

6. Market Access in Spain

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6.1 General Outlook of Healthcare System and Health Policies

The Environment

Spain has been a parliamentary monarchy since 1978. Political devolution to regional governments has been incrementally implemented over the last 30 years. Thus, the political organization of the Spanish state is made up of the central state and 17 highly decentralized regions (termed *Comunidades Autónomas*, that is, Autonomous Communities) with their respective governments and parliaments (Figure 1). With a population of 46,468,102 (December 2016), Spain covers 505,370 km² and has the third largest surface area in Western Europe (Table 1).

The fertility rate is one of the lowest in the EU (1.27 children per woman in 2014). The inflow of migrant population, especially in the last decade, has had a demographic impact in rejuvenating a population that is otherwise rapidly ageing. Life expectancy in Spain is one of the highest in Europe: 85.5 for women and 82.8 for men in 2015.

The top three causes of death in Spain since 1970 have been: cardiovascular diseases, cancer and respiratory diseases, albeit there has been a steady decrease in the actual mortality rates from these causes. Still, mortality rates for these causes are among the lowest in the WHO European Region. Maternal and child health indicators (neonatal, perinatal and maternal mortality rates) have experienced a dramatic improvement, current rates scoring below European averages.

Regarding lifestyle factors affecting health status, the proportion of daily smokers has been declining, though regular alcohol consumption is quite widespread and hazardous drinking affects some 7% of men and 3% of women. Obesity and overweight is increasing, doubling the 1987 rate for adult population to reach 15.6%.



Figure 1. Territorial organization of Spain: Regions

Capital	Madrid
Language	Spain has an official language for the entire State (Spanish) and four co-official languages in six of its 17 Regions (Galician, Basque, Catalan and Aranese).
Government	Parliamentary Monarchy
Area	505,370 Km ²
Population	46,468,102 Hab. [Census December 2016, INE]
GDP (PPP)	\$ 34,727.1 [2015 World Bank]
Per capita	€ 23,700 [2016 provisional, EUROSTATS]
Per capita	\$ 26,609 [FMI 2016]
GDP (nominal)	\$ 304.9 [December 2016, OCDE]
Currency	Euro

Table 1. Spain: an overview

The Healthcare System

In Spain, according to the principle of decentralization promulgated by the Constitution, and after the dissolution of INSALUD in 2002, healthcare competence was transferred to each of the 17 regions. The central government only provides this service directly in Ceuta and Melilla and carries out general and basic coordination work between the different regions.

The Ministry of Health, Social Services and Equity develops the Government's policy on health, planning and health care and consumption, as well as it has the competences for the General State Administration to ensure to the citizens their right to health protection.

The Inter-Territorial Council of the National Health System (NHS) of Spain is the organ of cooperation and intercommunication of the health services of the regions with each other and with the State administration to give cohesion to the system and guarantee citizens' rights throughout the territory. In Law 16/2003, of May 28, on cohesion and quality of the NHS, the article 69 reflects its current composition and functions.

The State, through the general taxes collected, finances all health benefits and percentage of pharmaceutical benefits; but this budget is distributed among the different regions according to several criteria of distribution, since the regions are responsible for healthcare in their respective territories.

Public expenditure on healthcare in Spain increased by € 2,031.4 million in 2015, or 13.91%, to € 68,007.1 million, accounting for 14.5% of the total public expenditure. This figure assumes that public spending on healthcare in 2015 reached 6.29% of GDP, a drop of 0.05 points compared to 2014, when spending was 6.34% of GDP.

Pharmaceutical expenditure accounts for approximately one third of the total health expenditure. Pharmaceutical expenditure on prescriptions among all regions grew by 4.08% in 2016 compared to 2015, while hospital spending fell by 6.22% in the same period, which together results in a flat growth of the total pharmaceutical expenditure (-0.06%).

However, this growth has not been homogenous in all segments of the pharmaceutical market. Public expenditure on innovative drugs has fallen by 41.6% between May 2011 and December 2016. In contrast, generic drugs units have increased and their average price has increased as well. Currently, the market at generic prices accounts for more than half of the Spanish market on prescription drugs in values and about 80% of the market in dispensed units.

Andalusia, Catalonia, Valencian Community and Madrid are the regions that present a higher level of public expenditure on drugs, and represent 55% of the total pharmaceutical expenditure.

The NHS is organized in two environments or levels of care: Primary Care and Specialized Care, in which the spontaneous access of citizens and technologies complexity are in inverse relation.

Given their disposition in the community framework, Primary Care is entrusted with the tasks of health promotion and disease prevention. As a maximum expression of accessibility and equity in access.

Specialized care is provided in the specialty centres and hospitals, on an outpatient basis or hospitalized. After the care process, the patient and the corresponding clinical information are returned to the Primary Care physician who, by having all the data in his/her clinic history, guarantees the overall clinical and therapeutic vision. This allows continuity of care to continue to be characterized by equity, regardless of the place of residence and the individual circumstances of the region, since healthcare reaches the patient's own home.

