in the field.

With regards to the determination of reimbursement amounts of hospitals for in-patient care (DRG lump sums) the so-called *InEK* Institute comes into play. The reimbursement tariffs for treatment in out-patient settings (EMB) is determined by the GKV-SV and the *National Head Association of SHI-accredited Physicians (Kassenärztliche Bundesvereinigung)*.

3. Pharmaceuticals (medicinal products)

3.1. Initial price setting and price maintenance

The initial price for a medicinal product can be freely determined by the manufacturer. This price has to be notified to an agency which is responsible for the data management of medicinal products in Germany. Save for some exceptions for certain pharmaceuticals, the notified price has to be applied for every sale of the product through Germany. For innovative products which undergo AMNOG, however, the freely determined price can only be charged within the first twelve months after launch. After this period, the AMNOG price will have been negotiated and needs to be charged going forward. Further, the negotiated price will apply retrospectively from the beginning of the seventh month after launch (with claw-backs for the time thereafter), so that the freely set price commercially is effective within the first six months after launch.

When selling medicinal products to hospitals, the manufacturer cannot sell beyond, and only in certain exceptional cases below the official manufacturer's selling price or the negotiated reimbursement price. In fact, prices for hospitals are usually lower than in out-patient care. In other words, rebates and discounts are not permissible for products sold to wholesalers or pharmacies. However, rebates and discounts granted by pharmaceutical manufacturers to hospitals are permissible. Pharmaceuticals sold to pharmacies, in addition to the price maintenance, are subject to mandatory margins and discounts (c.f. below).

Products which do not need to undergo AMNOG are subject to certain other limitations on free pricing and to cost curbing measures, so that there is effectively no free pricing for these products.

3.2. Benefit Assessment for New Pharmaceuticals (AMNOG)

Once a pharmaceutical is authorised, such product is, in general and within its indications, immediately eligible for reimbursement by SHI funds and private insurance funds. This is a special feature of the German reimbursement system. Upon launch, the AMNOG-process kicks in.

Pharmaceutical manufacturers are allowed to freely set the manufacturer's selling price for an initial period of twelve months from market launch. After that initial period, the AMNOG procedure ensures that a so-called reimbursement price for pharmaceuticals with new active ingredients is negotiated; negotiations take place on the basis of an HTA which assesses the additional benefit of a product brought to the patient – usually compared to an existing comparator therapy. Due to recent legislative changes, the negotiated reimbursement price applies retroactively from the seventh (formerly thirteenth) month from market launch. The gap between the (possibly higher) freely set manufacturer's price and the (possibly lower) reimbursement price in months seven to twelve must then be paid back to the SHI funds by the manufacturer.

Additional benefit assessment (HTA) – Section 35a SGB V

Under AMNOG, the price of an innovative pharmaceutical is based on the additional benefit that it demonstrated compared to the appropriate comparator therapy in the HTA. The comparator therapy is a therapy which is considered as an appropriate and efficient therapy and is determined by the G-BA for each indication of the product under assessment.

The AMNOG HTA applies to pharmaceuticals which are placed on the German market and which contain a new active substance. New indications of such product with new active substances, likewise, are mandatorily assessed.

For the mandatory HTA, the manufacturer has to submit a dossier at the latest in the moment of placing the pharmaceutical on the market or receiving the line extension. The G-BA then evaluates the submitted pharmaceutical or, rather, mostly instructs so-called IQWiG to do the scientific assessment. The IQWiG evaluation must be completed and the results published within three months. Subsequently, there is an advisory procedure under which the G-BA has to hear comments from the manufacturer concerned and other specialists from the health sector. The G-BA takes a final decision within three months of the results being published. With this decision, the G-BA determines whether an innovative pharmaceutical has an additional benefit or not and specifies the degree of this additional benefit. Please note that neither the evaluation of the benefit nor the decision of the G-BA determining the benefit is immediately contestable in court, but only very much later (c.f. under Price negotiations.)

Orphan drugs

Orphan drugs are also subject to the HTA and undergo an assessment and subsequent price negotiations. However, the law foresees that their additional benefits are deemed existent, and the extent of their additional benefit compared to a comparator therapy is not assessed. As a consequence, the value dossier which the manufacturer has to submit does not have to contain scientific information on the additional benefit. The dossier and the G-BA assessment only refers to other aspects which are needed to subsequently negotiate the reimbursement price of the orphan drug (e.g. patient groups, costs and treatment aspects). This alleviation applies as long as the sales of such orphan products with the SHI funds do not exceed €30 million in a twelve-month period. The sales threshold was lowered from €50 million to €30 million in 2022. Once the threshold is exceeded, the additional benefit has to be shown by way of submitting a full dossier within three months. Then, a fully-fledged AMNOG procedure assessing the scope of the additional benefit will be done.

Price negotiations – Section 130b SGB V

After the decision of the G-BA on the additional benefit of a product, there are mainly two possible scenarios: if the manufacturer was not able to demonstrate that its product has an additional benefit, it is checked whether the product can be integrated into a group of comparable substances within Germany's reference price scheme (c.f. 3.5 re Reimbursement Caps). Where there is no reference price group or a product has shown additional benefit, the manufacturer has to enter into negotiations on the reimbursement price with the Federal SHI Association. A manufacturer may opt out of price negotiations if the negotiable reimbursement price is likely to be too low. Even though this may also be quite a painful decision, it may be best to protect the selling price in other European and ex-European markets. This is because many other countries directly or indirectly make reference to the German prices of pharmaceuticals for their price determination. To address this situation also rather unfortunate for German patients, the pharmaceutical company can, under a new law, apply for the reimbursement price to remain confidential and to not be published in the official price list until the end of regulatory protection. In return for the confidentiality of the reimbursement price, the pharmaceutical company will have to grant an (additional) discount of 9% to the SHI funds. Where *no additional benefit* was assigned to the product by the G-BA, the reimbursement price may, however, not be negotiated at a higher level than the annual price of the appropriate comparator therapy. If the comparator medicinal product is patented, the annual price of the assessed

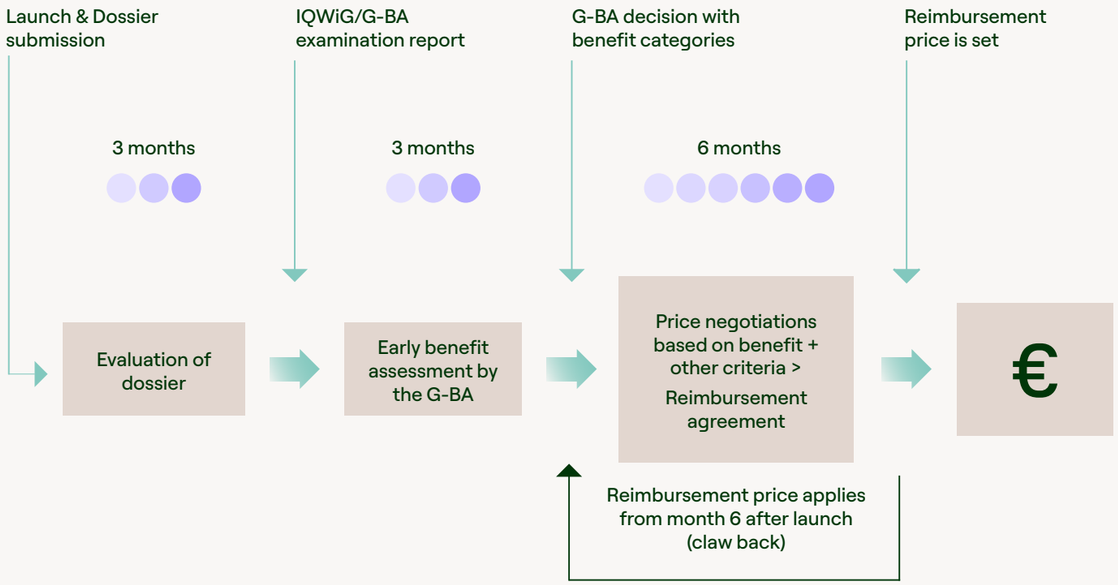
medicinal product must at least be 10% less than the comparator therapy. These price levels can be painful for the manufacturer of a newly developed pharmaceutical, since the comparator therapy could well be a low priced generic. Certain further mechanics may apply and may further curb the reimbursement amounts. Hence, under a newly introduced law, the guard rails following inter alia from a patented comparator therapy do not apply, if the G-BA in its benefit assessment concluded that a relevant portion of the clinical trials has been conducted in Germany, which will be re-assessed after 30 months. In such a case, a reimbursement price not higher than the comparator therapy can be agreed upon.

If the manufacturer was able to demonstrate an additional benefit in the HTA before the G-BA, the reimbursement price will be negotiated on the basis of the assessment and the degree of *additional benefit*. It is the idea that the price is appropriate to reflect the additional benefit compared to the comparator therapy.

If the parties do not agree on a reimbursement price within six months after the publication of the GB-A's decision on the benefit assessment, the reimbursement price will be fixed by the so-called "arbitration body" (*Schiedstelle*). If a manufacturer wants to have the G-BA assessment or the price negotiation challenged before the courts, the only way to do this is to refuse agreement on a price with the Federal SHI-Association and let the arbitration body impose a price. Only this decision (and then impliedly also the G-BA decision on the amount of benefit of a product) can be challenged before the courts by a manufacturer.

HTA and Price Negotiations in **Germany**

- **Initially free pricing**
- Innovative Drugs – Except orphan drugs – with < 30 Mio. Euro in Sales:



- Mandatory discounts imposed – and voluntary discounts possible!
- EU HTA not pictured

The reimbursement price (negotiated or determined by arbitration body) is available approximately twelve months after launch of a product (or implementation of a new indication). This is the nationwide valid and uniform reimbursement price for the respective product and all subsequently launched medicinal products with the same active ingredient, also applies to parallel importer's products. The AMNOG reimbursement price applies retroactively from the seventh (previously thirteenth) month of market launch. By way of a claw-back, the manufacturer must reimburse the SHI funds for any "overpaid" amounts from months seven to twelve, resulting from a (possibly higher) freely set manufacturer's price and a (possibly lower) negotiated reimbursement price.

3.3. Margins in the distribution chain

The Medicinal Products Act and the Ordinance on Medicinal Product Prices (*Arzneimittelpreisverordnung* – AMPreisV) regulate the prices and margins for prescription-only (Rx) and certain non-prescription (OTC) pharmaceuticals which are reserved for sale in pharmacies (pharmacy-only/ RX pharmaceuticals). As a result of fixed prices and margins, the retail price for every pharmaceutical is predetermined by either the set manufacturer's price or the subsequently determined AMNOG reimbursement price which is increased by the fixed wholesale margin and the fixed pharmacy margin. So, the retail price for a Rx pharmaceutical is the same in every pharmacy in Germany. The same applies to pharmacy-only OTCs whose costs are only exceptionally reimbursed by the SHI funds.

Retail prices are calculated as follows (all excl. VAT):

(Initially) freely set manufacturer's price ex-factory	€100.00	5,58% + €0.63
+ Wholesale margin[4]	Max. €3.85 (fixed charge of €0.70 and flexible margin of max. 3,15% of set manufacturer price; not more than €37.80)	5,51% + €1.31
+ Pharmacy margin	€11.88 (€8.35 lump sum + €0.41 lump sum + €3.12 (that is 3% of the wholesale price))	5,36% + €1.79
Retail price (excl. VAT)	€115.73	5,05% + €2.80

Once the AMNOG price is available, margins are calculated on the basis of the negotiated reimbursement price (see 3.4 below).

According to recent EU case law, these fixed margins do not apply to deliveries made to German customers by mail-order pharmacies located outside of Germany. According to a subsequent change in the law, however, they must comply with the above price regulation if they supply medicines to patients insured in SHI funds (90% of German patients).

For special pharmaceuticals whose use requires a high degree of preparation work or manufacturing in the pharmacy, for example formulations in the oncology sector, pharmacies receive compensation for the substances and their work efforts. Such compensation is determined by special provisions in the AMPreisV and an agreement between the GKV-SV and the Federal Pharmacists' Association (*Hilfstaxe*), or, if applicable, a special agreement with a private sick fund. Also special charges apply for repacking or mixing of pharmaceuticals by pharmacists.

4 Not applicable in case of mandatory direct supply from manufacturer to pharmacy.
5

3.4. Reimbursement of pharmaceuticals dispensed by pharmacies and used in in-patient care

So, generally a manufacturer of a medicinal product applies the notified manufacturer's price or later AMNOG reimbursement price when selling a product to its customer (i.e. a wholesaler). The wholesaler sells the product to pharmacies with a mark-up reflecting the fixed wholesale margin. Pharmacies dispense the product to patients with an additional mark-up reflecting the fixed pharmacist margin.

Pharmacies out in the field are reimbursed for such dispensing either directly by way of receiving the retail price from the patient, or by way of refunds from the SHI funds.

In the event that a product is not reimbursable by SHI funds (self-pay), the patient has to pay the retail price for the product to the pharmacy. If the patient is insured with a supplementary private sick fund, s/he will seek reimbursement of his/her expenses from such supplementary private sick fund. If a patient is insured through a SHI fund, the pharmacy will dispense the product without receiving any payment from the patient, but will seek reimbursement from the very SHI fund through which the patient is insured. However, the pharmacy will not be reimbursed for the entire retail price of the respective pharmaceutical. For mainly all pharmaceuticals which are not grouped in reference price groups (c.f. below), *mandatory discounts* are deducted from the pharmacy's reimbursement claim against a SHI fund:

Manufacturer's discount	7% on manufacturer's price for SHI and private insurance fund (6% on manufacturer's price in the case of generic drugs)
(Additional) Generic's discount	10% on manufacturer's price for SHI and private insurance funds
New: combination discount for certain medicinal products with new active ingredients that are used in combination therapy according to SmPC	20% on manufacturer's price for SHI and private insurance funds unless proven that combination therapy has a significant additional benefit (HTA); the combination discount was only introduced in 2022, it is disputed by pharma companies before courts, however.
Pharmacy's discount	€1.77/ from February 1, 2023 to January 31, 2025, : €2; or 5% of the retail price (see above) (to be granted by pharmacies out of their margin to SHI funds)

As seen above, there is a mandatory manufacturer's discount in force at 7%, or 6% for generics, on the set manufacturer's price. Additionally, a *price freeze* applies for all products which are not under AMNOG price determination anyway: If a manufacturer increases the price for a pharmaceutical compared to the price level at a certain date in the past, the amount of the mark-up has to be paid as an additional discount to the SHI funds. This effectively leads to a price moratorium, since any price increase will not go to the manufacturer, but to the SHI funds instead. Nonetheless, a certain inflation-related increase is permissible. The price freeze discount was expected to cease to be in force as of 31 December 2022, but will be extended until 31 December 2026.

Pharmacies out in the field are reimbursed for such dispensing either directly by way of receiving the retail price from the patient, or by way of refunds from the SHI funds.

The pharmacies necessarily have to bear the pharmacies' discount, however they will claim back from pharmaceutical manufacturers the manufacturers' discount, the generics discount, the combination discount and the price freeze discount (as far as applicable). If, ultimately, a pharmaceutical is dispensed to a privately insured patient, the manufacturers must pay the applicable manufacturer discounts to the private insurance fund which reimbursed the patient. Thus, although a manufacturer will, for example, initially receive €100 for a pharmaceutical when selling it to a wholesaler, the manufacturer will somewhat later have to pay a discount to a pharmacy, for example the manufacturer discounts and will, thus, eventually only receive €93 from such sale.

Pharmaceuticals used in hospitals

With regard to reimbursement for pharmaceuticals used in hospital, the following applies: SHI funds reimburse hospitals treating SHI-insured patients by way of lump sums for overall treatment depending on the type of disease (Diagnosis Related Groups – DRG). Thus, the costs of pharmaceuticals applied in a hospital usually have to be covered by the DRG lump sum which the hospital receives for the entire treatment of the patient. Certain, very expensive, drugs are reimbursed by sick funds separately by way of supplementary reimbursement (*Zusatzentgelte* – ZE).

3.5. Reimbursement caps (reference pricing) – Section 35 SGB V

A substantial number of pharmaceuticals (approximately 75% of effected prescriptions[6]) are subject to a fixed reference price scheme (*Festbeträge*). These reference prices are basically reimbursement caps determined by the G-BA and the GKV-SV for groups of similar or therapeutically comparable substances. The commercial result of a pharmaceutical being included into a reference price group is that SHI funds reimburse only the reimbursement cap which is to be determined for each product in this group based on a mathematical algorithm. If a product costs more than this cap (i.e. the manufacturer is unwilling to cut the price to the level of the reimbursement cap), the exceeding amount has to be paid for by the patient. In most cases, if patients do not wish to make any out-of-pocket payment, they may choose to be served with another medicinal product of the same therapeutic value which is fully reimbursable by the SHI fund. Because patients are reluctant to contribute towards their treatments additionally, pharmaceutical companies usually are forced to not set the price levels for their products above the reimbursement cap.

Reference price groups are widely established for generic products.

Patented substances can also be put into reference price groups, mainly in groups of substances on the same ATC level 4. SHI funds try to benchmark patented medicines against molecules that are already available as generics and then put patented and generic products into one group – with quite a detrimental effect on the level of cap. Innovative pharmaceuticals, whose mode of action is new and which bring a therapeutic improvement by proven higher efficacy or reduced side effects, are exempt from the scheme. The fixed price is calculated, very roughly speaking, by the SHI as the average of the prices of all the pharmaceuticals contained in the relevant group.

3.6. Prescription restrictions

Gatekeepers of the use of medicinal products (as well as medical devices) are SHI-accredited physicians, of course. They prescribe the products used out in the field. Their prescription is handed over to the patient and then dispensed by pharmacies.

In order to steer physicians in their prescribing, there are several means:

The G-BA can issue prescription advice on the cost-effectiveness of individual pharmaceuticals or preclude them from prescription for certain indications (Section 92 SGB V, *Arzneimittelrichtlinien*). Physicians disregarding the advice are at risk of paying damages to SHI funds. Moreover, SHI funds inform physicians about therapeutic alternatives and their respective prices.

6 http://www.bmg.bund.de/krankenversicherung/arzneimittelversorgung/wie-arzneimittelpreise-entstehen.html (source of the Federal Ministry of Health).