The Basic Services Catalogue of the NHS was established in Law 16/2003, of May 28, on cohesion and quality of the NHS and in the Royal Decree 1030/2006, of September 15, by which regulates the Common Catalogue of Services of the NHS and the procedures for its updating. Subsequently, the Health System reform established by the Royal Decree-Law 16/2012, of April, on urgent measures to ensure the sustainability of the NHS and improve the quality and safety of its services, modifies the Common Catalogue of Services of the NHS including the following modalities:

- Common Basic Catalogue of Services of the NHS. Includes all the assistance activities of prevention, diagnosis, treatment and rehabilitation carried out in health centres or socio-health centres, as well as urgent health transportation.
- Common Supplementary Catalogue of Services of the NHS. Includes Pharmaceutical services, Orthopedic services, dietary products and non-urgent medical transportation subject to medical prescription for clinical reasons.
- Common Ancillary Catalogue of Services of the NHS. Includes all activities, services and technical procedures that are not considered essential and/or which are adjuvant or a support for the improvement of a chronic pathology.
- Complementary Catalogue of Services of the Regions. Regions, within the scope of their competences, may incorporate a technique, technology or procedure not included in the Common Basic, Supplementary or Ancillary Catalogues of Services of the NHS, for which they will establish the necessary additional resources, informing, in a motivated manner, the Inter-Territorial Council.

The pharmaceutical supply includes medicines and medical devices and the set of actions aimed at patients receiving them adequately and their clinical needs, in the precise dosages, according to their individual requirements, during the appropriate period and at the lowest possible cost for them and for the community, to promote the rational use of the drug.

Patient's prescriptions include those drugs that have been authorized and registered by the Spanish Agency of Medicines and Health Products, masterful formulas and the official preparations made by the pharmacy offices as established in the National Formulary, and the vaccines.

The public funding of drugs is subject to the system of reference pricing and to mechanisms of selected prices as instruments of savings in the pharmaceutical spending, enhancing the use of generic drugs and adapting the packaging of the medicines to the duration of treatments.

The reform included in the Royal-Decree-Law 16/2012 modifies the system of user contributions in pharmacy that previously existed, establishing different levels of contri-

bution for the co-payment of drugs and/or medical devices reimbursed by the Social Security.

Drugs dispensed at hospital level have no co-payment. The ambulatory pharmaceutical supply of drugs and/or medical devices that are dispensed to the patient through a community pharmacy are subject to a user's contribution at the time of dispensing. For pensioners, monthly maximum limits of contribution are established as a function of income.

The Drugs' Law 29/2006, of July 26, devotes its VII title to regulate the public funding of drugs and medical devices. Article 89 of the aforementioned law established the procedure to decide, once a drug has been authorized and registered, to include it in the pharmaceutical supply of the NHS. Specifically, the inclusion of medicinal products in the reimbursement of the NHS is made possible through a "selective and non-indiscriminate funding", considering, among others, the criteria of "therapeutic and social usefulness of the medicinal product" and "the rationalization of public expenditure for pharmaceutical provision". According to the same article, the decision on public funding of new drugs corresponds exclusively to the Ministry of Health, Social Services and Equity.

The Royal-Decree-Law 9/2011, modified articles 89 and 90 of the Law 29/2006. Some of these modifications would be ephemeral, since, Royal-Decree-Law 16/2012 would change those same articles again. However, the new criteria introduced by Royal-Decree-Law 9/2011 for the inclusion of drugs and medical devices in the pharmaceutical supply are still present, so that instead of "therapeutic and social use of drugs", the "therapeutic and social value of the drug and the incremental clinical benefit thereof considering its cost-effectiveness". In addition to the "rationalization of public spending for pharmaceutical provision", the "budget impact for the NHS" should also be considered.

Thus, Royal-Decree-Law 16/2012 adds a new article, 89 bis, to Law 29/2006, which explicitly stated that the cost-effectiveness and the budget impact analyses, as well as the innovation component for indisputable therapeutic advances, would be considered for the decision of reimbursement of new drugs, if it contributes positively to the GDP.

Spain has 21,937 community pharmacies where 48,424 pharmacist work. At present in Spain, there are on average 2.2 pharmacists per pharmacy and there is one for every 2,125 inhabitants.

The pharmaceutical industry is one of the leading sectors of the Spanish investments in R&D. The pharmaceutical industry is the first Spanish sector by intensity in R&D.

On the other hand, it is worth noting the promising future of biotechnology companies, since it is an emerging science, with a long way to go. Although Spain joined the sector a little later in reference to other more competitive countries in research such as the USA, England, Germany, France or Canada, in recent years an extraordinary effort has been made that could gradually translate into levelling with the most scientifically potent countries.

The pharmaceutical industry exported drugs made in Spain worth € 11,084.3 million in 2015. Foreign sales grew by 7.9% in 2015, more than double the total of the country's foreign market (+3.8%), which means that they already represent 4.4% of the total Spanish exports.