Agreements between health insurance funds and associations of physicians in the federal states (§ 84 SGB V) can impose several 'economic objectives' on physicians with regard to their prescription of medicinal products: each state has its own set of regulations in this regard. Most common is a selection of the following:

- Physicians may be put under a personal budget for prescriptions of pharmaceuticals. It is usually calculated on the basis of an average value per patient (benchmark value) multiplied by the number of patients. Performance is controlled by quasi-public bodies. Physicians exceeding the budget may face increased scrutiny in future prescribing or even financial consequences – as said, all depending on the extent to which the local parties have specifically implemented the respective objective.
- Top selling groups of pharmaceuticals are often subject to quota (i.e. ratio of e.g. prescription of low-cost generics compared to more expensive originals). The achievement of quota by an individual physician is incentivized by certain benefits granted to the physician (e.g. a monthly lump payment) or by establishing sanctions in the event of non-compliance (service fee reductions). In some regions, manufacturers are able to obtain an opt-out of the quota system for a pharmaceutical by entering into rebate contracts with single SHI funds. A quota may, for example, be a so-called 'me-too quota': certain products may be deemed 'me-too products' and should subsequently not be prescribed; instead, the physicians should opt for, e.g., a product which may originally have been an innovator product, but is already off-patent and thus could be prescribed in its generic version. A similar objective would be to designate patent products as the 'leading substance' (mostly this happens when an innovator product gets off patent) and physicians are requested to primarily prescribe that leading substance, namely in its generic version or just prescribe a substance by naming the INN (International Non-proprietary Name). There are also quotas which compel physicians to prescribe a certain ratio of generic products compared to patented products.

Physicians missing these targets may be obligated to attend prescription courses teaching economic prescribing. Alternatively, they will eventually be liable to pay damages to the regional SHI funds.

3.7. Rule governing dispensing in pharmacies – import product incentivizing and generic substitution – Section 129 SGB V

Subject to the EU doctrine of free trade within the EU, importers are free to buy a pharmaceutical for a cheap price in another EU member state and sell it in Germany at a higher price. SGB V encourages such parallel imports. Pharmacists when dispensing pharmaceuticals are obliged to replace domestic pharmaceuticals with respective parallel imports, if their selling price is – depending on the price level of a product – 15% to 5% lower than the equivalent original products sourced in Germany.

As mentioned above, physicians are often encouraged or incentivized to prescribe a generic product or to name an active ingredient by mentioning the INN. In the case of an INN prescription, pharmacies are legally obliged to dispense a generic version. However, despite the 'economic objectives' which are being imposed on physicians, they are not precluded from prescribing a branded product. When they prescribe a branded product, pharmacies are obliged to verify whether there are generic products available and then have to dispense one of the cheapest generic versions. This applies, except in situations where the physician has specifically indicated on the prescription, that such generic substitution by pharmacies cannot be done.

However, dispensing parallel imports or generics can be prevented by the originator company by means of concluding an individual rebate contract with SHI funds (see 3.8 below), i.e. by giving an additional discount on the sales price of a product, in return for which the sick funds exclude the product from import or generic substitution at pharmacy level.

3.8. Rebate contracts – Section 130a SGB V

In addition to the mandatory discounts (c.f. 3.3), manufacturers are invited to grant contractual rebates to individual SHI funds. The law gives various incentives for manufacturers to voluntarily enter into rebate agreements with sick funds. For example, pharmacists are obliged to preferentially dispense rebated pharmaceuticals, if available, instead of non-rebated alternatives. Drugs subject to rebate contracts are, to a certain extent, exempt from the cost-effectiveness test that physicians regularly undergo regarding their drug issuing prescriptions. In issuing prescriptions, physicians use certified computer programmes displaying information on rebate contracts of all SHI funds. Finally, patients can be exempted from the personal out-of-pocket payments in respect of rebated pharmaceuticals. Further, products which are voluntarily discounted by the manufacturer are exempt, as mentioned above (see 3.7 above) from import substitution or generic substitution.

Rebates may only be granted to SHI funds, other social insurance funds and private insurers, but – as mentioned above – not to wholesalers or pharmacies.

3.9. Off-label use

Pharmaceuticals prescribed for off-label use are, in principle, not reimbursable. However, if: (i) the drug aims at curing or alleviating a life-threatening disease; (ii) there is no authorised drug available for this indication or patient; (iii) certain scientific data indicate good prospects of success; and (iv) the risk/benefit balance is positive, then the drug will be reimbursable (Section 2 para 1a SGB V and respective case law).

3.10. Non-Rx drugs, lifestyle drugs and other non-reimbursable products – Section 34 SGB V

Except for children and disabled adults, non-Rx pharmaceuticals are not reimbursable by SHI funds. Patients have to pay for such pharmaceuticals themselves. However, the Federal Joint Committee has listed indications where treatment with specific non-prescription pharmaceuticals is considered reimbursable. Pharmaceutical entrepreneurs may apply for a drug to be put on that list.

Pharmaceuticals aimed at improving private lifestyle, for example, treating non-pathological obesity or erectile dysfunction, are not reimbursable, whereby exceptions may apply.

Moreover, the Ministry of Health has drawn up a list of products/APIs which are considered 'uneconomical' or not sufficiently effective, and thus are not reimbursable. Drugs using or combining these APIs in a way described in the Ordinance on Uneconomical Pharmaceuticals (*Verordnung über unwirtschaftliche Arzneimittel*) are barred from reimbursement.

3.11. Out-of-pocket payments to patients – Section 31 SGB V

Each SHI-insured person is generally required to pay a fixed amount for each prescription, currently between €5 and €10 but not more than the price of the pharmaceutical. Pharmaceuticals can be exempted from this patient contribution if their price is at least 30% below the fixed reimbursement cap.

3.12. Reimbursement in clinical trials and early access scenarios

Under German law, there are generally three different legal paths for the supply of unauthorised medicinal products outside of the clinical trial setting and prior to the granting of a marketing authorisation for placing on the market in Germany:

- If the medicinal product is already authorised in another country, the medicinal product can be imported by a pharmacy for a specific patient (named patient import, *Einzelimport*).
- If the medicinal product is already in later stages of clinical trials or if a marketing authorisation has been applied for, a so-called compassionate use programs (*Härtefallprogramme*) for a group of patients can be set-up.
- Other than that the medicinal product can be supplied for emergency reasons for an individual patient, usually by way of an individual treatment attempt (*individueller Heilversuch*) under narrow justifications set out in the German criminal law (*rechtfertigender Notstand*).

Pharmaceuticals supplied from these pathways are eligible for reimbursement if narrow conditions are met. Reimbursement may require prior case-by-case confirmation from the respective health insurance fund.

With regards to reimbursement of products used in clinical trials: as a rule, a non-authorised product which is tested within the clinical trial is not reimbursable; after authorisation of the tested product and its use in a phase IV clinical trial there are good arguments for reimbursement, and limited arguments in phase III off-label studies. With regard to comparator, especially standard of care comparators in clinical trials, the result is case dependent; however there are in fact arguments for them to be reimbursable.

On the regulator details of such supply, please refer to our brochure early access to pharmaceutical products in major European markets.

4. Medical devices

4.1. Devices used directly by or for out-patient care (medical aids)

The German regulations on reimbursement of medical devices differs, depending on the kind of device and where it is used. Devices which are used by patients can be prescribed and the reimbursed; the same applies for reimbursed, so-called, digital health applications. Investment goods are, of course, bought by health care providers; they need to refinance them by collecting reimbursement/payment for their patient treatment.

4.1.1. Reimbursement requirements for patient-used devices

Medical devices substituting or supporting natural bodily functions ("*medical aids*") and complying with the marketing requirements of the Medical Devices Regulation, (for example, the requirement that such devices have a CE mark) are, in principle, eligible for prescription and reimbursement. However, several medical devices are generally exempt from any reimbursement.

For devices which are used by or for patients (for example, wheelchairs, ostomy or incontinence products, etc.) there are specialised retailers or health care service providers who use or supply the respective device, e.g. pharmacies, medical supply stores, home care service providers, opticians, hearing aid technicians or medical supply stores or homecare service providers. Manufacturers sell their products to wholesalers or directly to those intermediaries permitted to supply the patient with the device upon a physician's prescription. In principle, pricing is not regulated and rebates are permissible. However, reimbursement by sick funds (which greatly determines the manufacturer price) is subject to reference price schedules and contractual agreements with SHI funds (see 4.7 below).

Reimbursement of medical devices used by or for patients, i.e. medical aids (Hilfsmittel), is granted subject to a prescription. The prescriptions are usually issued by making reference to a product or product category number, which is assigned by the products being listed in the *medical technical aids reimbursement list* (*Hilfsmittelverzeichnis*). Products are initially listed or adjusted at the request of the manufacturer (or by third parties authorised by them). The listing takes into account the relevant statutory requirements imposed by the Federal Association of SHI funds (GKV-SV).The products available on the market are classified according to their applications in different product groups. The list provides comprehensive information on the performance, the type and quality of products available as well as requirements for the prescription. Each category contains a breakdown and a definition with high legal notices and a list of indications that justify a supply. It is continuously updated.

The medical technical aids reimbursement list is not binding in a legal sense, i.e. also products which are not listed can be prescribed and reimbursable. However, manufacturers seek listing their products to facilitate broader and easier prescribing and reimbursement for their products. As said, the list contains the minimum quality requirements for each product group and related service requirements. These requirements are referenced in contracts which the sick funds conclude with health care providers such as pharmacies, medical supply stores, home care service providers, opticians etc. and, thus, have to be abided by when a medical device, which is listed or belongs to a specific product category, is applied or used for a patient.

The *preconditions for the listing* of a device in the medical technical aids reimbursement list are mainly: the efficacy/functionality of the product, its safety and the fulfilment of the already stipulated requirements for the product group to which the device belongs. If the product introduces a new diagnostic or treatment method into the German out-patient care a further precondition for the listing is G-BA assessment of this new diagnostic or treatment method and approval for out-patient care.

In order to qualify for prescription, any medical device must be medically necessary to ensure the success of a medical treatment, to compensate for an impairment, to remedy a weakness supposedly leading to a disease, to ensure the healthy development of a child or to prevent the need for permanent care. Devices not serving one of these goals are not eligible for reimbursement. Moreover, the Ministry of Health has drawn up a list of medical devices which are excluded from reimbursement, because they are considered as being of little therapeutic benefit or low value (for example, eye patches).[7]

4.1.2. Advice/instructions on prescription of medical devices

The G-BA has issued detailed binding advice on the prescription of selected medical devices such as artificial limbs, orthopaedic equipment or vision aids (section 92 SGB V). Physicians disregarding the advice risk paying damages to SHI funds.

7 Ordinance on medical devices of little therapeutic benefit or low value (*Verordnung über Hilfsmittel von geringem therapeutischen Nutzen oder gerin-gem Abgabepreis*).

4.1.3. Reimbursement caps

A substantial number of medical devices substituting natural bodily functions are subject to a fixed reference price scheme *(Festbeträge, Section 36 SGB V)*. The associations of SHI funds classify comparable devices and set a fixed amount to be reimbursed by SHI funds. Sums exceeding this amount have to be paid for by the patients themselves.

4.1.4. Reimbursement of Digital Health Applications used by patients

Digital health applications (*Digitale Gesundheitsanwendungen*, "DiGA") are reimbursable by SHI funds upon prescription, under certain conditions. The digital solution needs to be a medical device of low-risk (Class I or IIa under MDR) with a mainly medical functionality based on digital means (apps or mainly software-based solutions). The solution's purpose of usage has to be the diagnosis, monitoring or treatment of diseases or improvement of related health care provision. Non-medical devices or digital applications used alongside or in combination with other medical devices, which are not primarily based on digital means, are not included. Medical devices with higher classification are not subject to reimbursement as a DiGA; they will be reimbursed by other means, e.g. as medical aids (see 4.1.(a) above) or they will be sold to health care providers (e.g. hospitals) and then need to be refinanced by collecting treatment remuneration (see 4.1 (b), (c), (d)).

DVG: Claim or digital health applications Art. 33a SGB V

Scope – Digital Health Applications
Purpose of use: Support of insured persons and support of care in rendering of services

Medical products acc. to MPV (Art. 33a Sec..2 SGB V)

Stand-Alone Software | Med. product based on dig. technologies

and

Low-risk classification

Class I | Class IIa

Circulating acc. to MPV

Admitted by BfAM to registry for digital health products acc. to Art. 139e SGB V (or in SHI fund contracts for specific modes of care (Art. 140a Sec. 4a SGB V))

Basis: Manufacturer application with information about

Security, eligibility & quality

Data protection- and security

Benefits to patient care

Upon presription by responsible doctor/psychologist

and

Patient's own initiative, after obtaining approval of insurer

No legislative or G-BA exclusion of services (Sec. 4)

Provision as benefit-in-kind (sec. 3): electronic transmission/ media carriers or digital sales platform (reimbursement)

The reimbursement coverage is subject to the competent authority (*Bundesinstitut für Arzneimittel und Medizinprodukte – BfArM*) listing the DiGA in the DiGA register. The listing is binding in a legal sense – no reimbursement without registration. Such registration is triggered by a respective application to be submitted by the manufacturer/designer of the solution. The BfArM takes three months to decide. The requirements for a listing in the DiGA register are quite demanding: The application has to be supported by evidence showing the safety, functionality, interoperability and quality of the digital health solution and its compliance with data protection and cyber security requirements (to a large extent also required by MDR). For the challenging part, the manufacturer/designer of the solution must also provide evidence of the solution's positive impact on health care provision. If evidence for the latter is not yet available, manufacturers may apply for a preliminary listing for a twelve months' testing period. The testing period can be prolonged for another twelve months if the results generated within the first twelve months show a strong likelihood that such evidence will be obtained later.

Such positive impact can be demonstrated either by establishing that the digital solution has a medical (i.e. clinical) benefit or by establishing that the digital solution improves the 'structure or procedure of health care provision' in Germany. A medical benefit is likely to be unverifiable without collecting clinical patient data. An improvement of the structure and procedure of health care is somewhat easier to demonstrate – but still requires supporting data. Where the data required to support a listing is not (yet) available, an application for preliminary listing can be submitted. Where such submission is accepted by BfArM, the manufacturer of the application will be granted one year of use on a preliminary basis – subject to the manufacturers obligation to collect data from the use of the product. After one year, a final decision is made, though there is the option to prolong this period for another year.

The reimbursement amount in the first twelve months after registration matches the manufacturer's freely set price. During that time period, manufacturers and the GKV-SV negotiate the reimbursement amount which applies from the 13th month onwards.

Listed DiGAs can be prescribed like medical aids and their costs can then be reimbursed. Guidance and instructions imposed on prescribing physicians may be imposed.

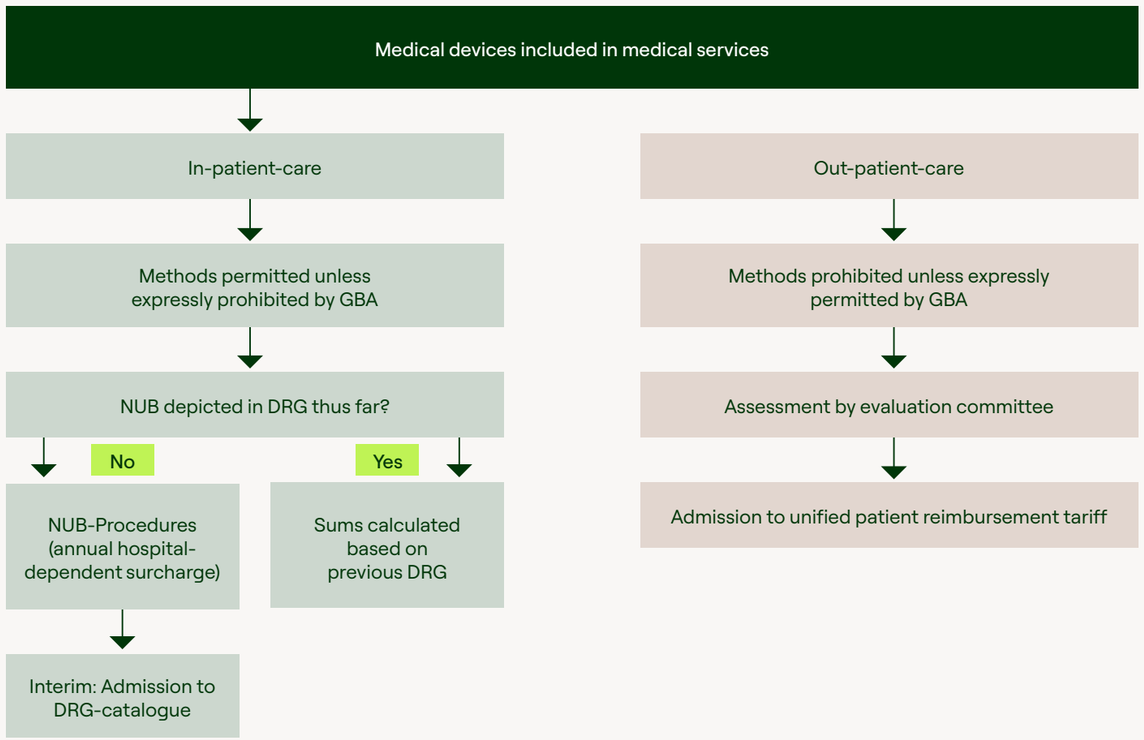
4.2. Devices used by health care providers

Products mainly used in the in-patient care (e.g. stents, implants, MRTs etc.) by health care providers (e.g. hospitals, physicians) are sold to these in-patient care health care providers. The costs, which such health care providers incur, are not directly reimbursed by SHI. The health care provider will rather use the device for the treatment of patients and would then refinance these device costs by collecting DRG lump sums for the treatment of patients from SHI funds or privately insured patients.

With regard to new and innovative therapeutic or diagnostic methods, including those using innovative devices, the general rule in Germany is:

- As a rule, new innovative methods can be applied in *in-patient care* at hospitals once they emerge and can, in general, also receive reimbursement without any governmental or reimbursement body needing to pre-approve such procedures. This rule does not apply for certain procedures using certain high-class medical devices which follow a new therapeutic-scientific concept.
- New innovative methods which are meant to be used *out in the field* will only be reimbursed upon them having been assessed by the G-BA and G-BA has approved them expressly for reimbursement for out-patient care.