Spain is the fifth largest pharmaceutical market in Europe by volume of sales and employment generation (behind Germany, France, Italy and the United Kingdom) and the sixth European market in terms of production (after the four previously countries and Ireland).

In 2015, in this market have been introduced 91 new drugs, of which 43 were generics, 5 biosimilars and 20 components correspond to new active principles, the latter concentrated in the antineoplastic and antiviral areas. From them, 4 new drugs have been marketed as “orphan”.

6.2 Pricing and Reimbursement

As we mentioned before, the Spanish Ministry of Health (MoH) oversees the pharmaceutical policy. Specifically, the General Direction of Basic Health Services and Pharmacy (*Dirección General de Cartera Basica y Farmacia – DGCSBF*) is the department which designs, develops and implements these policies in relation to medicines and medical devices.

The most important functions of this entity in relation to Pricing and Reimbursement (P&R) procedure are the following:

- Decide if a medicine or a medical device has public funding for the whole indications or for some of the approved indications for this product.
- Determine the conditions for the prescription and dispensation for the Health National System.
- Coordinate with regional governments all the decisions taken in relation to medicines and medical devices through the Sectorial Health Conference.
- Support a specific intersectoral commission, *Comisión Interministerial de Precios (CIPM)*, which has the competence of approving the P&R proposals for medicines and medical devices.
- Capture and analyze data about the pharmaceutical expenditure in retail and in hospitals. They are also in charge of making the annual Spanish pharmaceutical expenditure report.
- Maintain updated all the databases of medicines and medical devices funded by the public system.
- Establish distribution margins and retail sales.

The DGCSBF has a Sub-directorate which oversees the implementation of all these activities, *Subdirección General de Calidad de Medicamentos y Productos Sanitarios (SGCMPS)*. This Sub-directorate has two different sections, the first one in charge of the P&R procedure and the funding of medicines and medical devices, the other section has the responsibility for the databases of medicines and medical devices and to analyze the pharmaceutical expenditure.

Moreover, this Sub-directorate has three different advisor Committees.

1. *Comité Permanente de Farmacia del Consejo Interterritorial de Salud (CPF)*: The MoH and all regional governments have representatives in it. Their main task is the coordination of pharmaceutical policies at national and regional level.

2. *Comisión Interministerial de Precios (CIPM)*: This Committee has an intersectoral character. Four different ministries are part of it, MoH, Ministry of Industry, Ministry of Economy and Ministry of Finances, and regions are represented. Its main task is to approve the price of the drugs.
3. *Comité Asesor para la Financiación de la Prestación Farmacéutica del Sistema Nacional de Salud*: This Committee would be integrated by experts in Pharmaeconomy and Outcomes Research to advise about those topics to the Sub-directorate. This Committee has not been set up yet.

Pricing and Reimbursement Procedure

In Spain, the funding of medicines is selective, not all the approved medicines have to be funded and have reimbursement by the NHS, not even all the indications of the same medicine should be funded by the NHS.

The national regulation establishes several criteria for reimbursement:

- The severity of the disease.
- The duration and the sequela of the pathology.
- The added value of the drug.
- The unmet need.
- The cost-effectiveness ratio.
- The alternatives in the market.
- The degree of innovation.

As we mentioned previously, the CIPM decides if a new medicine or a new indication should be funded and reimbursed by the NHS and establishes at the same time the price of this medicinal product considering the cost-effectiveness data and the budget impact.

If these medicines are not funded or cannot be funded by the public system, they would be commercialized after a communication of the price to the Sub-directorate to assure that this is in line with the pharmaceutical policies of the MoH.

When a new medicine is authorized, the Spanish Medicines Agency send a communication to the SCMPs to start the procedure of P&R. First, the SGCMPs check up on if this product is included in one of the ATC (Anatomical Therapeutic Chemical) groups funded by the MoH. Otherwise, they do not initiate any procedure. As we stated before, in this case the company should communicate the price to de SGCMPs.

If the new product can be funded, the SGCMPs initiates the procedure of P&R (Figure 2) and requests the company the documentation for assessing this new product. So, they start the evaluation considering the dossier from the company which contains data related to clinical data, pharmaco-economic issues, budget impact and added value (the most relevant aspect is the budget impact). After the assessment, the evaluators begin the negotiations about the price and the type of reimbursement with the company. After that, the SGCMPs includes this agreement in the following meeting of the CIPM for decision. If the decision is positive the SGCMPs communicates the approved price and the reimbursement conditions to the company and to the regional governments. If the deci-