Reimbursement of new treatment methods (NUB) with medical devices



4.2.1. Use of medical devices in in-patient care

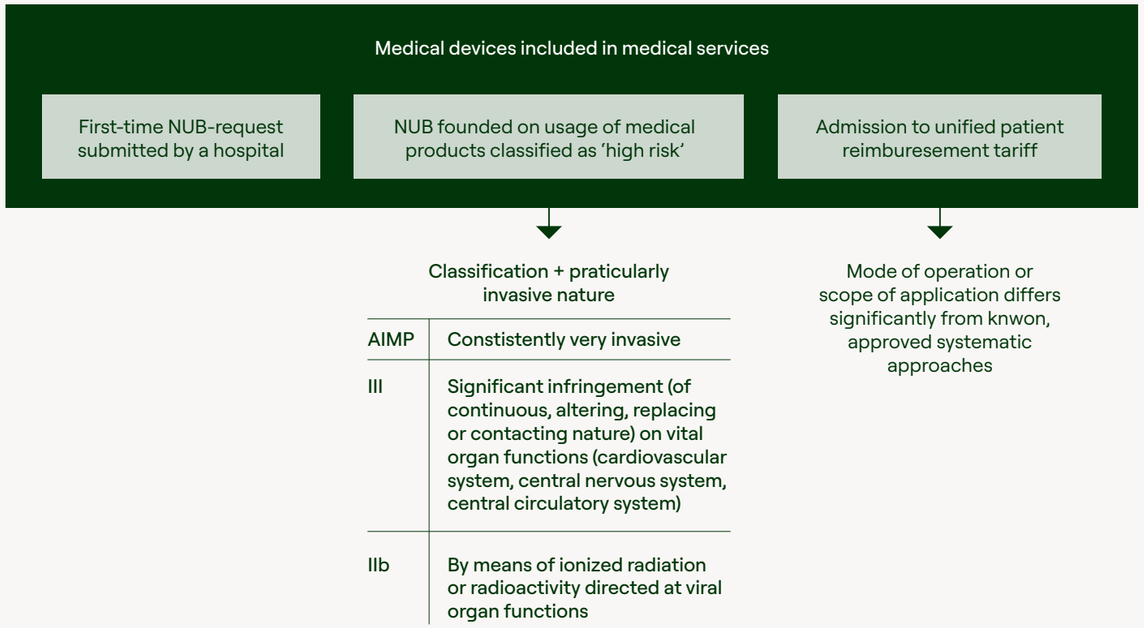
As mentioned above, the use of innovative new devices which represent a new diagnostic or treatment method in in-patient care does not require the prior approval of the G-BA or any other governmental body. Thus, new diagnostic or treatment methods (which may involve using a CE-marked innovative medical device) can be done in hospitals and such in-patient care is generally reimbursable (i.e. not precluded from reimbursement or requiring prior reimbursement approval by G-BA). Though, as mentioned above, the G-BA does not have to pre-approve new innovative methods being applied in in-patient care, the G-BA has the right to assess a new measure and declare it ineffective, not safe, not necessary or not commercially viable – and hereby exclude the method from reimbursement in the SHI.

However, despite the general reimbursability of new inpatient treatments, the administrative hurdles to obtain reimbursement coding and a reimbursement agreement for new treatment measures are troublesome for hospitals. Simply speaking, the given DRG coding and allocated DRG lump sums to an already coded procedure may not be fit for the new but adjacent or bar recovery of a sufficient reimbursement amount. Thus, an update of an existing DRG Code may need to be pursued for an innovative treatment by the hospital and the medical device company which sells the involved medical device. Where the current DRG coding system does not even contain an adjacent procedure (i.e. the new procedure is completely new), reimbursement for such new treatment needs to be sought on an interim basis as long as a new DRG code could be set up. This is to be done by applying for the procedure to be eligible for interim reimbursement with the so-called INeK institute. Such an application is called NUB application, NUB standing for 'new diagnostic or treatment method' (*neue Untersuchungs- oder Behandlungsmethode*).

Once a favourable assessment of INeK is obtained, the procedure is available for interim reimbursement by way of hospitals negotiating the individual reimbursement amount with SHI funds in their regular annual negotiations.

There is one exception from the rule that new innovative in-patient treatment methods do not require G-BA approval before in-patient care use and reimbursement. This exception applies to a number of methods which use high-class (IIb, III), invasive medical devices as the core of that method and the method is considered using a 'new theoretical-scientific' treatment concept. For those methods, the NUB application to INeK will need to be triggered in order to get interim reimbursement coding as mentioned above. However, for these methods the law also requires that the INeK process is supplemented by an assessment of G-BA of the method and the medical device used within that process. Only when the G-BA approved the in-patient use of that method (using that device, it can be reimbursed (see slide below).

Early benefit assessment of NUB relating to medical products classified ‚high risk' (2)



4.2.2. Devices used in out-patient care as a means for diagnosis or treatment

Other medical devices which are intended to be used by health care providers in the out-patient care as a mere means to diagnose or treat patients (e.g. an MRT) are simply sold by device manufacturers or their distributors to physicians, hospitals or other health care providers. Such long-term investment goods are paid for by physicians and hospitals and are not reimbursed. However, SHI funds reimburse such health care providers treating SHI insured patients for their services. The costs of the providers for the purchase and maintenance of medical devices used within such service rendering need to be amortized by the service fee (in hospitals, the DRG lump sum).

Where an innovative medical device is used in out-patient care within a new diagnostic or treatment method, that method can only be used in out-patient care after the G-BA has adopted that method. Once adoption is obtained the method can be applied, coded and reimbursed – and hereby the costs of the medical device used therein be amortized.

4.2.3. Devices in reimbursement test period for in-patient or out-patient care

As mentioned above, the G-BA is entitled to decide upon the application and reimbursement of new diagnostic or therapeutic methods (which often involve the use of an innovative medical device). Simply speaking, in out-patient care the application of a new diagnostic or treatment method can only be done and is only reimbursed (some exceptions apply), if the G-BA has explicitly approved the new method; whereas in in-patient care the new method can be applied and is reimbursed as long as the G-BA has not explicitly excluded the method from reimbursement. There may be a situation in which the G-BA has no sufficient data to decide whether a new method/device is effective, safe, necessary and commercially viable and, thus, not in a position to decide upon the reimbursement of the same. In this situation the following procedure can be pursued: subject to this procedure the G-BA can allow the application of the new method in hospitals and/or out in the field for a test phase. The services rendered by hospitals, physicians and other health care service providers will be reimbursed subject to reimbursement agreements concluded between the service providers and SHI funds. The test phase will be accompanied by a scientific body.

If the new method is mainly based on the use of a medical device, the reimbursement test phase can only be implemented by the G-BA, if the manufacturer of the respective medical device is obliging itself to contribute to the costs of the test phase.

4.3. Companion diagnostics

Companion diagnostics are usually categorised as in vitro diagnostics (IVD). Where the treatment of the pharma product for which the companion diagnostic is used is done in in-patient care, their reimbursement is governed by specific regulations under the DRGs system. Companion diagnostics utilised in conjunction with AMNOG-reimbursed products undergo evaluation overseen by the G-BA which also assesses the patient benefits of the pharma product. As mentioned above, when a pharmaceutical company seeks reimbursement for a new product under the AMNOG process, it is required to submit data and evidence supporting the clinical efficacy and cost-effectiveness of the product, which may include data related to the companion diagnostic's utility. For companion diagnostics used in conjunction with AMNOG-evaluated products, their medical benefit is intrinsically linked to the efficacy and appropriate use of the therapeutic intervention. Therefore, the G-BA assesses the diagnostic's performance and validity in identifying the patient population that would benefit most from the specific treatment. The companion diagnostic's ability to stratify patients and predict treatment responses significantly influences the evaluation of the overall product's added value. Where the pharma product receives G-BA assessment and reimbursement, the companion diagnostic utilised in conjunction with the product will also be reimbursement if it is deemed to be integral to the product's therapeutic pathway.

4.4. Contracts on provision of medical aids – Section 126 SGB V

SHI funds conclude contracts with service providers (e.g. homecare companies) on the provision of health care services which entail the supply, use or application of medical devices. For comparable services and related devices used when rendering these services, the contracts contain detailed provisions on prices and quality requirements etc. Based on such contract, the service provider is retained by a SHI fund. Other health care providers may also enter into similar contracts with the respective SHI funds and, thus, will also be allowed to render health care services for the patients of this very SHI fund based on such contracts. Health care providers which do not have any contract with the SHI fund are generally not entitled to render health care services (and supply, use or apply medical devices) to the patients of such SHI fund. However, recent judgements confirm the patients' right to procure a necessary medical aid themselves and have it reimbursed by the respective SHI if the product supplied by the service provider, for which the patient's SHI concluded a contract, does not prove to be sufficient, appropriate or functional.

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Italy.

1. Summary

- A significant part of the medicinal products are reimbursed from the Italian National Health Service, which is funded through taxation, and is managed by the Ministry of Health and the Regions. Medical devices are not subject to reimbursement by the NHS, with the exception of a medical device which is involved or required in performing one of the so called essential levels of care ("LEA"), which are the medical treatments and services that the National Health Service ("NHS") is required to provide at its expense to all citizens.
- There is a positive list of reimbursed medicinal products, which is handled by the Italian Medicines Agency ("AIFA").
- Pricing and discounts of pharmaceuticals are strictly regulated at each level of the channel, including: wholesale, distribution and pharmacies.
- Various measures are in place or are being introduced by the Government to cut back on the costs of medicinal products, e.g.:
  - maximum expenditure thresholds fixed for the state and for each region;
  - maximum prices for medicinal products;
  - mandatory discounts; and
  - annual budgets for pharmaceutical companies.

2. The Italian health care system: overview

The Italian NHS was established in 1978 and replaced the previous system of state insurance founded after the Second World War. The aim of the NHS was to create an efficient and uniform health system covering the entire population, irrespective of income or contributions, age, gender, employment or pre-existing health conditions.

The NHS provides health care services to all residents and their families and emergency care to visitors irrespective of their nationality. All in-patient treatments, that is (or i.e.) treatments requiring hospitalisation, are free under the NHS.

The NHS is composed of various bodies and entities, namely the Ministry of Health ("MoH"), the Superior Institute of Health, AIFA, the regional health authorities, the regional health institutions (ASLs, ATSs, ASSTs, ASPs, etc.) and the hospitals through which health care services are provided.

The NHS is largely funded through direct and indirect taxation, while the remainder is derived from the incomes of the regional health institutions and from patients directly. Regions are allocated a proportion of the health care budget. This proportion varies annually and is established by the MoH.

For 2024, the maximum expenditure for each region is fixed at: (i) 6.8% of the National Health care budget with regard to the total expenditure referable to medicines reimbursed by the NHS (class A medicines) distributed through public and private[amend as shown or review] pharmacies (so-called *"tetto della spesa farmaceutica convenzionata"*); and (ii) 8.5% of the total health budget, with regard to expenditure referable to medicines provided in hospitals (class H medicines) which are purchased or made available for use by health facilities directly managed by the NHS (so-called *"tetto della spesa farmaceutica per acquisti diretti"*).

If these thresholds are exceeded, any overspend is borne respectively by pharmaceutical companies, wholesalers, and pharmacies for threshold (i) and 50% by pharmaceutical companies and 50% by the regions, in proportion to their respective quotas for threshold (ii). Pharmaceutical expenditure in 2024 amounted to approximately 7/8 billion Euro with regard to expenditure (i) and 13/14 billion Euro with regard to expenditure (ii).

2.1 Major legislation

The main legislative provisions on reimbursement, prescription and distribution of medicinal products and medical devices are contained in Legislative Decree n. 219 of 24 April 2006, which implemented the European Pharma Code, and Legislative Decree 137/2022, which implemented EU Regulation 2017/745 on medical devices and repealed, exception made for some provisions, Legislative Decree n. 46 of 24 February 1997, which implemented EU Directive 93/42/EEC on medical devices.

The provisions regulating the methods of determination of prices for reimbursable medicinal products are mainly contained in the Decree of the Ministry of Health dated August 2, 2019, and the prices of non-reimbursable medicinal products in class C are largely governed by Law Decree n. 390 of 20 September 1995 and Law Decree n. 87 of 27 May 2005 (as subsequently amended).

In addition, the prices of medicinal products in classes A and C are determined by various subsequent financial laws and the decisions of the major players in the pharmaceutical industry.

2.2 Prescribers – physicians

Prescription-only ("Rx") medicinal products are prescribed by accredited physicians. Class A Rx medicinal products subject to reimbursement by the NHS are prescribed by the so-called "*medici di base*", physicians on call, ER physicians, outpatient specialists and hospital physicians according to different provisions of regional laws. In principle, there are no provisions limiting the autonomy of prescribers; such prescribers are thus free to prescribe any medicinal product they deem advisable.

However, in practice, prescription behaviour is strictly monitored by national and regional health authorities. In addition, guidelines are normally issued by the Regions to address the physicians' prescribing practice in relation to generics.

Furthermore, the power of physicians to use certain medicinal products is often conditioned by the actual availability of products within the hospitals.

2.3 Decision-makers – the Italian Health Authorities

The AIFA is vested with the power to permit or prevent the reimbursement of individual medicinal products or categories thereof on the basis of cost/benefit evaluations and take other major decisions which apply nationwide. Regions may adopt special measures, for example, patient co-payment schemes, to reduce regional expenditure; moreover, Regions may provide for measures to rationalise pharmaceutical spending and to allocate the limited resources in a manner deemed most congruent to the needs of the population.

3. Pricing and reimbursement of pharmaceuticals

3.1 Distribution and pricing

Medicinal products sold to hospitals are subject to a compulsory discount equal to 50% of the relevant price (net of VAT) charged to the public. This discount applies to both reimbursable and non-reimbursable medicinal products. No compulsory discounts are required by law for medical devices.

The NHS reimburses hospitals by way of lump sums for overall treatments, depending on the type of disease and the treatment (*Diagnosis Related Groups*). Thus, the costs of medicinal products applied in a hospital usually have to be covered by the DRG lump sum which the hospital receives for the entire treatment of the patient. The purchase of pharmaceuticals by hospitals is usually carried out through bid and tender procedures, under which further discounts, in addition to the compulsory ones, are provided by pharmaceutical companies.

In out-patient care, the chain of distribution and pricing mechanism is as follows:

(a) Pharmaceuticals are classified as prescription-only ("Rx") and non-prescription ("non-Rx"). Rx medicinal products may only be distributed to patients by pharmacies, while non-Rx medicinal products may also be distributed from a dedicated section of a commercial store in the presence of a pharmacist in compliance with Law no. 248 of 4 August 2006.

(b) The mechanism for determining the prices of medicinal products differs depending on whether they are reimbursable (class A) or not (class C). In principle, the prices of class C medicinal products are freely set by pharmaceutical companies. However, in practice, the prices of medicinal products in class C have been increasingly regulated by Law no. 149 of 26 June 2005, according to which pharmaceutical companies may only increase the prices of class C pharmaceuticals every other January. Nevertheless, section 1, paragraph 801 of Law n. 296/2006 has specified that the above limitation on price increases only applies to Rx class C medicinal products, while the price of non-RX class C medicinal products can be freely set at any time. There are no compulsory margins for wholesalers and pharmacies with respect to non-Rx medicinal products, although the most common practice is to apply the same margins as provided by law for Rx medicinal products (see 3.1(d)).

(C) Prices of medicinal products in class A are subject to negotiation with the AIFA, in accordance with the provisions of the Decree of the Ministry of Health dated August 2, 2019 (see 2.1 above). An agreement reached between the AIFA and the manufacturer on the medicinal product price lasts 24 months and is subject to an implied renewal for an additional period of 24 months unless previously terminated by either party, or unless one of the parties communicates to the other a proposal concerning the amendment of the contractual terms before the expiration of the agreement. In the event of changes in the therapeutic

indications of the medicinal products leading to a potential increase in their use, the negotiation may be reopened by each party before the expiry of the agreement. Moreover, AIFA can reopen the negotiation before the expiration of the agreement in the event that: (i) market variations occur such that an excessive increase in the use of the medicine or an unfavourable cost-therapy ratio is expected; (ii) there is new evidence on the efficacy and safety of the medicine such that the positioning in therapy is deemed modified or that the estimated clinical benefits are substantially reduced; or (iii) there is an overt shortage of the medicine in the Italian territory. It is common practice to establish under the negotiation procedure a proportionate relationship between the price paid and, among others, the volume of sales of the medicinal product.

(d) Wholesalers' margins for reimbursed medicinal products are fixed at 3% of the ex-factory price (net of VAT), while pharmacies' margins are fixed at 30.35% of the ex-factory price (net of VAT).

(e) In addition, when reimbursing pharmacies the retail price of reimbursable medicinal products, the NHS applies the following compulsory discounts:

- 3.75% for medicinal products whose price is lower than €25.82 (1.5% for pharmacies with revenue between EUR 150,000 and EUR 300,000);
- 6% for medicinal products whose price ranges between €25.83 and €51.65 (2.4% for pharmacies with revenue between €150,000 and €300,000);
- 9% for medicinal products whose price ranges between €51.66 and €103.28 (3.6% for pharmacies with revenue between €150,000 and €300,000);
- 12.5% for medicinal products whose price ranges between €103.29 and €154.94 (5% for pharmacies with revenue between €150,000 and €300,000); and
- 19% for medicinal products whose price is higher than €154.94 (7.6% for pharmacies with revenue between €150,000 and €300,000).

In addition, NHS applies an additional compulsory discount equal to 2.25% of the price.

(f) In relation to reimbursable class A medicinal products, pharmacies may not grant discounts to patients and pharmaceutical companies and wholesalers may not grant discounts to pharmacies.

3.2 Reimbursement

(a) Once a medicinal product is authorised, it is not immediately eligible for reimbursement. As a very general principle, reimbursement is provided for essential medicinal products, namely products:

- for diseases for which no therapeutic alternative exists; or
- for which the medicinal products, already available on the market, do not provide a satisfactory or appropriate answer; and
- which present a better cost/benefit and risk/benefit analysis than those offered by medicinal products already on the market.

Even in the absence of the above characteristics, medicinal products which are as safe and effective as those already on the market may be reimbursable depending on the result of their cost/benefit evaluation. However, medicinal products that do not display a clinical advantage compared to products already available on the market can be reimbursed only if they present a therapy cost equal to, or lower than, those already available on the market.

When evaluating eligibility for reimbursement, the AIFA also takes into consideration, among others, the following factors in relation to the medicinal products: (i) the reimbursability, use, and sales price in other EU countries; (ii) information about the production capacity of the marketing authorisation holder, as well as the capacity of contingency management and the distribution model adopted to cover the national territory; (iii) the foreseen market share in the following 36 months; (iv) the impact on expenditures for the NHS; and (v) estimate of the financial/economic impact (business impact assessment) and relating consumption following the commercialisation of the product.

(b) In certain cases with respect to non-reimbursable medicinal products, AIFA entitles a product to reimbursement but limits the reimbursement to a particular disease and/or specific therapeutic indications. Relevant determinations are known as the "Note AIFA" and are published on the national reimbursement list (*Prontuario Nazionale*). Physicians disregarding the notes without a justifiable reason may be sanctioned and asked by the competent local health institution to refund the price of the prescribed medical product.

(c) As approval of a Marketing Authorisation (MA) and pricing (and reimbursement) were decided in the past in the course of the same procedure, it appeared that such disposition could be effectively enforced in order to prevent generic manufacturers from entering the market before patent expiry. However, more recently AIFA issued a communication, according to which the route for the grant of the MA may be split from the procedure of reimbursement and pricing. According to the AIFA's new guidelines, if an MA application is filed for a medicinal product that is still under patent protection, AIFA shall decide on the grant of the MA and on the price and reimbursement afforded to the medicinal products, while the latter shall be published in the Official Journal as "C – nn" (i.e. medicinal products in class "C" – not reimbursed by the NHS – and nn as non-negotiated) for the period in which the patent protection is still effective.

(d) Law Decree no. 158/2012 introduced a provision that sets forth that if a medicinal product (e.g. generic) is granted an MA but infringes the patent protection of another medicinal product (e.g. originator) such medicinal product (e.g. generic) cannot be reimbursed in Italy until such patent protection has expired. Law no. 118/2022 has confirmed such provision, specifying that the marketing authorisation holder of the generic medicine can apply for reimbursability even before the patent protection of the originator has expired. This is without prejudice that reimbursement will still be granted after that patent protection has expired.

(e) Class C medicinal products are not reimbursed by the NHS.

3.3 Generic substitution

Physicians are encouraged to prescribe the generic name of an active ingredient, although they are not precluded from prescribing the brand name of a medicinal product. With respect to reimbursable medicinal products, whenever the prescribing physician does not indicate on the prescription only the name of the active ingredient, if applicable the pharmacist should inform the patient of the availability of a generic version. However, if the prescribing physician inserts the words "*not to be replaced with generics*", or the patient decides to purchase the branded medicinal products regardless of the pharmacist's advice, the difference between the price of the product prescribed and the generic medicinal products shall be met by the patient.

For class C medicinal products which are not reimbursable, if applicable, the pharmacist is obliged to inform the patient of the availability of a generic medicinal product. Moreover, if the prescription does not mention anything to the contrary, upon the patient's request the pharmacist is obliged to dispense the generic version of the medicinal product concerned.

Generics are reimbursed to the pharmacist by the NHS up to the lowest price of the corresponding medicinal products available on the regional distribution channel, on the basis of specific directives provided for by each region.

3.4 Import quotas

Due to the low prices of medicinal products in Italy compared to other EU countries, Italy is one of the most important source markets for parallel trades.

Parallel imports of medicinal products are subject to relevant authorisation by the AIFA, in compliance with the Ministerial Decree of 29 August 1997. There is no obligation on pharmacies to replace domestic medicinal products by parallel imports if they cost less.

3.5 Off-label use

Medicinal products prescribed for off-label use are not reimbursable unless the relevant use is included in a specific list by the AIFA. To be entitled to be included in such a list, no therapeutic alternative should exist and favourable results of at least phase II clinical trials should be available.

The inclusion in the list mentioned above is also possible in the event a therapeutic alternative exists. In this case, the medicine to be included in the list must be prescribed for a therapeutic indication different from the one authorised, provided that such indication is grounded on research conducted within the national and international medical and scientific community, according to parameters of cost effectiveness and appropriateness.

The relevant request is not submitted directly by the manufacturer, but should come from patient associations, scientific societies, health institutions, universities or AIFA's Technical-Scientific Committee.

3.6 Non-Rx drugs, lifestyle drugs and other non-reimbursable products

Lifestyle drugs, for example, treating non-pathological obesity or erectile dysfunction are always classified as non-reimbursable class C medicinal products.

3.7 Out-of-pocket payments by patients

In order to reduce and/or cover the regional health expenditure, the regions may require co-payments from patients with respect to certain reimbursable medicinal products. The co-payment policy varies from Region to Region. Certain categories of people, for example disabled people or people whose income does not exceed certain thresholds, are usually exempted from co-payments.

3.8 Price reductions and discounts

Since 2005, for the purpose of regulating national health expenditure, the AIFA has issued resolutions imposing on pharmaceutical companies mandatory reductions and discounts on the retail prices of reimbursable medicinal products. Such reductions have ranged from 5% to 7% of the retail price and have been considered cumulative.

The Financial Law for 2007 confirmed the reduction set forth in the AIFA resolutions for the previous years. In addition, the Financial Laws for 2007 and 2008 provided that pharmaceutical companies could switch to the payback system rather than reducing the price of their medicinal products.

The payback is a financial mechanism that allows pharmaceutical companies to ask for the suspension of the AIFA price reduction of 5%, compared with simultaneous payment in cash (payback) of the relative value of specific accounts identified by the regions.

3.9 Annual market share for pharmaceutical companies

To reduce expenditure by the NHS, the Financial Law for 2008 introduced a new system whereby pharmaceutical companies were assigned individual budgets for reimbursement. Such a budget identified the maximum spending allowed by the NHS for medicines owned by that pharmaceutical company which, if this budget was exceeded, had to contribute to replenishing the expenditure.

The budgets were calculated by the AIFA on the basis of the turnover generated by the medicinal products sold during the previous year and taking into account the estimated reduction of such turnover in the subsequent year due to the expiry of patents. How much each pharmaceutical company contributed to overspending by the NHS is determined proportionally to the amount each pharmaceutical company exceeds its budget. The Financial Law mechanism for 2019 has amended this by replacing the budget system with the market share system. Differently from the budget system, the market share system is not based on estimates but rather measures the actual weight of the company on the market in the reference year.

In relation to innovative medicinal products, the quota for overspending is allocated to all marketing authorisation owners in proportion of their market share.

Due to the low prices of medicinal products in Italy compared to other EU countries, Italy is one of the most important source markets for parallel trades.

4. Price and reimbursement of medical devices

Medical devices are not subject to reimbursement by the NHS, save in the context of LEAs. Similarly, the pricing of medical devices is not regulated. However, the MoH, which is the competent authority for medical devices, establishes the maximum prices at which the latter may be purchased by hospitals in the event in which medical devices are involved in LEAs.

4.1 Registry of medical devices

Medical devices which are not registered on the special register of the MoH (*Repertorio dei Dispositivi Medici*) and may not be sold to hospitals and other public institutions within the NHS.

4.2 Point of sale

The point of sale for medical devices may vary depending on the device.

National and European legislation on medical devices does not provide for restrictions on the point of sale of medical devices. However, special legislation may envisage restrictions with regard to specific types of medical devices (e.g., prescription glasses may only be sold by opticians).

4.3 Advice on the use of medical devices

The Unique Commission of Medical Devices, a division of the MoH, publishes evaluations of the cost/benefit relationship of medical devices registered on the National Register of Medical Devices to provide health operators with guidelines on the appropriate use of the same.

4.4 Contract on the provision of medical devices and public tenders

The purchase of medical devices by hospitals is carried out through bid and tender procedures.

The relevant starting price for such tenders, in relation to some medical devices, is established by the Unique Commission of Medical Devices.

More recently, the National Anti-Corruption Authority has been entrusted with the task of identifying "reference prices" in the health sector – including medical devices – and publishing them regularly. Reference prices are not mandatory but NHS entities may re-negotiate contracts concluded at a price that differs of at least 20% from the reference price.

4.5 Payback mechanism for medical devices

Law no. 111 of 2011, converting Law Decree no. 98/2011, introduced a cap on public spending on medical devices for the first time. Originally set at 5.2% of the health care budget, the cap in question was amended several times and, from 2014 onwards, it has been set to 4.4%.

The Financial Law for 2015 has provided a mechanism for repayment of health spending similar to the one envisaged for medicinal products. Specifically, in the event of a region exceeding the above mentioned cap, a portion (equal to 40% in 2015, 45% in 2016 and 50% from 2017) of the excess spending is to be reimbursed by medical device companies, each company in an amount equal to the percentage incidence of its turnover on the total expenditure for the purchase of medical devices borne by the Regional Health Service.

After several years in which this provision was not enforced, the Ministry of Health's Decree of July 6, 2022, certified the overrun of the cap for the years 2015, 2016, 2017 and 2018, and quantified the amount owed by companies for the repayment.

This measure triggered a strong political and judicial debate. The Italian lawmakers granted several postponements of payment deadlines while companies brought numerous appeals to Lazio's Regional Administrative Tribunal. Subsequently, pursuant to Law Decree 34/2023, companies that waived their right to appeal against the payback measures were given the chance to pay an amount equal to 48% of the original due amount. The Campania region and Lazio's Regional Administrative Tribunal referred the question on the constitutionality of the payback mechanism to the Italian Constitutional Court.

With two rulings issued on 22 July 2024, the Italian Constitutional Court established the legitimacy of the payback mechanism for medical devices and that all companies are entitled to reduce their payment to 48% of the original due amount.

4.6 HTA and observatory on prices of medical devices

Pursuant to the Legislative Decree 137/2022, which implemented EU Regulation 2017/745 on medical devices, the Ministry of Health drafted a National Health Technology Assessment Plan for Medical Devices, which aims: (i) to ensure the proper management of medical device expenditure; (ii) to ensure uniformity in the national system; (iii) to ensure the early identification and evaluation of innovative health technologies recognised as having a potentially high clinical, economic and organisational impact; (iv) to ensure that the NHS decision-making processes are informed by scientific evidence on the potential clinical, organisational, economic, social, legal and ethical impact; (v) to ensure the development of recommendations on the use of evaluated technologies; and (vi) to ensure the introduction of specific classifications and conditions of purchase at the expense of the NHS for the use of medical devices after they are marketed. Pursuant to the afore mentioned Legislative Decree, the Ministry of Health also provided for the activation of the National Observatory of Medical Device Prices, with the task of supporting public entities in procurement and tender processes and verifying consistency between purchase prices and reference prices defined by the National Anti-Corruption Authority for homogeneous categories of products.

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Portugal.

1. Summary

- The maximum retail price of prescription only (Rx) medicinal products and of non-Rx medicinal products subject to reimbursement must be authorised by INFARMED (the authority responsible for conducting the reimbursement and prior assessment procedure) before these medicinal products can be commercialised in Portugal. The retail price for non-reimbursed non-Rx medicinal products (OTCs) can be freely determined by each pharmacy.
- The maximum retail price ("*Preço de Venda ao Público*" or "PVP") is calculated using the prices of certain "reference countries" (currently Spain, France, Italy and Belgium).
- Reimbursed medicinal products are fully or partially paid for by the State. When purchasing reimbursed medicinal products in pharmacies, patients do not pay, or they pay only a part of the medicinal products. The National Health Service (NHS) is responsible for the cost of all in-patient medicinal products administered within the NHS.
- The reimbursement is established mainly by means of a percentage of the PVP of the medicinal product (according to different reimbursement categories) and a system of reference prices (when medicinal products are clustered in homogeneous groups of medicinal products).
- All Rx medicinal products to be purchased by the NHS (except those that are already reimbursed) are subject to prior assessment (*"avaliação prévia"*) and to the execution of a prior assessment contract with the marketing authorisation holder ("MAH"), which sets out the purchasing conditions, including the price. Entities of the NHS cannot purchase Rx medicinal products without a valid prior assessment contract in place (except for reimbursed Rx medicinal products).
- INFARMED is responsible for conducting the reimbursement and prior assessment procedure. The final decision is, however, a competence of the Minister of Health (who may delegate this competence to the directive council of INFARMED). There is a single common procedure for the prior assessment and for the reimbursement of medicinal products (provided by Ordinance no. 195-A/2015, of 30 June).
- As for medical devices, in most cases the price can be freely determined by the relevant economic operators. However, certain medical devices or generic groups of medical devices can be subject to special maximum price systems for reimbursement and prior assessment purposes.
- When there are public health reasons or proven economic advantages, the State can reimburse the acquisition of medical devices to beneficiaries of the NHS and of other public health sub systems. For this purpose, the manufacturer shall submit a reimbursement application to INFARMED. In this case, the rules on pricing and reimbursement of medicinal products apply (with the necessary adaptations).

2. Overview of the health care system in Portugal

2.1 Overview

The Portuguese health care system consists of three coexisting systems:

a) National Health Service (NHS)

The NHS comprises all institutions and services that are dependent on the Ministry of Health. The NHS is a universal service (available to all citizens and residents in Portugal) funded mainly by taxes. Health care provided by the NHS is essentially free of charge. However, when accessing hospital emergency services without prior referral by the NHS, patients need to pay user fees called *"moderation fees" ("taxas moderadoras"*), which take into consideration the economic and social conditions of patients. There are certain beneficiaries who are exempt from the payment of moderation fees (e.g., pregnant women, unemployed people, low-income pensioners, patients with certain chronic diseases, blood donors, firefighters, etc).

b) Health subsystems for certain professional sectors

Apart from the NHS, there are several health subsystems created within the scope of various ministries, banking and insurance companies and other institutions, to provide health care to their employees or associates. These are special public and private health insurance schemes for certain professional sectors (e.g., ADSE – Assistance in Disease to Civil Public Servants; SAMS – Medical and Social Assistance Services, for bank employees and their families). Beneficiaries of these systems have access to the NHS, but also to private sector entities that have agreements with the respective systems.

c) Private systems

Various private health institutions and professionals complete the offer of health care services, providing their services on a private basis or through agreements or conventions with both the NHS and some of the above mentioned subsystems.

Part of the population subscribes to voluntary private health insurance offered by privately owned insurance companies, which enter into agreements/conventions with private health care institutions and professionals.

2.2 Major legislation

The key legal provisions on pricing and reimbursement of medicinal products and medical devices are provided in DecreeLaw no. 97/2015 of 1 June, setting up the National System for the Evaluation of Health Technologies.

In addition to this DecreeLaw, there are other relevant legislative texts such as Ordinance no. 195-A/2015, which provides the common procedure for the reimbursement and prior assessment of medicinal products, Ordinance no. 195-C/2015, of 30 June setting out the rules for the maximum price system and Ordinance no. 195-D/2015, of 30 June providing the reimbursement categories and corresponding reimbursement percentages.

2.3 Payors – the State

Reimbursed medicinal products are paid by the State (in the percentage that is subject to reimbursement). When purchasing reimbursed medicinal products in pharmacies, patients do not pay, or they pay only a part of the medicinal products. This, however, requires that the medicinal products are prescribed to patients using the official medical prescription model.

For beneficiaries of health subsystems and of private (voluntary) health insurance, part of the costs of the medicinal products may also be copaid by the health subsystems or by the private insurance companies.

The NHS is responsible for the cost of all in-patient medicinal products administered within the NHS.

2.4 Prescribers

Medicinal products are classified, in terms of dispensing to the public, as: (i) medicinal products not subject to medical prescription; and (ii) medicinal products subject to medical prescription (these ones with further subcategories).

A medical prescription is defined as the document by which one or more specified medicinal products are prescribed by a medical doctor or, in cases provided for in special legislation, by a dental practitioner or dentist (Article 3(1)(ooo) of DecreeLaw 176/2006). Nurses are not allowed to prescribe medicinal products.

The prescription of medicinal products shall necessarily include the international nonproprietary name (INN) of the active substance, the pharmaceutical form, the dosage, the presentation and the posology. The prescription may also include a commercial name, brand name or indication of the MAH name. The prescription shall be carried out electronically or, in exceptional cases, manually.

Rx products can only be sold to the public in pharmacies. Non-Rx products (OTCs) can be sold in pharmacies and in other specialised stores (parapharmacies). When reimbursed non-Rx products are sold outside of pharmacies, however, the reimbursement or state co-payment is not applied (i.e., the consumer pays the entire price).

2.5 Decision-makers

INFARMED ("*Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.*") is the competent authority for medicinal products. It is the authority responsible for authorising the maximum retail price of medicinal products. INFARMED is also the authority responsible for conducting the reimbursement and prior assessment procedures.

The reimbursement or prior assessment decision, including the authorisation to execute reimbursement or prior assessment contracts, is a competence of the Minister of Health (who may delegate this competence to the directive council of INFARMED).

3. Pricing and reimbursement of medicinal products

3.1 Pricing overview (outpatient setting)

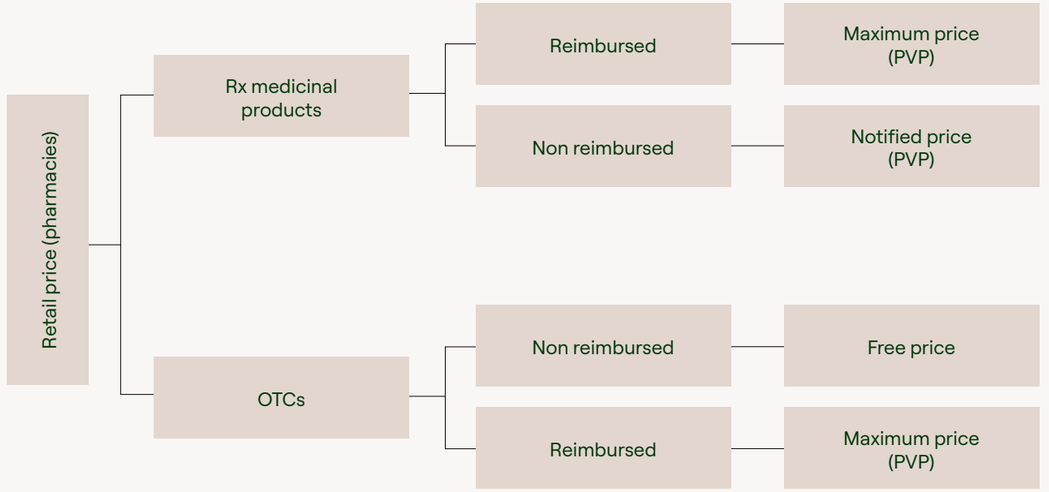
The retail price (i.e., public selling price in pharmacies) of medicinal products is determined according to one of three main systems: the maximum price system, the notified price system or the free price system. As a general rule, only medicinal products that are authorised to be placed on the market in Portugal under a valid marketing authorisation can be granted a price and a reimbursement status.