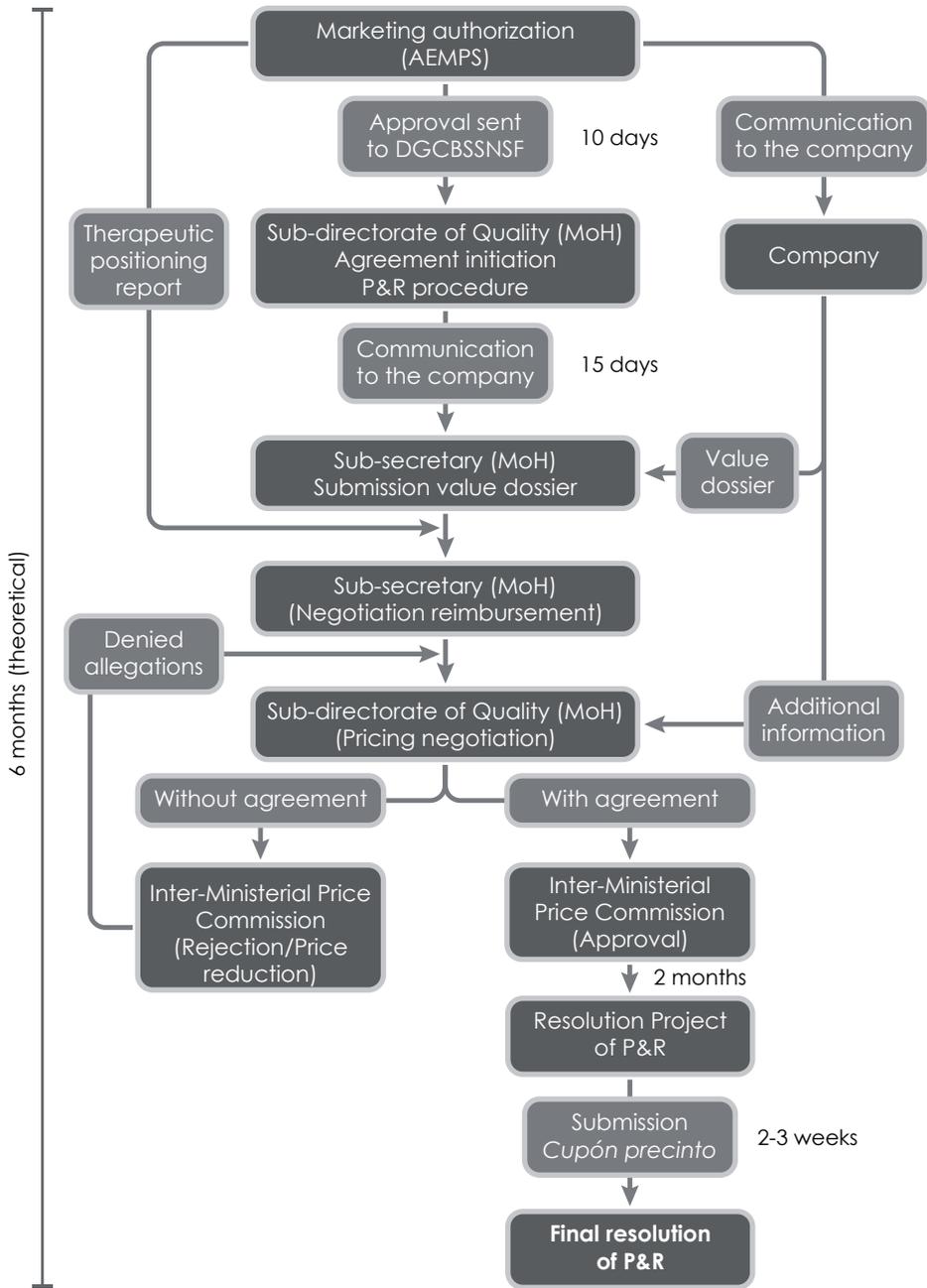


Figure 2. Current pricing and reimbursement process

sion is negative the company can submit more documentation taking into account, the objections proposed by the CIPM.

In case of generic products, there is no need to be reviewed by the CIPM because there is a specific policy for this type of drugs which we will comment afterwards.

This price agreed by the CIPM is not the final official price; some specific margins (distribution, pharmacies) and taxes (VAT) should be added.

As we stated formerly, it is mandatory that all new drugs with a new active ingredient and those authorized but with a new indication should be assessed by the SGCMPs and by the CIPM.

Control of Prices and Pharmaceutical Expenditure

Reference Price System and Homogenous Groups System

As commented before, the P&R procedure is decided by the MoH. There is a 10-year protection period for new medicines. After this period, they are included in specific price systems: Reference Price System (RPS) and/or Homogeneous Groups System.

A RPS is composed by different groups of drugs with the same active ingredient and the same route of administration. Each group must include at least two different presentations with the same active ingredient, one of them should be the original drug and the other one must be a generic or biosimilar medicine or another drug with the same active ingredient but different to the original one. The price of each group is established taking into consideration the lowest cost/treatment/day and the number of daily doses that has each package. This reference price system establishes the maximum price for each group. All drugs included in every group have the same price per unit. All prices are reviewed every year and the groups are updated considering the expiration of patents during the ongoing year.