Non-Rx medicinal products (OTCs) that are not subject to reimbursement are covered by the free price system. This means that the retail price is defined by each pharmacy (or store authorised to sell OTCs) and the margins are defined by the MAH and the operators in the distribution chain.

3.2 Maximum price system (outpatient setting)

Reimbursed Rx medicinal products and reimbursed non-Rx medicinal products (not a common situation, since they are as a general rule non-reimbursable) are covered by the maximum price system.

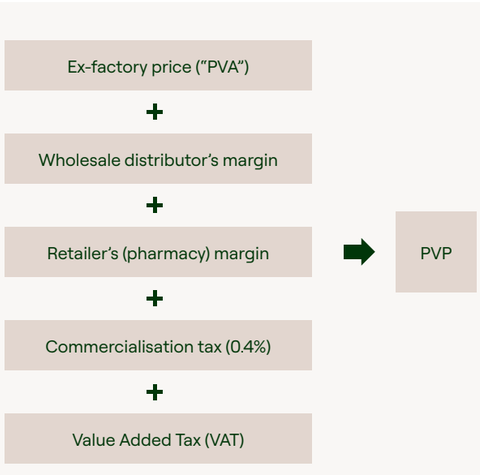
Medicinal products covered by this system have a fixed retail price decided by the directive board of INFARMED, which cannot be exceeded. This *maximum retail price* is called "*Preço de Venda ao Público*" or "*PVP*". Rx medicinal products that are not subject to reimbursement also have an approved PVP, but they can be subject to the notified price system (explained below).



Medicinal products covered by the maximum price system cannot be commercialised in Portugal before the PVP is determined. For that purpose, the MAH shall apply for PVP authorisation to INFARMED (through the SIATS platform). The timeline for INFARMED to authorise the PVP is 15 days (after which the price is considered as tacitly authorised).

The MAH may voluntarily determine prices lower than the authorised PVP. Changes to the authorised PVP must be communicated at least 20 days before the date of their implementation and they become effective on the first day of the month. The practice of discounts is also allowed throughout the whole distribution chain, from the manufacturer to pharmacies (discounts by pharmacies may however be limited by the Minister of Health for reasons of public interest, namely public health or sustainability of the sector, or the protection of competition).

The PVP is calculated according to the following formula:



The PVP of medicinal products to be placed for the first time on the Portuguese market is calculated using the average of the PVAs in force in *"reference countries"* for the same product or, where there is no such product, for identical or essentially similar products. This reference PVA is then added alongside the margins, commercialisation tax and VAT to determine the final PVP. The reference countries are determined by ordinance of the Minister of Health on an annual basis. The reference countries for 2025 are Spain, France, Italy and Belgium (Ordinance no. 293/2024/1, of 15 November).

For the purposes of determining the PVP, the PVA to be considered in Portugal cannot exceed:

- The average of the PVAs in force in the reference countries for the same product or, if the product is not available in all reference countries, the average of the PVAs in force in at least two of those countries.
- If the same product exists in only one of the reference countries, the PVA in force in that country.
- If in a reference country the same product is available at different prices, the lowest price.
- If the same medicinal product is not available in any of the reference countries, the average of the lowest PVAs of identical or essentially similar products (excluding generics) in force in the highest possible number of those countries.
- In the event that neither the same nor identical or essentially similar products are available in any of the reference countries, the PVA for an identical or essentially similar product being commercialised in Portugal.
- In the event that neither the same nor identical or essentially similar products are available in any of the reference countries or in Portugal, the PVA in force in the country of origin.

The price comparison is made by reference to the smallest sized pack/presentation in Portugal. The PVA is determined on the basis of the comparison, in each of the reference countries, with the PVA of the nearest sized presentation or, if they are equidistant, with the smallest presentation among those.

The PVP is reviewed annually, based on the comparison with the prices in force in the reference countries. For this purpose, the MAH shall submit to INFARMED, until 15 December of each year, the lists of prices for the following year (which come into force on 1 January). If the comparison with the prices in force in the reference countries would determine a higher PVP than that currently in force, the PVP will remain unchanged. Medicinal products with a PVP of up to EUR 5,00 are exempted from the annual price review.

The PVP may also be reviewed on an exceptional basis, for reasons of public interest or at the initiative of the MAH (exceptional review of the price or "REP"). When requested by MAHs, the REP essentially aims at getting a PVP higher than the one currently approved. The request for REP shall be submitted by the MAH to INFARMED, but the final decision takes the form of an ordinance of the Minister of Health. The decision on a REP depends on how indispensable the product is and on the budgetary affordability for the NHS. It takes into consideration factors such as the cost of production of the product and the price of existing alternative products for the same therapeutic purposes and with an equivalent risk-benefit ratio.

(a) PVP of generics (outpatient setting)

The PVP of generics shall be at least 50% less than the maximum PVP of the reference medicinal product in the same dosage, or in the closest dosage and in the same pharmaceutical form. However, if the PVA of all presentations (pack sizes) of the reference product (with the same dosage or, in the absence of such dosage, of the closest dosage and in the same pharmaceutical form) is below EUR 10,00, then the PVP of the generic shall be only at least 25% lower than the maximum PVP of the reference product.

The maximum PVP of the reference product to be taken into consideration is the average of the maximum PVP of the reference product in the two years immediately preceding the pricing application for the generic.

(b) PVP in case of parallel imports

The PVP of medicinal products subject to parallel import to be introduced in the Portuguese market must be at least 5% less than the maximum PVP of that product and of identical or essentially similar products with a marketing authorisation in Portugal.

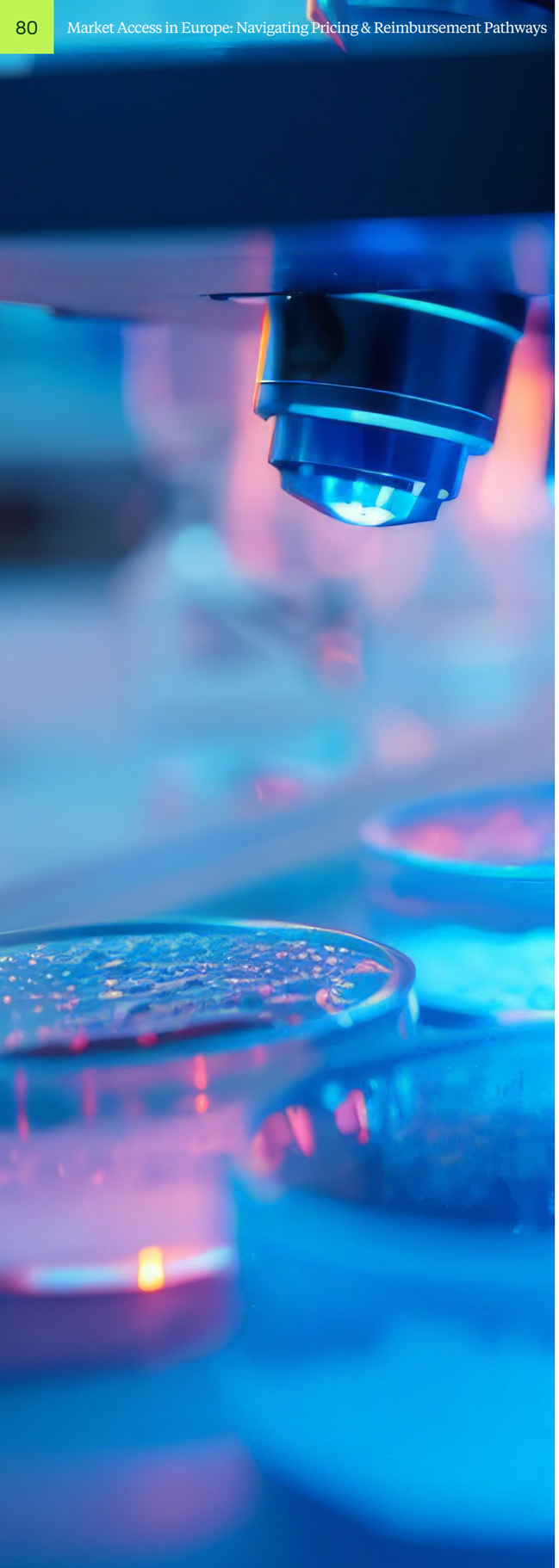
Where the medicinal product in question does not have an approved PVP in Portugal, a PVP will be calculated on the basis of the general rules explained above (including those for generics, if that is the case).

(c) Maximum marketing margins

The commercialisation of Rx medicinal products (re-imbursed or not) and of reimbursed non-Rx medicinal products is subject to maximum marketing margins. This means that the price of medicinal products sold in pharmacies in Portugal includes a margin for the pharmacists and wholesalers, which is subject to maximum percentages and amounts. The marketing margins depend on the PVA amount:

PVA (EUR)	Margin Wholesaler	Margin Pharmacy
Up to €5.00	2,24% + €0.25	5,58% + €0.63
€5.01 to €7.00	2,17% + €0.52	5,51% + €1.31
€7.01 to €10.00	2,12% + €0.71	5,36% + €1.79
€10.01 to €20.00	2,00% + €1.12	5,05% + €2.80
€20.01 to €50.00	1,84% + €2.20	4,49% + €5.32
From €50.01	1,18% + €3.68	2,66% + €8.28

(percentages calculated on the PVA)



3.3 Notified price system

Non-reimbursed Rx medicinal products can be subject to the notified price system. This system provides certain flexibility to the MAH in terms of price. Contrary to what happens to medicinal products that are fully subject to the maximum price system, medicinal products under the notified price system may have a PVP higher than the maximum approved PVP through an additional annual variation of up to a maximum of 10% of the PVP in force, with a limit of €2.50 each year. Products covered by this system are not subject to the annual price revision for the maximum price system explained above.

When the MAH intends to apply a PVP higher than the maximum approved PVP, it shall notify INFARMED with a minimum prior notice of 20 days. The new price shall be applicable from the first day of the following month. The marketing margins on the additional variation shall be 20% for pharmacies and 8% for wholesalers (excluding VAT). INFARMED may oppose the application of the notified price system, namely for market or public health reasons.

3.4 Prior assessment for medicinal products to be purchased by the NHS (inpatient)

All Rx medicinal products to be purchased by the NHS are subject to prior assessment. There is an exception for Rx medicinal products that are already reimbursed, which are exempt from prior assessment. Other medicinal products with substantial sales volume to the NHS may also be subjected to prior assessment.

Medicinal products subject to prior assessment can only be purchased and used by entities of the NHS after a prior assessment contract has been signed, which requires a favourable prior assessment decision. The medicinal products can only be purchased by entities of the NHS in the conditions provided in a valid prior assessment contract. The prior assessment establishes the conditions for the purchase of medicinal products by the NHS, including the price, considering:

- the technical scientific criteria that demonstrate therapeutic innovation, or its therapeutic equivalence, for the claimed therapeutic indications; and
- its economic advantage.

The burden of proof as regards to the added or equivalent therapeutic value of the medicinal product, as well as its economic advantage, lies with the MAH.

The economic advantage in the case of therapeutic equivalence shall consist of: (i) price reduction in relation to the alternative, in cases of new pharmaceutical form, new dosage forms, or significantly different packaging size in relation to the packaging of medicinal products with the same qualitative composition; (ii) price reduction of at least 10% in relation to the (non-generic) alternative in cases of a new medicinal product, with the same qualitative composition as other medicinal products, in identical pharmaceutical form, dosage and packaging. For generics, the economic advantage shall be at least 30% in relation to the reference medicinal product. For similar biologics, the economic advantage shall in general correspond to at least 20% of the PVA of the reference biologic.

Entities of the NHS may purchase medicinal products that can also be sold to the public in pharmacies, or "hospital use only" medicinal products. For the first ones, if they are already reimbursed, a prior assessment will not be required as mentioned above. Otherwise, they need to go through a prior assessment procedure.

Medicinal products for "hospital use only" have no PVP (retail price), since they cannot be sold to the public, and are also not subject to reimbursement by the State. For this reason, they do not follow the typical pricing and reimbursement pathway. The price of these medicinal products is the *hospital selling price* ("preço de venda hospitalar" or "*PVH*").

The prior assessment establishes a *maximum acquisition price for entities of the NHS* (the "PVH"). The PVA of these medicinal products, subject to annual review, shall not exceed (for nongenerics) the *lowest PVA* in force in the reference countries for any of the essentially similar pharmaceutical forms existing in each of those countries. For generics, the PVA shall be at least 30% lower than the maximum price of the reference medicinal product with the same dosage and pharmaceutical form.

The PVH is calculated according to the following formula:

PVA + 0.4% commercialisation tax + VAT

INFARMED is the authority responsible for conducting the prior assessment procedure, at the request/application of the MAH. The prior assessment decision is, however, a competence of the Minister of Health (who may delegate this competence to the directive council of INFARMED).

There is a single common procedure for the prior assessment and for the reimbursement of medicinal products (provided by Ordinance no. 195-A/2015, of 30 June). Therefore, the rules explained below for the reimbursement procedure are also applicable to the prior assessment procedure of medicinal products to be purchased by the NHS. The prior assessment is without prejudice to the application of public procurement rules.

(a) Early Access Programme (PAP)

As a general rule, only medicinal products that were subject to prior assessment and for which a prior assessment contract has been signed can be purchased and/or used by the NHS .

However, INFARMED may authorise the use in Portugal or medicinal products without a valid marketing authorisation (and therefore without prior assessment contract) when: (i) by clinical justification, the products are considered indispensable for the prevention, diagnosis or treatment of certain pathologies; (ii) they are necessary to respond to the actual or potential propagation of pathogenic agents, toxins, chemical agents or nuclear radiation, which may cause harmful effects; or (iv) in exceptional cases, they are acquired by a pharmaceutical service or pharmacy and dispensed to a specific patient.

In this case, medicinal products are supplied according to the terms of the Early Access to Medicines Programme (*Programa de Acesso Precoce a Medicamentos* or "PAP" – *cf.* INFARMED Deliberation no. 80/CD/2017).

In exceptional cases, authorised medicinal products may also be used by entities of the NHS without the signing of a prior assessment contract (as long as there is no decision rejecting the prior assessment procedure), by decision of INFARMED under the terms of authorisation for exceptional use, when such products are purchased by a pharmaceutical service or pharmacy and dispensed to a specific patient. The authorisation for exceptional use shall be submitted by the institution or service, explaining that there is no therapeutic alternative and the patient is at immediate risk of life or at risk of suffering serious complications. These medicinal products are supplied, from the date of granting of the MA and during the prior assessment procedure, also under the terms of the Early Access of Medicines Programme.

3.5 Reimbursement of medicinal products (in pharmacies – outpatient setting)

The State may co-fund (also mentioned as "reimburse") the purchase of medicinal products prescribed to beneficiaries of the NHS and other public health subsystems. Reimbursed medicinal products are required to be available for dispensing in pharmacies (in accordance with the notification of the start of the commercialisation made by the MAH to INFARMED).

The State reimburses the purchase of certain medicinal products. The reimbursement is established mainly by means of a percentage of the PVP and a system of reference prices.

The reimbursement is established by means of:

- a percentage of the PVP of the medicinal product;
- a system of reference prices;
- the weighting of factors related to the characteristics of the patients, the prevalence of certain diseases and public health objectives.

The reimbursement of medicinal products is granted by a reimbursement decision with or without the signing of a reimbursement contract.

The reimbursement of the medicinal product expires for all presentations and dosages if one of the following situations occurs with regard to one of them:

- The medicinal product is not commercialised within the NHS within one year (counting from the notification of the reimbursement authorisation).
- After the beginning of the commercialisation, the medicinal product is not available in the market for a period exceeding 90 days.

The reimbursement also expires if the MAH does not comply with the obligation to supply the medicinal products or if the MAH shows the intention to suspend or interrupt the supply and for that reason creates a danger to public health.

3.6 Reimbursement in the maximum price system (PVP)

The reimbursement of medicinal products by reference to the PVP requires:

- the technical-scientific demonstration of the therapeutic innovation or therapeutic equivalence, for the claimed therapeutic indications; and
- demonstration of its economic advantage.

The burden of proof as to the added therapeutic value or therapeutic equivalence of the medicinal product and its economic advantage lies with the MAH. The reimbursement requires the medicinal products to fall under one of the following situations:

1) Innovative medicinal product that fills a therapeutic gap, presenting greater efficacy, effectiveness and/or safety than existing alternative treatments.
2) New medicinal product, with a similar qualitative composition as other products already commercialised and reimbursed, if, in an identical pharmaceutical form, dosage and packaging, it presents an economic advantage in relation to non-generic reimbursed products.
3) New pharmaceutical form, new dosages or significantly different packaging of already reimbursed medicinal products with the same qualitative composition, provided that the therapeutic need and advantage, as well as the economic advantage, are demonstrated.
4) New medicinal product that does not constitute a significant therapeutic innovation where it presents economic advantages in relation to already reimbursed products used for the same therapeutic purposes.

3.7 Reimbursement in the reference price system

Reimbursed medicinal products are subject to the reference price system when clustered in homogeneous groups of medicinal products. These are groups of medicinal products with the same qualitative and quantitative composition in active substances, dosage and route of administration, with the same or equivalent pharmaceutical forms, in which at least one is a generic. The lists of homogeneous groups are published by INFARMED quarterly. Other medicinal products that, although not meeting these criteria, belong to the same pharmacotherapeutic group or subgroup and are considered therapeutically equivalent to the other products belonging to the group, may also be included in the same homogeneous group.

The determination of the reimbursement level for medicinal products that are covered by the reference price system is subject to specific rules.

The reimbursement of these medicinal products is determined as follows:

- The maximum amount of the reimbursement is determined according to the applicable reimbursement category or system, calculated over the reference price of the respective homogeneous group – that is, the reimbursement percentage is applied to the reference price (not to the maximum approved price for each individual medicinal product).
- Where the PVP of the product is lower than the amount calculated under the terms of the previous sub paragraph, the reimbursement shall be limited to that PVP only.

The reference price of each homogeneous group corresponds to the average of the five lowest PVPs of the products that are part of the group and are on the market. However, where the average of these five lowest PVPs exceeds the price of the most expensive generic that is part of the homogeneous group, the reference price shall correspond to the price of the generic.

Where a homogeneous group already exists, the maximum PVP of the new medicinal products to reimburse shall be 5% lower than the maximum PVP of the generic with the lowest price with at least 5% market share in the generics of the homogeneous group.

3.8 Reimbursement of generics

There are certain special rules for determining the reimbursement level of generics. For reimbursement purposes, as from the 5th generic (inclusive), the maximum PVP of the generic shall be 5% lower than the maximum PVP of the generic object to the immediately prior reimbursement application (irrespective of the decision). This shall, however, not result in a PVP that is inferior to 20% of the PVP of the reference medicinal product.

3.9 Reimbursement of similar biologics

Similar biologics are also subject to special rules for determining their reimbursement level. For the purposes of reimbursement, the PVP of the similar biologic cannot exceed 80% of the PVP of the reference biologic. Where similar biologics already exist under a given INN with at least 5% market share of the respective active substance, the PVP of the similar biologic cannot exceed 70% of the PVP of the reference biologic.

3.10 Reimbursement decision process

The MAH may request the reimbursement of a medicinal product for which a PVP was already determined. When the medicinal product has no PVP yet, the MAH may also request the PVP to be determined in the context of the reimbursement procedure.

The request/application for reimbursement shall be submitted to INFARMED. INFARMED is the authority responsible for assessing the reimbursement application. The reimbursement decision, however, is a competence of the Minister of Health (who may delegate this competence to the directive council of INFARMED).

In the context of the assessment of the reimbursement application, a pharmacotherapeutic evaluation and economic evaluation will be conducted. INFARMED may request the MAH to present an economic evaluation study prepared in accordance with the applicable methodological guidelines.

After the assessment is completed, INFARMED prepares a draft decision on the reimbursement application which may consist of: (i) rejection of the application; (ii) acceptance of the reimbursement application; and (iii) proposal for the signing of a reimbursement contract.

The MAH is given the opportunity to comment on the draft decision. After the prior hearing of the MAH, INFARMED prepares the final draft decision and submits it to the competent decision-making authority (Minister of Health or directive council of INFARMED). In cases where INFARMED proposes the signing of a reimbursement contract or the MAH does so during the prior hearing, negotiations shall take place within 30 working days.

Reimbursement or prior assessment contracts, besides the price definition, may include provisions on:

- Maximum amount of charges to be borne by the State, across all NHS establishments and services, with the acquisition of the medicinal products, based on a given number of patients, and respective guarantee mechanisms (and consequences of exceeding the previously agreed upon amounts of charges).
- Definition of objectives to be achieved after implementation of the contract, for purposes of reevaluation of the same.
- Limited period of time, at the end of which the reimbursement percentage shall be reduced, with an equivalent reduction in the price of the medicinal product, or the exclusion from reimbursement.
- Limited period of time during which an additional set of evidence shall be submitted to substantiate the decision to maintain the reimbursement or change the category, or to allow the purchase by entities of the NHS (in case of prior assessment).
- Mechanisms for sharing risk with respect to the use of the medicinal products.
- Duration, renewal, modification and termination of the contract.

The decision on reimbursement shall be taken within the following timelines (added of any clock-stops):

- 30 calendar days for generics and similar biologics;
- 75 calendar days for non-generic medicinal products whose INN or therapeutic indication is already reimbursed; and
- 180 calendar days for medicinal products whose INN or therapeutic indication is not yet reimbursed.

In practice, INFARMED is not able to comply with these timelines in the majority of cases (published statistics available).

Where the reimbursement request is rejected, the MAH may only submit a new application to INFARMED after 6 months (except when the reasons for rejection are the non-demonstration of economic advantage and/or financial affordability and the MAH intends to submit a new price proposal or contractual conditions).

Following the notification by the MAH of the start of the commercialisation of the reimbursed medicinal product, the product is included in the lists and files of reimbursed medicinal products.

As mentioned above, there is a single common procedure for the reimbursement and prior assessment of medicinal products (provided by Ordinance no. 195-A/2015, of 30 June). Therefore, the procedural rules explained in this section also apply to the prior assessment of medicinal products to be purchased by the NHS.

No measures have yet been adopted to implement the EU HTA Regulation, so changes may occur in the future.

3.11 Reimbursement categories on the general scheme

Under the general reimbursement scheme, the State pays a percentage of the price of medicinal products dispensed in pharmacies (outpatient setting) in accordance with the pharmacotherapeutic classification of the medicinal products. Each medicinal product that is included in the list of reimbursed medicinal products is attributed to a reimbursement category, which corresponds to the percentage of the PVP of the medicinal product that is reimbursed. This is a product-specific reimbursement (i.e., the medicinal products are reimbursed when prescribed for all of their approved therapeutic indications, for all patients, by any prescriber). The reimbursement categories are the following:

- *Category A:* 90% of the PVP (includes medicinal products for the treatment of chronic diseases or life-saving medicinal products, such as medicinal products for the treatment of Parkinson's disease, Cystic fibrosis, diabetes, cancer and medicines specific for haemodialysis).
- *Category B:* 69% of the PVP (includes medicines for serious diseases, such as anticoagulants, and products for cardiovascular and respiratory diseases).
- *Category C:* 37% of the PVP (includes nonpriority medicinal products with proven therapeutic value, such as anti-infectives, hormones and products used in the treatment of endocrine disorders, anti-inflammatory and antihistaminic medicines and vaccines.
- *Category D:* 15% of the PVP (may include new medicinal products, those whose reimbursement is adjusted in the reimbursement contract, or those that, for specific reasons, are covered by a transitory reimbursement regime).

3.12 Reimbursement levels on special schemes

There are two special reimbursement schemes:

- *Beneficiary-specific:* extra reimbursement for pensioners with low incomes. The reimbursement of the price of the medicinal products in Category A is increased by 5% and in Categories B, C and D by 15%.
- *Disease-specific:* reimbursement for defined pathologies or special groups of patients. The reimbursement depends on specific conditions regarding the prescription, such as the pathology or group of patients and the clinical speciality of the prescribing physician, among others. The list of pathologies covered by special regimes and the reimbursement conditions are published by INFARMED. Some examples of pathologies or conditions covered by this scheme include ichthyosis (reimbursed at 100%), psoriasis (90%), medicinal products for medically assisted procreation (69%), moderate to strong oncologic-related pain (90%), Alzheimer disease (37%), haemophilia (100%), Crohn's disease or ulcerative colitis (100%) and Multiple sclerosis (100%).

4. Pricing and reimbursement of medical devices

4.1 Pricing of medical devices

In most cases, the price of medical devices can be freely determined by the relevant economic operators. However, certain medical devices or generic groups of medical devices can be subject to *special maximum price systems* for NHS beneficiaries for reimbursement purposes and/or for purchasing by NHS entities (for the purpose of prior assessment). The determination of these special maximum prices can be based, without prejudice to other criteria, on a retrospective analysis of the prices charged to NHS entities over a period of not less than six months.

4.2 Prior assessment for pricing of medical devices purchased by the NHS

Certain types of medical devices may be subject to prior assessment in order to establish the conditions for purchase and use by NHS entities. The types of medical devices subject to prior assessment are established by ordinance of the Minister of Health.

The prior assessment of medical devices considers whether a medical device presents: (i) a demonstrated therapeutic innovation for the claimed clinical purposes; and (ii) a demonstrated economic advantage.

The prior assessment may establish a maximum purchase price for NHS entities. A prior assessment contract can be signed with the manufacturer subject to a prior assessment procedure with a favourable opinion. NHS entities can only purchase medical devices for the indications and under the conditions approved in the prior assessment contract. The prior assessment decision is a competence of the Minister of Health (who may delegate this competence to the directive council of INFARMED). The rules concerning the prior assessment procedure for medicinal products are applicable to medical devices with the required adaptations.

4.3 Reimbursement of medical devices

When there are public health reasons or proven economic advantages, the State can reimburse the acquisition of medical devices to beneficiaries of the NHS and of other public health subsystems.

For this purpose, the manufacturer shall submit a request for reimbursement to INFARMED. INFARMED is the authority responsible for assessing the reimbursement application, but the reimbursement decision is a competence of the Minister of Health (who may delegate this competence to the directive council of INFARMED). For the purposes of reimbursement, maximum prices may be determined for the medical devices. The rules concerning the reimbursement procedure for medicinal products apply to medical devices with the required adaptations.

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Spain.

1. Summary

- In Spain, there is a public health care system which operates in parallel with a network of private health insurance companies. Over 90% of the population uses the National Health System ("*NHS*") for their medical needs.
- Pharmaceutical assistance is jointly financed by the NHS and patients. Medicinal products reimbursed by the NHS that are dispensed to patients who are not hospitalised are subject to a co-payment system.
- Only doctors, dentists and podiatrists can prescribe medicinal products by means of an official prescription.
- The inclusion of a medicinal product within the reimbursement system is selective and based on general and objective criteria. Once a medicinal product has been authorised and registered, the Ministry of Health will decide whether or not to include it within the reimbursement system.
- In compliance with the principle of rational use of medicinal products, public health authorities must encourage, as a general rule, the prescription of medicinal products based on the active ingredient (rather than the brand name).

2. The Spanish health care system: overview

In Spain, the main regulation applicable to price and reimbursement of medicinal products is established in the Spanish Medicinal Products Law (Royal Legislative Decree 1/2015 of 24 July) ("*Spanish Medicinal Products Law*") and the Reference Price Regulation (Royal Decree 177/2014 of 21 March ("*Reference Price Regulation*").

2.1 Main legislation

The regulation of the pricing of medicinal products is mainly established by the Spanish Medicinal Products Law and the Reference Price Regulation. In addition, there are other relevant legal texts such as Royal Decree 823/2008 of 16 May on margins, discounts and deductions for distribution and dispensation of medicinal products, Royal Decree 271/1990 of 23 February on the reorganisation of price intervention for medicinal products for human use and Order of 17 December 1990 on certain parameters for the application of Royal Decree 271/1990.

2.2 Payors – insurance funds

In Spain, there is a public health care system which operates in parallel with a network of private health insurance companies.

(a) National Health System

The public health care system provides universal health care to all citizens under a tax financed scheme run by the NHS. The various Autonomous Regions pay for all health care services from their budgets and have flexibility in how and what products and services procure and somehow incorporate into the NHS.

Over 90% of the population uses the NHS for their medical needs. The system allows Spanish citizens to choose their primary care doctor, through whom they have access to the rest of the system. In order to consult a specialist, patients must first be referred by their primary care doctor (except in emergencies).

In addition, emergency care is universally available to anyone (irrespective of the patient's nationality and of the patient contributing to the NHS).

(b) Private health insurance

The private system coexists with the NHS. The private insurance system is used either as a supplement to, or as an alternative to, the NHS. The advantage of private insurance is that the insurance companies have their own network of hospitals, clinics and labs.

The patients of private health insurance usually have a shorter waiting time for treatment than patients in the NHS. The only downside is that these insurance companies can insist that patients only use doctors who are members

of their group. However, most companies have programs that refund around 80% of the fees charged by physicians outside the approved group.

2.3 Prescribers – doctors, dentists and podiatrists

Only doctors, dentists and podiatrists can prescribe medicinal products by means of an official prescription, which must include the necessary data to identify the prescribing health care professional, the patient and the prescribed medicinal products.

Medicinal products are classified as prescription and non-prescription/over-the-counter ("*OTC*"). OTC medicinal products are excluded from reimbursement by the NHS and may be advertised to the general public.

All medicinal products are dispensed to patients solely through pharmacies or hospital pharmacies (primary care and specialised care).

2.4 Decision-makers – the Ministry of Health and Regional Health Authorities

The Ministry of Health is the main body involved in the pricing and reimbursement process of medicinal products.

The Ministry of Health is generally in charge of pharmaceutical legislation and assessment and authorisation of medicinal products, and it carries out some of these duties through the Spanish Agency for Medicinal Products and Medical Devices ("*AEMPS*"), the Directorate General for the Common Portfolio of Services of the NHS and Pharmacy ("*DGCYF*") and the Interministerial Medicinal Products Pricing Commission ("*CIPM*").

The DGCYF is responsible for deciding on the reimbursement of medicinal products, as well as for co-ordinating with the health services of the Autonomous Regions the measures and actions related to the pharmaceutical provision of the NHS, meaning the set of medicinal products, medical devices and actions aimed at ensuring that patients receive them in a manner appropriate to their clinical needs, in the precise doses according to their individual requirements, during the appropriate period of time and at the lowest possible cost.

In addition, the DGCYF is assisted by the so-called Advisory Committee, a body of a technical nature providing advice, evaluation and consultation on the relevance, improvement and monitoring of the economic evaluation to support the decisions on reimbursement.

In terms of pricing, the competent authority is the CIPM, which is made up of both national and regional public authorities.

The AEMPS has an important role in the reimbursement process by means of the Therapeutic Positioning Reports ("*IPT*").

In practice, both pricing and reimbursement procedures run in parallel. The DGCYF has considerable influence over the process, and de facto leads the negotiations with the marketing authorisation holders ("*MAH*") (or their local representatives) and co-ordinates the work of the evaluation teams.

3. Pricing and reimbursement of medicinal products

3.1 Decision to reimburse the price of medicinal products

Reimbursement of medicinal products is made selectively and not indiscriminately. The criteria for the funding of medicinal products are set forth in Article 92 of the Spanish Medicinal Products Law:

- severity, duration and sequelae of the different pathologies for which the medicinal product is indicated;
- specific needs of certain groups;
- therapeutic and social value of the medicinal product and its incremental clinical benefit, taking into account its cost-effectiveness ratio;
- rationalisation of public spending on pharmaceutical services and budgetary impact on the NHS;
- existence of medicinal products or other therapeutic alternatives for the same conditions at a lower price and lower treatment cost; and
- degree of innovation of the medicinal product.

In terms of the pricing and reimbursement process as such:

- As soon as the AEMPS informs the DGCYF about the new medicinal product, the initiation team within the DGCYF sends a communication to the MAH (or its local representative) informing about the initiation of the pricing and reimbursement process and granting a 10-20 working day period for the submission of the pricing and reimbursement dossier.
- Once the pricing and reimbursement dossier is submitted, the evaluation team within the DGCYF carries out the relevant evaluation to make a decision, including cost-effectiveness, budgetary impact and degree of innovation, which are set out in an evaluation report (including, where appropriate, the so-called IPT) that is then forwarded to the CIPM to make a decision on pricing.
- Pricing and reimbursement is then executed by means of an express decision on inclusion or non-inclusion within the pharmaceutical provision of the NHS issued by the decision team within the DGCYF. If included, the decision lays down the reimbursement conditions and the price within the scope of the NHS (and the notified price, as the price of the medicinal product when sold outside the NHS).
- The medicinal product in question may be subject to special reimbursement conditions, the most common of which are as follows:
  - submission of annual sales certification, in order to verify the actual sales of the medicinal product against the estimated sales provided by the companies during the P&R process;
  - updated information on the situation of the medicinal product in other markets, mainly in neighbouring countries, in order to proceed accordingly to an adaptation of the price of the medicinal product to the lower price in the countries of the EU;
  - expenditure caps, a way of setting a maximum expenditure for the medicinal product throughout the NHS for a given period of time; or
  - payment based on results, usually reserved for high-cost therapies (e.g. cell and gene therapies).

OTC medicinal products, medicinal products which are not use for a specific pathology, cosmetics, dietetic products, mineral waters, elixirs, dentifrices, toothpastes and similar products will not be reimbursed, as well as those medicinal products indicated for syndromes of minor severity and those which do not respond to therapeutic needs.

3.2 Fixing the price

The decision on the price of reimbursed medicinal products is made on the basis of the price proposal formulated by the MAH (or its local representative) according to technical, accounting and financial documentation that must be made available to the CIPM so that it can prepare the relevant economic report. In this sense, Article 97 of the Spanish Medicinal Products Law provides that *"for the purposes of pricing, pharmaceutical companies must provide the Ministry of Health with all the information on the technical, economic and financial aspects"*.

The ex-factory price, reimbursed price or PVL is set based on the identification of the manufacturing costs to which a business profit is added. The purpose is to identify the real cost of the medicinal product in an objective and transparent manner, so that the adjusted manufacturing costs are included, and a reasonable business profit is added, avoiding unjustified or unnecessary costs.

For the purpose of quantifying the manufacturing costs, the following variables are taken into account:

- level of activity;
- evolution of the company's costs and sales volumes;
- estimates of sales of the new medicinal product; and
- the impact on structural costs arising from the manufacture of the new medicinal product.

It also includes expenses for research and development, as well as for promotion and advertising.

In addition to the manufacturing costs, other complementary criteria is involved in fixing the PVL, some of which are very similar to the criteria for deciding on reimbursement, including: (i) therapeutic usefulness; or (ii) cost-effectiveness and budgetary impact analyses.

As a matter of practice, the price-approval process entails a negotiation with the MoH where the cost and the profit margin are not the only variables which are considered. These variables have actually been replaced by factors such as therapeutic usefulness, PVL of similar medicinal products, activities performed by the company in Spain (R&D, manufacturing, etc.), or the price of the medicinal product in other EU Member States, as well as other criteria applicable to the reimbursement leg, such as the degree of innovation or the contribution to the sustainability of the NHS.

Based on the application of the aforementioned criteria, the CIPM decides whether or not it is feasible to reimburse the price of the medicinal product. The CIPM's decision is incorporated into the subsequent DGCYF's decision of inclusion or non-inclusion in the pharmaceutical provision and the price within the scope of the NHS.