The Homogeneous Groups System is an extension mechanism of the RPS and establishes different groups. These are composed by drugs that have the same active ingredient related to dose, pharmaceutical form, quantity and method of administration. The price of each group is based on the minimum price of any of these drugs on the market when the group is created. Companies can request to be entitled to lower prices and this reduction is applied to the other drugs of the group. These prices are reviewed every three months.

In summary, both systems are complementary; the RPS is based on the application of the maximum price of each group reviewed annually and the Homogeneous Groups System is based in the minimum price of each group reviewed every three months.

Deductions

In 2010 due to the crisis, the Spanish MoH establishes general discounts for all innovative drugs. Both, retail and hospital drugs, have a general deduction of 7.5%. This discount is different for orphan drugs, 4%. For those medicinal products that do not have generic or biosimilar products but have lost exclusivity, this discount is 15%.

CAP

There is another specific mechanism at national level, the CAPs. This mechanism establishes the maximum budget that the NHS can spend in a specific drug. The companies should periodically report to the MoH the sales to the NHS to know when the CAP is reached.

There are three different models of CAP in Spain:

- CAP based on the maximum number of units supplied to the System. Once achieved the maximum, the remaining units are free for the System.
- CAP based on the maximum cost of the treatment per patient. This model established the number of packages per treatment. The exceeded packages are free for the System.
- CAP based on both models

National Tendering

There is a new mechanism for lowering the pharmaceutical expenditure, the National Tendering. The *Instituto de Gestión Sanitaria* (INGESA) oversees this entity. They publish the conditions for a national tendering for drugs and medical devices. The implementation of this agreement is done at regional level by the Regional Government. Hospital medicines, vaccines and invasive medical devices are included in these tendering. These agreements have a duration of two years.

6.3 Mapping and Structure of Decision Makers (Reimbursement/HTA)

Autonomous Communities (Regions)

Regarding the health system, starting in 1981 in Catalonia and finalized in 2002, the implementation of the roadmap been established by the 2003 NHS Cohesion and Quality Act. The Quality Act foresees that the MoH at national level will no longer has executive capacity over the running 17 regional systems. It has evolved to a role of guarantor of rights and entitlements.

One of the consequences of that Law was the creation of regional health ministries (17 in total all over Spain) in addition to the national one. This decision represents a division of competences at national and regional level as well as the necessity of establishing a coordination body: The NHS Inter-Territorial Council (CISNS) and the development of coordination and cohesion tools in a mature system. One key objective is to guarantee equity across the country.

The coordination body (CISNS) meets regularly with the National Ministry and the 17 Regional Ministries of health. This coordination body includes different *ad-hoc* commissions, committees and taskforces for discussing more in depth any relevant matters. Specific groups have been established to discuss related topics such as pharmaceutical policy, public health, benefits basket etc. Decisions in the CISNS must be adopted by consensus,

but in those matters, that have been transferred to the Regions; they can only take the form of recommendations. Thus, regions are free to implement the recommendations issued by the CISNS but signed agreements or regulations have more binding effect and may become mandatory for regions.

Nowadays, the Spanish NHS is in a complex equilibrium facing major challenges in terms of sustainability, equity among regions and obtaining major benefits from the decentralization.

During this decentralization process, the key factors have been:

- The creation of governing bodies at national and regional level.
- Allocation of funds to national and regional administration.
- Definition of the common benefits package at health level.
- Development of the information system allowing interconnection among regions.
- Development of tools to track performance and resources distribution.

At regional level the health systems (*Consejerías de Sanidad*) consists of a Regional Ministry holding health policy and health care regulation and planning responsibilities, and one or more regional health care providers.

In the regions, the ministry of health is responsible for the territorial organization of health services within its jurisdiction. Usually, the most frequent model consists of two separate executive organizations, one for primary and one for specialist care (ambulatory and hospitals) and a pharmacy division is also created at a high organogram level in the organization. Drugs are seen as major expenses in the regions and in consequence ad-hoc structures have been created, mainly, to keep under control the drug expenditure.

In terms of drugs, the P&R process has been described in the previous chapter but since regions are fully responsible for pharmaceutical management and modulation of the consumption, additional measures have been put in place.

Retail Drugs Evaluation Committees

Since 2003 some regions have organized to perform joint drugs evaluation. The aim was to share methodology, findings and maximize resources. Under the name of Joint Committee for the Evaluation of New Medicines (CENM), Andalusia (CADIME), Aragon, Catalonia (CANM), Balearic Islands, Navarra, Bask Country and Castile and Leon are running evaluations. The aim is to share results and maximize resources by distributing the work among the different regions.

All reports are public as well as the methodology applied. It is mainly addressed to new innovative drugs but it also evaluates new pharmaceutical forms, presentations, and combinations etc. of already existing drugs.

Comparisons are made with already existing alternatives in terms of efficacy, safety and cost. No formal pharmacoeconomic evaluation is included and cost comparison is mainly based in terms of cost per defined daily dose (DDD) since most drugs are considered alternatives. Drugs are rated in five categories based on their relative innovation value: no added value, minor, moderate or significant added value and non-assessable due to insufficient information. More than 80% of evaluations performed are considering that

drugs do not add any value to current alternatives available or there is insufficient information to evaluate and in consequence do not recommend the new alternative.

Other Regions have their own evaluation committees or although not being a formal part of the CENM take into consideration their recommendations available at websites.

In practice, those classifications play a variable role in the Regions. Some of them use incentives based on prescriptions recommendations and selection of drugs with high therapeutic benefit and try to avoid those with low benefit according to the evaluation of their committees.

The more the electronic prescribing and recording of medical records evolves, the more the Regions implement prescribing control systems under which an IT programme may select the most efficient drug, advice on those not recommended and include follow-up systems to track deviations according to the forecast.

The degree of implementation varies among Regions and meanwhile in some of them it has an impact on physician's prescribing choices, in some others stay as recommendations.

Hospital Drugs Evaluation Committees

At hospital level, the Commission of Therapeutic and Pharmacy (CFT) is the entity that decides on the therapeutic arsenal available in each hospital.

The commission has representatives from the hospital management, physicians, pharmacist etc. As within any evaluation, the elements considered for incorporating a product into the hospital are quality, safety, relative efficacy and cost.

Physicians can prescribe drugs not listed on the hospital's formulary, if they obtain previous authorization by the CFT and medical director.

The rational use of medicines is also monitored by the CFT and in some cases internal mechanisms for validation of prescriptions are put in place prior to dispensation.

In Spain, it is also very common to reach price-volume agreements and obtain discounts at hospitals level products. In some regions, especially in Catalonia there are also experiences in risk-sharing agreements with some specific products.

There has been a considerable budget impact increase in the hospital innovative drugs. Therefore, many regions have created commissions for the evaluation of these high impact, high price drugs at regional level. The details may vary from region to region but the major worry is how to cope with an increasing budget due to higher prevalence figures and the incorporation of high priced new drugs in this setting.

In practice, in some Regions the decision of incorporation of a medicine at the hospital is not taken at hospital level but at regional level. Thus, some hospital formularies may vary from region to region and even within the same region. Equity among Spanish citizens is questioned by most of Pharma companies.

The Spanish Society of Hospitals Pharmacist (SEFH) constituted a working group in the early 2000 with the objective of developing an evaluation guideline for hospital products. The group was named GENESIS group. The objective of this group was to develop a tool to support the evaluation of the therapeutic options at hospital level. The meth-

odology is standardized and has been agreed by the members of the working group. In addition, the collaboration among the pharmacy departments of different hospitals is aimed to increase the efficiency, quality, speed and independency in the evaluation process. The methodology is publicly available and the reports performed by the participant's hospitals as well. This initiative is recognized by the Ministry of Health as well as by the Regions and considered as a best practice.

In November 2016, has been published a Guideline for the economic evaluation and budget impact of the products that has been integrated into the already in place evaluation guideline for hospital products created by the GENESIS group. This is a clear recognition not only of the relevance of the economic part of the reports but of the requirements of improving its economic evaluation. The Guideline is accessible at the web page of the scientific society. Among other recommendations, it has been established a threshold of € 21,000/QALY with a range varying between € 11,000 and € 50,000/QALY. A follow up of this guideline and its implementation should be carefully considered by all stakeholders.

Evaluation Agencies of Health Technology

The Spanish Network of Agencies for Evaluation of Health Technologies of the NHS is made up of agencies or evaluation units of the general administration of the state and the Regions, which work in a coordinated way, with a common methodology under the principle of mutual recognition and cooperation.

The Spanish Network is created by the NHS Inter-Territorial Council in 2012, to promote quality, efficiency and sustainability in health technology assessment in the NHS.

The Network's mission is to generate, disseminate and facilitate the implementation of information aimed at informing decision making in the NHS, contributing to the increase of quality, equity, efficiency and cohesion in the NHS.

The General Directorate for Public Health, Quality and Innovation is responsible for the management, financing, monitoring and dissemination of reports and products produced within the framework of the Network, in collaboration with the DGCBSF. Major focus of these institutions is on health technologies and the cooperation for the evaluation of drugs varies from Region to Region.

The institutions assigned are ISCIII (at national level), AQUAS (Catalonia); Avalia-t (Galicia); AETSA (Andalusia); Osteba (Bask Country); UETS (Madrid); SECS (Canary Islands) and IACS (Aragon).

Other Regional Prescribing Control Measures

Some Regions use prescribing incentives for generics and biosimilars. Some others have adopted a very strict approach for international non-proprietary name (INN) prescription being mandatory such as in Andalusia. The wide use of electronic prescribing systems has facilitated this type of measures.

Tenders at the retail market are another initiative with Andalusia playing a leading role. A lot of controversy has been generated. A series of tenders have been implemented

since 2012 in the retail market for out-patented products such as: statins, antihypertensive, gastro-protectants, analgesics etc. Although all controversy generated, the process is not only still in place but also incrementing the type of products included in those tenders.