3.3 Reference prices/selected prices

The public reimbursement of a medicinal product is subject to the reference price system set out by Article 98 of the Spanish Medicinal Products Law and the Reference Price Regulation.

The reference price is the maximum amount with which the medicinal product presentations included in each of the reference groups that will be reimbursed, provided they are prescribed and dispensed from public funds.

The groups shall include all presentations of funded medicinal products that have the same level 5 of the World Health Organisation's anatomical-therapeutic-chemical classification of medicinal products (ATC5) and the same route of administration. The group must include at least one biosimilar or generic presentation reimbursed by the NHS (unless the medicinal product or its main active ingredient have been authorised for a minimum of 10 years in a EU Member State and additionally there is a medicinal product different from the original one and its licenses, in which case the existence of a generic product will not be essential to establish a group).

The reference price shall be calculated by reference to the lower cost per treatment per day of the presentations included in the group. This price will be established dividing the wholesale price of each product by the number of defined daily dosages.

There are two other relevant concepts: lower price and lowest price. These two concepts will have a decisive impact on the prescription and dispensation of medicinal products as explained in section 4 below.

The lower price is set by the Ministry of Health for each homogeneous group (the homogeneous group is made up of presentations of reimbursed medicinal products with the same active ingredient by reference to the dosage, content, pharmaceutical form and route of administration, which could be inter-changed in dispensation) and is incorporated into the NHS "nomenclátor" (list of products included in pharmaceutical assistance updated every month by the Ministry of Health), but this price does not necessarily have to be the same as the lowest price in the market. The lowest price is the lowest market price and refers to individual presentations (not to homogeneous groups). However, the market forces are equating lower prices and lowest prices.

The lower prices of homogeneous groups are reviewed every three months. The new lower price reviewed for each homogeneous group will correspond to the lowest priced presentation at the time of each quarterly update. Therefore, in the month in which the update occurs, lower prices are the same as the lowest prices. But during the next two months following the update, pharmaceutical companies may request voluntary price reduction for their presentations and in these cases the price will be below the lower price and will be the lowest price of the homogeneous group until the next quarterly update.

3.4 Co-payment

Pharmaceutical assistance is jointly financed by the NHS and patients. Pharmaceutical products reimbursed by the NHS that are dispensed to patients who are not hospitalised are subjected to a co-payment system.

The Government may adjust the patient's contribution by taking into account the following criteria:

- the ability to pay;
- the therapeutic and social utility of the medicinal products and medical devices;
- the needs of specific groups;
- the severity, duration and after-effects of the different pathologies for which the products are prescribed;
- the rationalisation of public expenditure for pharmaceutical provision; and
- the existence of available medicinal products or medical devices or other similar or better alternatives for the same disease.

In general, the patient's contribution will be as follows:

- 60% of the retail price for patients and beneficiaries whose yearly gross income is equal to or greater than €100,000.
- 50% of the retail price for patients and beneficiaries whose yearly gross income is equal to or greater than €18,000 and less than €100,000.
- 40% of the retail price for patients and beneficiaries who are not included in the previous groups.
- 10% of the retail price for social security pensioners and beneficiaries.
- 40% of the retail price for foreign citizens not registered or authorised as residents in Spain.

4. Prescription and dispensation

As mentioned above, in compliance with the principle of rational use of medicinal products, public health authorities must encourage, as a general rule, prescription of medicinal products based on the active ingredient rather than the brand name.

When the prescription is made by active ingredient, the pharmacist must take into account the price of the medicinal products for dispensation and for this purpose the monthly lists related to lower and lowest prices mentioned above are essential.

In accordance with the Reference Price Regulation, when the prescription is made by active ingredient, the pharmacist will dispense the lowest priced medicinal product of its homogeneous group. In the case of shortages or urgent necessity, the available presentations should be dispensed in order of lowest price. If taking this into account it is possible to dispense several presentations, the corresponding generic or biosimilar product will be dispensed. When prescription is made by brand name these rules will be applicable only if the prescribed medicinal product is priced higher than the lower price of the homogeneous group. Accordingly, there is a clear push in favour of the generic product and a significant pressure generally on the pricing of products.

As described above, this situation, which involves price changes every month, was creating stock problems in pharmacies. Moreover, some generic pharmaceutical companies were lowering their prices aggressively and were then unable to meet the demand, which was causing supply problems.

To avoid this situation, the Spanish Medicinal Products Law considers as a very serious infringement the *"failure by the MAH to comply with its obligation to keep the market adequately and continuously supplied in order to enable compliance with the legally established requirements regarding the pharmaceutical provision of the NHS and to guarantee the supply to pharmacies and pharmacy services of medicinal products included in homogeneous, lowest price and lowest price groups"*, punishable with fines between €90,000 and €1,000,000.

5. Coming changes

In Spain, we currently find ourselves in the process of reviewing and developing the legal framework that will govern all issues related to pricing and reimbursement of medicinal products, including amendment/update of the Spanish Medicinal Products Law, Spanish HTA Regulation and Spanish Pricing and Reimbursement Regulation:

5.1 Spanish Medicinal Products Law:

The new Spanish Medicinal Products Law is currently in the Draft Bill phase, so we are still in the very early stages of the review process, although a draft text is already available. In summary, the text of the Draft Bill as we know it today incorporates the following developments:

- reinforces prescription by active ingredient;
- amends the homogeneous groupings system;
- suggests selected prices, harshly criticized by the sector in general;
- addresses incremental innovation and strategic medicinal products;
- makes prescription requirements more flexible; or
- introduces new developments in advertising, including issues that affect the already long debate on promotion in the period between authorization and pricing and reimbursement.

The Draft Bill is generating a lot of discussion and addresses issues of great relevance to the industry in general. There is still a lot of work to be done, and the debate over the coming months is expected to be intense.

5.2 Spanish HTA Regulation

In Spain, we are still working on the Spanish HTA Regulation, although we already have a draft text that sets out the Ministry of Health's initial ideas on how to approach HTA more locally, highlighting, among other issues:

- reports produced at national or regional level must take into account joint clinical assessments produced at European level;
- creation of the so-called "system for the assessment of the efficiency of health technologies," composed by the Governance Council, the Office for the Assessment of the Efficiency of Health Technologies, and the Health Technology Positioning Group;
- HTA must include, separately, a report on comparative clinical assessment and another on the evaluation of non-clinical aspects; and
- mechanisms are incorporated to involve patient organizations, consumer organizations, and health care professional organizations in HTA.

As said, the draft Spanish HTA Regulation has undergone an initial consultation process and is moving forward for final approval.

5.3 Spanish Pricing and Reimbursement Regulation

The new Spanish Pricing and Reimbursement Regulation has also begun the drafting process, although in this instance we do not yet have a draft text. The main goals of the future regulation include:

- regulating and defining procedures and methodology for pricing and reimbursement decisions;
- establishing procedures and conditions for accelerated, conditional, and provisional reimbursement authorizations;
- setting up procedures to complement the generation of knowledge on real-life performance of medicinal products;
- modifying the reference pricing system by introducing elements that increase competition;
- reforming the procedures for pricing and reimbursement of generics and biosimilars;
- establishing mechanisms for monitoring and basic rules for price review;
- defining procedures to ensure transparency, as well as confidentiality of those aspects that must be confidential; or
- establishing procedures and systems for monitoring pricing and reimbursement decisions.

We are currently in an earlier stage and expect to see the first draft of the text soon, accompanied by the relevant consultation process.

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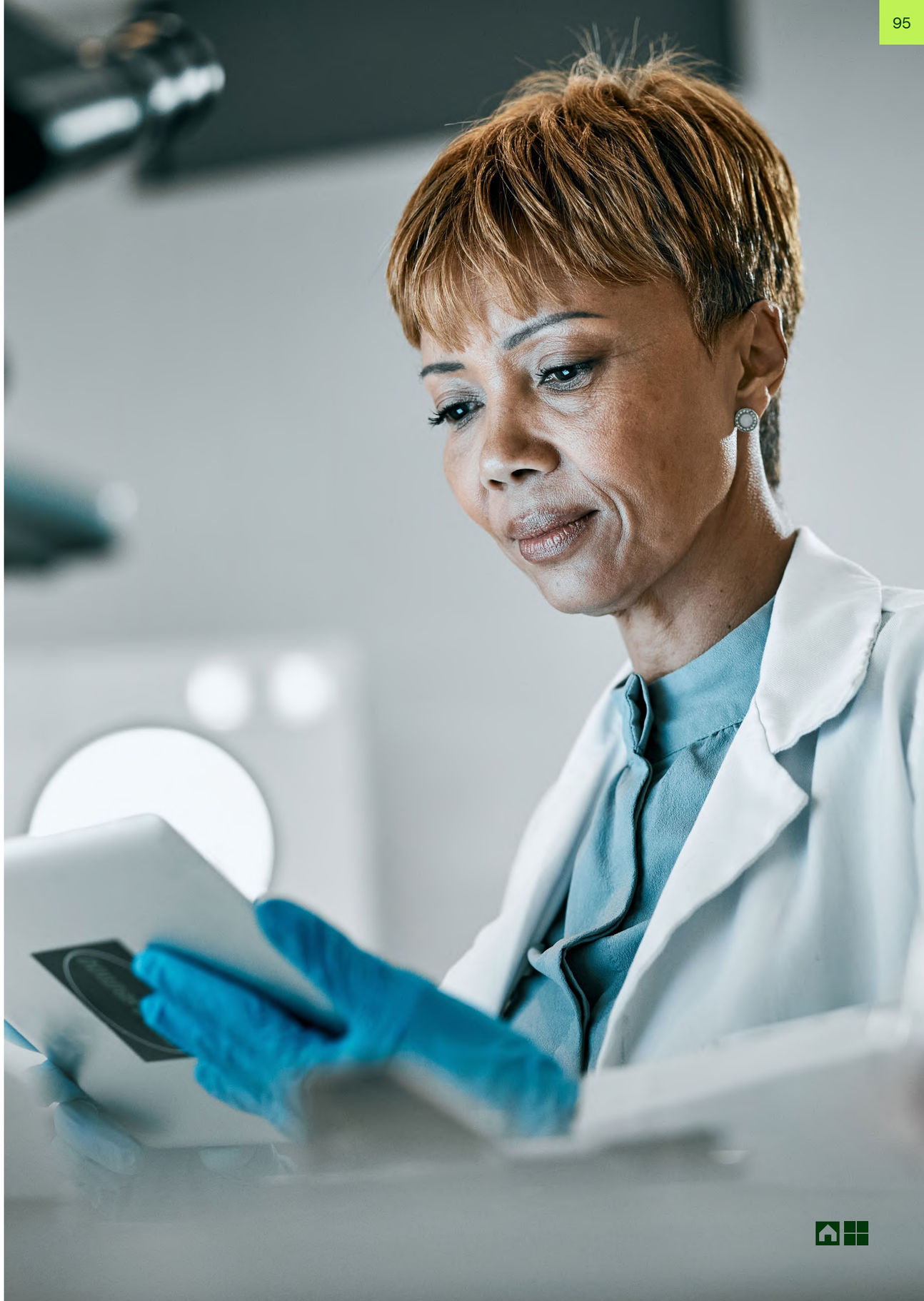


The Netherlands.

1. Summary

- The majority of the medicinal products and medical devices are reimbursed from a basic package of health insurance which is mandatory for each citizen.
- There are 4 major health insurers in the Netherlands that dominate the health insurance market.
- There is a positive list of reimbursed medicinal products for outpatient use. The availability of medicinal products within the hospital is decided by the individual hospitals.
- Health insurers apply reimbursement restrictions mainly for outpatient reimbursement:
  - Reimbursement limited to medicinal products designated by the health insurer, whereby the insurer is obliged to designate at least one medicinal product of each active substance included in the positive list (preference policy).
  - Various contractual arrangements between health insurers and pharmacists whereby pharmacists are forced to dispense cheaper medicinal products.
- Health insurance companies however also apply some restrictions to inpatient reimbursement:
  - Provide a fixed budget for which a health care provider (pharmacist/hospital) must buy medicinal products (closed-end financing of medicinal products).
  - Health insurers enter into agreements with pharmaceutical companies regarding reimbursement of hospital products.
- Various measures are in place or are being introduced by the government to cut back the costs of medicinal products, e.g.:
  - Maximum prices for medicinal products in the Medicine Prices Act.
  - Agreements between health care providers, health care insurers, patient organisations regarding expensive medicinal products.
  - Medicine Reimbursement System (*Geneesmiddelenvergoedingssysteem*) for medicinal products for outpatient use and the maximum personal contribution for medicinal products for outpatient use.
  - New and expensive hospital medicinal products may temporarily be excluded from reimbursement. Such products may be moved to reimbursed status. Prior to moving such a product to a reimbursed status, the Minister may require that a financial arrangement be agreed upon with the pharmaceutical company, which would involve a discount.
  - Subsidy scheme for promising care (*Subsidieregeling veelbelovende zorg*) whereby the government provides subsidy for research for, among others, new promising medicinal products of which there is no evidence (yet) that it is (cost) effective compared to existing treatments.[1]
  - Conditional authorisation orphan drugs, conditionals and exceptionals (*Voorwaardelijke toelating weesgeneesmiddelen, conditionals en exceptionals*) which provides for the possibility to have new, promising medicines of which there is no evidence yet that it is (cost) effective compared to existing treatments, included under conditions in the basic health insurance.
  - Measures to ensure that certain expensive medicinal products are only reimbursed from the hospital (inpatient) budget, by excluding these medicinal products from the positive list for outpatient use, because the inpatient system is based on budget (closed-end) financing, whereas the outpatient system is based on an open-end financing.
  - Policy decision “health care insurance in relation to rules for the admission of medicinal products to the basic health care insurance” (*Besluit van 23 April 2018, houdende wijziging van het Besluit zorgverzekering in verband met regels voor de toelating van geneesmiddelen tot het basispakket*) which allows for the (temporary) exclusion of reimbursement for new indications for in-patient use of already existing medicinal products.

1 The subsidy scheme for promising care ceases to apply as of January the 1st 2026.

2. The dutch health care system: overview

Under the Health Insurance Act (*Zorgverzekeringswet*) which came into force on 1 January 2006, it is mandatory for all residents of the Netherlands to take out basic health insurance which consists of a standard package of insured services. The health care system in the Netherlands is one of private health insurance with public social conditions. The system is operated by private health insurance companies which must accept all Dutch citizens, regardless of their age or condition of health. A system of risk equalisation enables the acceptance obligation and prevents direct or indirect risk selection. All people pay the same nominal insurance premium to their health insurer for the basic health insurance. The Health Insurance Act also provides for an income related contribution to be paid by the employer of the insured. Employers contribute by making a compulsory payment towards the income related insurance contribution of their employees. The Health Insurance Act aims to increase competition between insurance companies and health care providers to economise health care costs, while safeguarding the public interest by introducing the standard package of insured services. This system has led to extensive consolidation of the market for health insurance companies through mergers. In addition to mandatory policies, health insurance companies can offer additional insurance packages, in which case no mandatory acceptance applies.

2.1 Major legislation

The pricing of medicinal products is regulated by the Medicinal Products Prices Act (*Wet Geneesmiddelenprijzen* – "WGP").

Reimbursement and regulated tariffs are regulated by the Health Insurance Act (*Zorgverzekeringswet* – "Zw") and the Health care (Market Regulation) Act (*Wet Marktordening gezondheidszorg*).

2.2 Payors – insurance funds

In the Netherlands, insured parties pay a fixed premium (the nominal premium), which averages approximately €1,880 per person per year. The insurer determines the level of the nominal premium, but is obliged to provide everyone with the same care for this premium. Health insurers are allowed to make a profit.

Most health care policies provide for benefits in kind, where insurers negotiate with health care providers on the price, content and organisation of the care. Until recently, insured parties could also choose a restitution policy where they could choose their own health care provider, also if the health care provider did not have a contract with the patient's health insurance company. In case law from the Supreme Court in 2022, it was confirmed that health insurers are not obliged to reimburse the full amount of treatments under a restitution policy. This means that in principle health insurers are allowed to apply a generic discount on the costs to be covered by the health insurer for a medical treatment under a restitution policy. In practice, the number of restitution policies offered by insurance companies declined rapidly over the past few years. As of 2025, no restitution policies are offered, but health insurance companies currently offer combination policies which still allow patients, to a certain degree, to choose a health care provider that does not have a contract with the patient's health insurance company.

All people pay the same nominal insurance premium to their health insurer for the basic health insurance.

The government set a public framework condition that health care must be affordable for all. People who cannot pay for the fixed premium due to low income, can apply for a care allowance.

2.3 Prescribers – physicians and dentists

In the Netherlands, prescription-only medicinal products are prescribed by physicians, dentists and certain designated nurses. Midwives can prescribe certain prescription-only medicinal products in specific circumstances.

2.4 Decision-makers – the Ministry of Health

The Minister of Health decides which new medicinal products shall be placed on the Drugs Remuneration System (*Geneesmiddelen Vergoedingssysteem* –"GVS"), which consists of a positive list of reimbursed products. The GVS is included in the Health Insurance Decree (*Besluit Zorgverzekering* – the "Decree") and the Health Insurance Regulation (*Regeling Zorgverzekering* – the "Regulation"). The execution of the GVS is assigned to the Minister of Health, Welfare and Sport (*Minister van Volksgezondheid, Welzijn en Sport* – the "Minister"). Before the Minister decides on an application, it will consult with the Health care Institute Netherlands (*Zorginstituut Nederland*).

In addition to the formal decision-makers, there is a trend towards an increased influence on actual reimbursement decisions by other stakeholders. Health insurers have an increasing influence on actual reimbursement decisions for both the outpatient and the inpatient system as a result of e.g. contractual arrangements and budget measures. Hospitals and other health care providers also have an increasing influence as a result of e.g. purchasing decisions and the drafting of treatment guidelines which may include first choice medicinal products.