6.4 Challenges and Catalyzers for Market Access

Challenges

One of the important challenges for market Access in Spain, seems to be the methodology used for price regulation. Shifting from the current method to a value based pricing system appears to be the future although major changes in the current structure should be done e.g. strong HTA evaluation system, develop of the cost-effectiveness committee. Along with the methodology, the lack of transparency through the price regulation process appears to be a major issue because makes that the final decisions are quite a bit unpredictable. Within the lack of transparency there is an ignorance of real prices mainly in the hospital setting which concentrate an elevated proportion of high price drugs. Official list of prices exists but does not reflect real ones due to confidential discounts offered by the pharmaceutical companies and not included in any public document. This situation is sustained by some pharmaceutical companies but not all of them.

Other recognized challenge is related to the policy of generic drugs which it should be widely introduced but results in a modest impact.

A proposal for a change in Spain, should focus on fixing the price of those medicines protected by exclusive Intellectual Property Rights and not in those in the generic competition.

Price regulation based on criteria of international reference prices can be an appropriate option for other kind of countries but it does not seem to be a feasible option for Spain. Value based pricing appears to be the best option although not in the short term because the aforementioned need of a new Health Technology Assessment structure and more rigorous evaluations of every of the new technologies.

Catalysts

As a facilitator to change the situation and overcome the described challenges, emerge a new legislation that promote a new framework transparent and predictable along with a replicable methodology that provide clear guideline to companies to regulate prices adequately. This would avoid the ambiguous legislation around the current criteria for price regulation. New legislation should also develop a value based pricing system, what is demanded by experts from all areas.

A new structure to record use of resources, expenditure and prices could contribute to the development of an information system that helps government and companies to deal with innovative contracting and agreement formulas which facilitate the quick introduction of innovative medication based on equity criteria.

6.5 Innovative Mechanisms for Funding, Purchasing and Paying for Drugs

In Spain, the responsibilities for funding, buying and paying for drugs within the public health system are spread among the different levels of health administration. On the one hand, the decision of public funding and fixing the price is a competence of the Central Government. On the other hand, the Regional Governments should face the purchase and payment of these drugs with their budgets.

This is a system that largely transfers the pressure of funding the drugs to the Regional Governments that can influence little in the decisions of supply and pricing but who then have to prioritize and manage the existing resources to pay the pharmaceutical bill.

The payment of the prescription drugs is made directly from the health services of the Regional Governments to the community pharmacies based on the products dispensed each month. The payment of hospital drugs occurs in two stages: The payment that Regional Government makes to hospitals and the payment of hospitals to pharmaceutical companies through the purchase.

In relation to the purchase, it is usually done directly by hospitals or hospital groups in the case of hospital drugs, or by community pharmacies concerted with the public sector for prescription medicines. In the first case, the price set is a maximum price on which hospitals or groups of hospitals try to reduce by multiple mechanisms according to the product and the purchasing capacity. In the second case, it is a fixed price that incorporates the price of the pharmaceutical company and the margins of the wholesaler distribution and the community pharmacy.

The models of payment to the hospitals by the different Regional Governments are usually made through a payment by global annual budget or directly by the payment for dispensed product.

The payment by budget transfers the risk directly to the hospitals that with the amount allocated have to face the costs incurred. In the case of payment for dispensed product, this is not unlimited. For this, maximum limits of invoicing are established, from which the hospital has to face costs that exceed the limit. Most hospitals establish indicators and incentives for clinical services and physicians to stay within these limits.

In the case of the payment of prescription drugs, the Regional Governments pay directly to the community pharmacies through contracts with the Pharmaceutical Association of each Region. These contracts establish the payment of the drug dispensed at the official price established by the central Government. This payment includes the cost of the drug at the price set by the central government plus the margins of distribution (wholesaler) and dispensing (community pharmacy).

In recent years, in the traditional funding, purchasing and payment systems have been incorporating new mechanisms linked to the concepts of financial agreements, agreements based on the value of the drug and incentives for clinical and purchasing management. As innovative payment models, we also highlight some of the ini-

tiatives that have been recently developed that go beyond the established traditional payment. Specifically, we emphasize the payment by rate/patient/month in hospitals and the payment for pharmaceutical services, both in hospitals and in community pharmacies

The following section includes some more detailed information of the different innovative mechanisms adopted at each stage.

Funding of Drugs

The funding of drugs has traditionally been established through a central pricing system by the central government where, apart from the criteria established in the law, a fundamental element is the comparison of the price with other countries.

Two prices are established, one general price and the one for the National Health Service. The central government advertises the general price but not the price for the NHS which remains not visible outside the public health system.

Once fixed the price this can be revised periodically, either by a particular form or by a systematic form, as is the case of the RPS. Specifically, the RPS generates an automatic review of drugs when patents expire and the first generic appears.