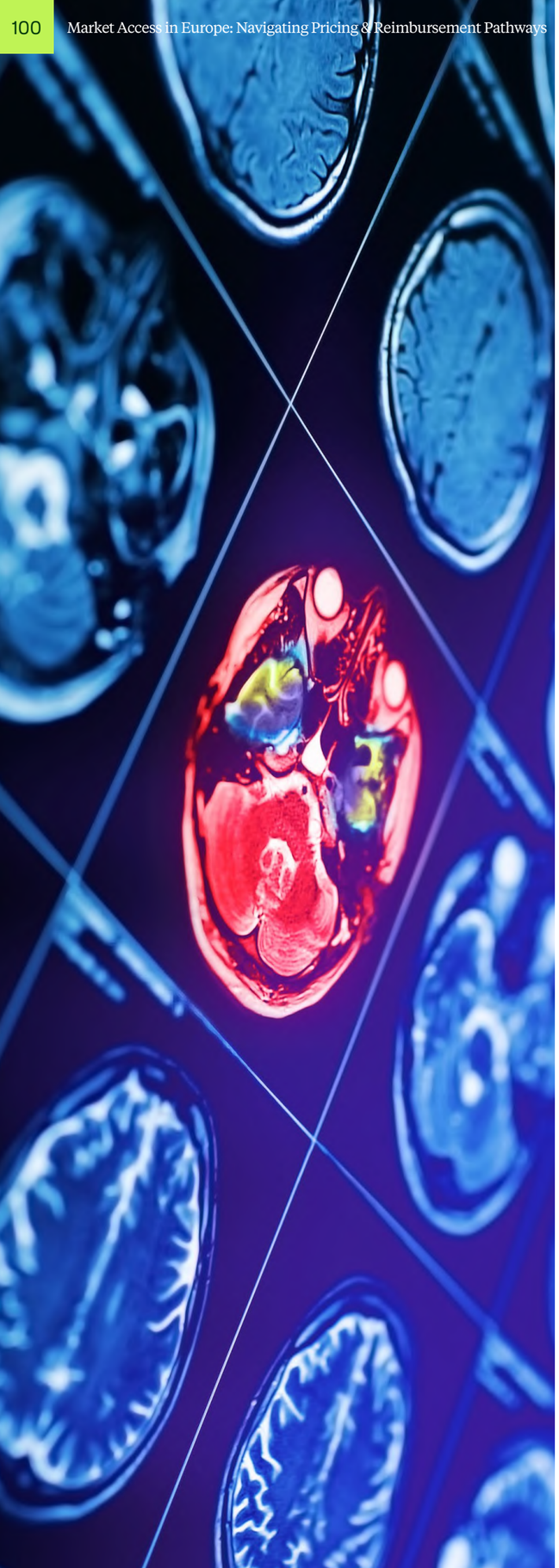
2.5 Pricing

The pricing of medicinal products is regulated by the Medicinal Products Prices Act (*Wet Geneesmiddelenprijzen* – "WGP"). The pricing of medical devices is not regulated.

The WGP allows the Minister to fix maximum prices based on the average official list price of comparable medicinal products in Belgium, Norway, France and the United Kingdom. A maximum price can be calculated if a comparable product is marketed in at least two of the four countries and the product is eligible for reimbursement. A comparable product is a product with the same active substance, the same or almost the same unit strength of active substance and the same pharmaceutical form (including generics and biosimilars). Maximum prices are calculated using set price lists from each country to determine the cheapest available "comparable" product. The average of these prices is equal to a prescription-only medicinal product's maximum price for which the product may be sold to those who are authorised to dispense such medicinal product (retail price). The maximum retail prices of generics also fall under the WGP. Hospital prices are also covered by the WGP. The prices of OTC products are not controlled.

The WGP offers a legal basis for, among others, manufacturers of medicinal products for which a maximum price is set, to request the Minister to increase the maximum price in the situation that it would otherwise not be profitable to market the respective medicinal product on the Dutch market. For the year 2024, hundreds of such requests have been submitted and are now under review by the Minister.

In addition to the statutory maximum prices it is common for hospitals, wholesalers and pharmacies to negotiate and obtain discounts and bonuses when purchasing medicinal products.



3. Prescription and reimbursement of medicinal products

3.1 Drug remuneration system (outpatients)

Once a prescription-only medicinal product has obtained a marketing authorisation, it can be included in the positive list of the Drugs Remuneration System (GVS). The GVS provides a positive list of reimbursable products for use outside the hospital. A medicinal product is reimbursable if it is either (i) interchangeable (equivalent therapeutic value) with one or more other medicinal products on the list with a similar indication or (ii) it has a unique therapeutic value. Furthermore reimbursement may be subject to a statutory condition. This is designed in the Annexes to the Regulation as follows:

(a) Annex 1A: prescription-only medicinal products grouped in Annex 1A are "similar" interchangeable products, meaning that the products in the same group have an equivalent range of indications, an equivalent manner of administration, are designed for the same general age group and there is an absence of clinically relevant differences. For interchangeable products the reimbursement is limited to a maximum amount. The reimbursement limit is the average of the pharmacy purchase prices of the products within one group on a particular reference date, which is currently October 1998, for medicinal products that were registered by that date. For medicinal products registered after the aforementioned date the reference date is the earliest date a "similar" interchangeable medicinal product is registered. If a medicinal product is priced above the maximum reimbursement amount, the patient must co-pay the difference.

(b) Annex 1B: prescription-only medicinal products that are not interchangeable, and which can therefore not be clustered are placed on Annex 1B if such products have added therapeutic value and are cost-effective compared products already included in the GVS. The applicant must provide results of pharmaco-economic research and forecast budgetary implications. These unique products are reimbursed at the manufacturer's recommended price.

Reimbursement may furthermore be conditional on specific indications. Pursuant to Article 2.5(2) of the Regulation, the Minister is permitted to stipulate conditions for the reimbursement regarding e.g. age, indication, etc. These conditions are included in Annex 2 of the Regulation.

An application for admission of a medicinal product in the GVS must be filed with the Minister. The procedure for such an application consists of three parts:

(a) Filing the official application, containing a standard application along with the supporting dossier.

(b) The Minister of Health requests advice from the Health care Institute Netherlands (*Zorginstituut Nederland – "ZiN"*) establishing a product's therapeutic value and, in some cases, also the financial consequences of including it on the positive list. An important part of ZiN's advice is the opinion of the Scientific Advice Board (*Wetenschappelijke Advies Raad* – "WAR"). The WAR will assess on the interchangeability of the prescription-only medicinal product. If the medicinal product is not interchangeable, the evaluation relies on the balance of the product's therapeutic value and cost-effectiveness and will take into consideration therapeutic efficiency, therapeutic efficacy, possible side-effects, past experiences, number of patients that could benefit, ease of administration, improvement in the quality of a patient's life and the cost of reimbursement. As of February the 1st 2025 the ZiN has a new working procedure. The new working procedure involves new document formats that must be used by the applicant, next to the already existing document formats. From February the 1st 2025 it is optional to use the new documentation for applications. However, from May the 1st 2025 using the new document formats is compulsory. This new working procedure also applies to reimbursement submissions filed under the Regulation (EU) 2021/2282 on the Health Technology Assessment (the EU Health Technology Assessment Regulation), although separate instructions are to be followed.

(c) A decision should be made by the Minister within 90 days, excluding any clock-stops. If a decision is made to include the medicinal product in the GVS this decision is published in the Government Gazette (*Staatscourant*) and will have effect thereafter.

If the application is refused, it is possible to request that the Minister reconsiders the application. This is usually done by the marketing authorisation holder in writing and must contain information on new facts or changed circumstances. The procedure for reconsideration is identical to the procedure for a regular application.

For certain specialised and more expensive medicinal products, reimbursement is only made through the hospital budget and not in the GVS. For example, TNF alpha inhibitors and certain cancer medicinal products and growth hormones have been removed from the GVS and are only reimbursed within the hospital. The same happened in 2021 also for total parental nutrition and certain medicinal products for the treatment of Gaucher and in 2022 for epoetins and G-CSF.

3.2 In-patients

In contrast to the outpatient system there is no independent reimbursement system such as a positive list for medicinal products used in a hospital setting. Medicinal products used in the hospital form part of the general entitlement to medical care. The content of what comprises medical care is defined by the state of scientific knowledge and practice. If a certain medical treatment, including the medicinal product used in the treatment, forms part of the "state of the art" medical care, a hospitalised patient is entitled to such care. Generally health insurers decide whether a new medicinal product meets the "state of the art" criterium; if this is the case the medicinal product is charged as part of the overall costs of the medical treatment. For new medicinal products that cost more than €1,000 per patient per year, health insurers decide jointly whether those medicinal products meet the "state of the art" criterium. In case this assessment is positive the health insurers request the Dutch Health care Authority to include the medicinal product in a list for "add-on medicinal products". Consequently the health care provider can claim the costs of those medicinal products as a surcharge on the other costs for the medical treatment.

New expensive hospital medicinal products may, however, be temporarily excluded from reimbursement. The Minister could place such products in a so-called "lock" (*sluis*). While placed in the lock, the ZiN will provide advice on the necessity, effectiveness, cost effectiveness and practicability of the product. The Minister will decide on the basis of the advice whether the medicinal product will be allowed to be reimbursed or whether it will be "locked" from reimbursement permanently. Prior to moving a product from the "lock" to a reimbursed status, the Minister may require that a financial arrangement be agreed with the pharmaceutical company, which would involve a discount and potentially other arrangements regarding appropriate use of the product.

3.3 Conditional reimbursement (both in-and outpatient)

As of 2019, there is a system of conditional reimbursement under two regulations: the Subsidy scheme for promising care (*Subsidieregeling veelbelovende zorg*) and the Conditional authorisation orphan drugs, conditionals and exceptionals (*Voorwaardelijke toelating weesgeneesmiddelen, conditionals en exceptionals*). The Subsidy scheme for promising care offers financial support for research into (cost) effectiveness of the medicinal product compared to existing treatments. The subsidy scheme for promising care ceases to apply as of January the 1st 2026. The Conditional authorisation orphan drugs, conditionals and exceptionals offers patients with a serious and rare disease access to new and promising medication through conditional admission.

3.4 Reimbursement

(a) Reimbursement out-patients

Insured parties (patients) have the right to reimbursement of medicinal products appointed by the Minister in the GVS to the extent that these medicinal products are also appointed by the health insurer. Health insurers are obliged to appoint at least one medicinal product of all the medicinal products with the same active substance available within the positive list (GVS), this is also known as the "preference policy". In addition to a joint preference policy for certain substances, several health insurers have, as of 1 July 2008, also started an individual preference policy.

This means that each health insurer designates different medicinal products it will reimburse and apply such reimbursement conditions in different preferred periods of time at the choice of the health insurer. With the preference policy, for each active substance health insurers aim only to include the medicinal products with the lowest gross pharmacy cost price in the insurance claim of the insured parties. Non-preferred medicinal products are not reimbursed and pharmacists are obliged to dispense the preferred medicinal products, unless the p rescribing doctor specifies another product with the instruction "medical need".

In 2024 several measures were taken in relation to the functioning of the preference policy and medicinal product shortages. One of these measures include that as of 2025 health insurers appoint a preferred medicinal product for a period of two years, instead of one year. Further, some of the health insurers will apply a one-time period of three years. As of 2027 health insurers, in turn, appoint their preferred medicinal product. This should incentivise manufacturers to keep their medicinal products available for a longer period on the Dutch market, which is intended to reduce the risk of product shortages.

In addition to the preference policy, health insurers enter into various contractual arrangements with health care providers such as pharmacists to cut back on costs of medicinal products, e.g. generic substitution arrangements, lowest price range arrangements or an arrangement in which a pharmacist receives a fixed price per multisource medicinal product regardless of the actual price. Preference policy and all other contractual arrangements are based on the prices included in the general price list Z-Index.

Health insurers may set additional conditions for reimbursement aimed at an appropriate use of a medicinal product, e.g. limited to a prescription from specialised doctors.

(b) Reimbursement in-patients

The availability of medicinal products used in a hospital is decided by individual hospitals. The purchase of medicinal products is paid for through the total price paid by health insurers for each diagnosis treatment combination (DBC). As of 2012, the prices of the majority of the DBCs must be negotiated between hospitals and health insurers.

Additional financing is available for hospital products (expensive and orphan medicinal products) that are placed on an add-on list.

3.5 Homeopathic products and OTC products

Homeopathic medicinal products and OTC products are not reimbursed by the basic health insurance. However, it is possible to conclude a supplementary insurance policy for reimbursement of homeopathic products.

3.6 Out-of-pocket payments by patients

Most prescription-only medicinal products are reimbursed by the insurers. However, on the basis of the preference policy and contractual arrangement reimbursement may differ for each insurer and according to the kind of insurance policy the patients have. There are several health insurers that leave the choice of the medicinal products to the patients, physicians and pharmacists. The first €385.00 for the costs of health care, including medicinal products, has to be paid by the patients themselves, the so-called "personal excess" (eigen risico).

Further, patients will, under certain circumstances, have to pay an amount of up to €250.00 if they use a medicinal product that is more expensive than the maximum reimbursement limit that is set for that medicinal product in the Medicine Reimbursement System, i.e. the "personal contribution".

3.7 Off-label use

Medicinal products listed in Annex 1A and 1B of the Regulation prescribed for off-label use may in principle be reimbursed by the health insurer. This is understandable, as for most of these medicinal products no further requirements in the form of indication limits have been set. However, this may be different for those medicinal products prescribed for off-label use which are listed in Annex 2 of the Regulation.

For Annex 2 medicinal products, requirements must be fulfilled before a patient is entitled to the reimbursement of that medicinal product.

4. Prescription and reimbursement of medical devices

Medical devices used in the hospital form part of the general entitlement to medical care. The content of what comprises medical care is – similar to the system for medicinal products – defined by the state of scientific knowledge and practice.

For outpatient use of medical devices a different system applies; the Minister appoints certain categories of medical devices. These categories of medical devices are listed in the Regulation.

The categories of medical devices that are listed in the Regulation are reimbursed by the health insurer for all patients with basic insurance. The reimbursement of medical devices is further regulated by the health insurer. The health insurer determines which type of medical device within a certain category is reimbursed; this may differ for each health insurer. The health insurer may also regulate whether the medical device must be prescribed by doctors or specialists and/or whether permission of the health insurer is necessary before a medical device is provided.

5. Coming changes

In the Netherlands, the National Health care Institute announced on its website what the national assessment procedure looks like with the new EU HTA legislation: after the Dutch authorities receive a Joint Clinical Assessment (JCA) report, the Dutch authorities will prepare a pharmacoeconomic report, a budget impact analysis and (if applicable) send a letter to the Minister of Health, Welfare and Sport containing advice whether or not to reimburse the medicinal product or the medical technology. The National Health care Institute announced on its website that it will analyze the effects of the new HTA legislation at the national level for the national assessment procedures. It is unknown if, and when, the National Health care Institute will publish changes to the national HTA process.

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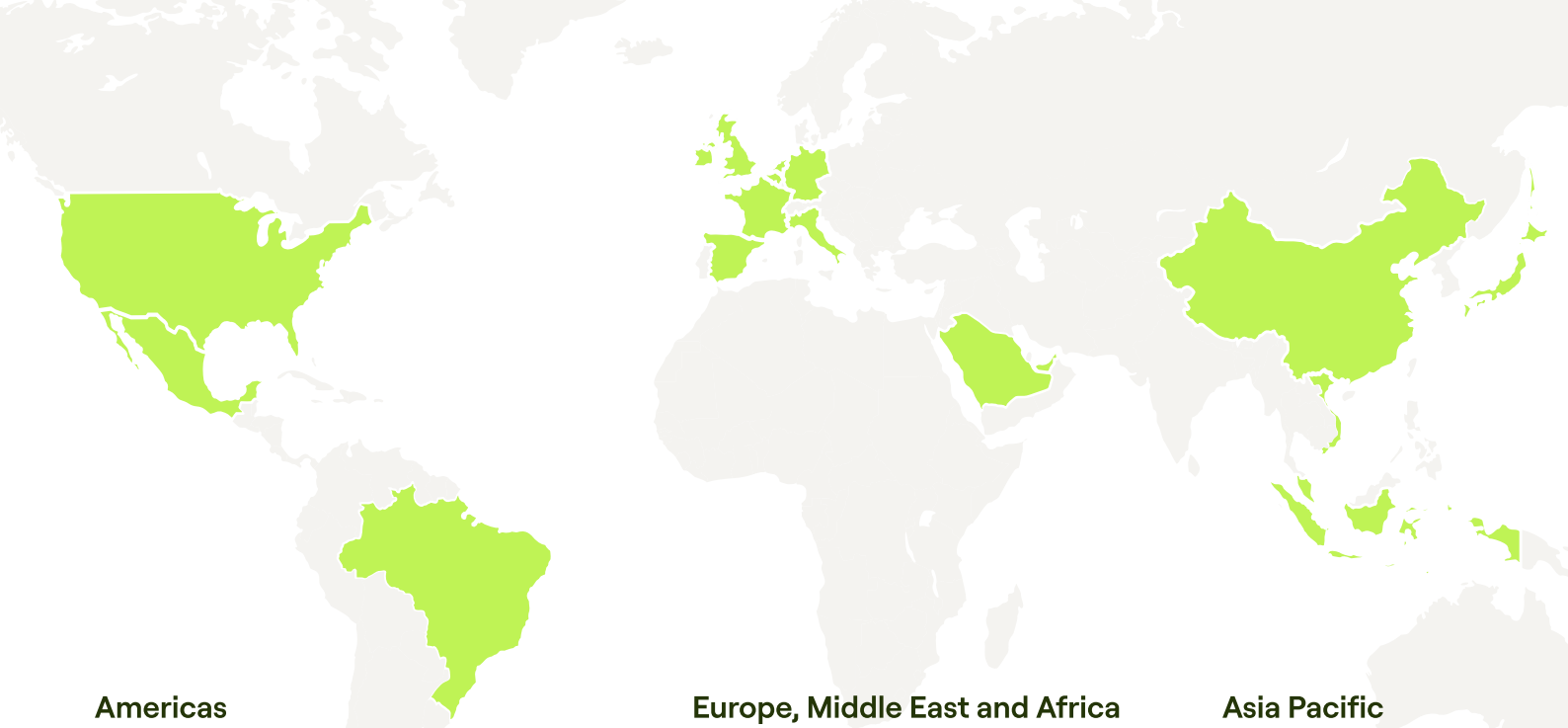

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