Undoubtedly, the RPS is the pricing mechanism that has brought more returns to the sustainability of the system. It is a system more like a selective reimbursement model than a reference price in the strict sense. At the first stages of its implementation there was a maximum price to be paid by the public health system and the citizen had to cover the difference between the maximum price and the price of chosen drug. Over time, the system evolved to a model where the reference price became the price above which no product is publicly funded.

The central government has recently developed new pricing and reimbursement scenarios to try to finance new treatments with dynamic price mechanisms and minimizing budgetary risk. Specifically, we highlight the system of spending ceilings, price/volume agreements and maximum prices per treatment.

Spending ceilings

Spending ceilings are used to insure a maximum outlay for a drug or group of drugs. From a certain amount established as a ceiling, the pharmaceutical company should run with the costs that are generated above it. These ceilings try to minimize the uncertainty of the budgetary impact, so that without modifying the unit price of the product this is conditioned to the overcoming or not of the established ceiling.

Specifically, the central government has established spending ceilings for different molecules such as new antivirals for hepatitis C or some cancer treatments. The system has proved to be a safeguard to the budgetary deviation but its success has been conditioned by the difficulties of managing these ceilings from the central Government. The difficulty lies in being able to add in time and form all the necessary information, as well as the procedure of compensation by the companies to hospitals for the amounts paid above the ceiling.

Price/volume agreements

The price/volume agreements have recently been used by the central government to decide the reimbursement of some drugs. This has been the case for the new antivirals for the treatment of hepatitis C. Specifically, for the different active principles price ranges were established according to the number of patients treated at a global level and by regions. When the estimated volume of sales is reached to move from one range at national level to the next one where the price is reduced. Those regions that have contributed to comply with their regional range can benefit from the price reduction of the drug.

As in the case of spending ceilings, the main difficulty is the complexity of managing the price cuts for each range of sales volume. This is due to the time difference between the date when the agreed volume is reached and the date when this information is received at central level. Thus, the system requires complex invoicing regularizations with hospitals for drugs purchased at the price of the previous range from the day it is officially established that the range has been exceeded and the date on which it is notified.

Maximum cost per treatment

The maximum costs per treatment have also been used in the case of the new treatments for hepatitis C. They consist of setting a maximum cost for the treatment of a patient regardless of the duration of treatment. In this way, the company should pay the additional costs of those patients that exceed the established cost.

Payment by rate/patient/month

This system has been implemented at the hospital setting and consists in establishing a fixed monthly payment to the health provider for the pharmacological treatment of a patient with a certain pathology, independently of the drug or drugs administered.

This system has been implemented mainly in Catalonia for certain pathologies such as treatment of HIV, hepatitis C, rheumatoid arthritis, psoriasis and Chron's disease, growth hormone deficiency, and recently the treatment of cholesterol with the new monoclonal antibodies inhibitors PCSK9.

This payment model aims to encourage the hospital to develop not only purchase management mechanisms but also clinical management, selecting for each patient the most efficient drug for their clinical condition, the best therapeutic regimen and the use of doses and vials, explicitly implicating physicians in this task.

In addition, with this system, the Regional Government can periodically set and modify fees based on the appearance of new medicines for pathology and adapt the economic value of the therapeutic mix regardless of the prices of each drug. With this system, the pharmaceutical companies should adapt their offers according to the rate assigned to each pathology, thus gaining some control over the costs outside of the prices.

The Government of Catalonia has obtained significant efficiency advantages thanks to the implementation of this model compared to the traditional system of paying for each drug dispensed and administered. In addition, clinical hospital management and companies have been encouraged to compete in the market to offer purchase conditions to hospitals that facilitate compliance with these rates.

Payment for pharmaceutical services

In Hospitals: There are, in some cases, payments to hospitals for the pharmaceutical services associated with the preparation and dispensing of drugs. Specifically, in the region of Catalonia there is a program called “pharmaceutical care program” provided with funds from the efficiency obtained in the purchase of drugs that is distributed among different hospitals through a payment mechanism based on so-called pharmaceutical care units (Unidades de Atención Farmacéutica – UAF). These UAFs are calculated based on the workload that the hospital must perform to prepare, dispense, and administrate the treatment to a patient.

In Community Pharmacies: In the case of community pharmacies, several regions have established payment programs that are not linked to the dispensing of drugs. These programs establish payments for services such as the treatment of methadone withdrawal to patients addicted to parenteral drugs and the screening activities of colon cancer and HIV infection. In all of them, a fee is established per patient treated or test performed. There are currently several pilot trials underway to study new forms of payment linked to the development of customized dispensing systems based on unit doses and for the pharmacotherapeutic follow-up of chronic polymedicated patients.

Purchase of Drugs

The purchase of drugs in hospitals is done by tenders, generally for products that are adjudicated to those companies that offer the best conditions for each public offering, or by negotiation without competition in the case of exclusive products.

In the case of prescription drugs that are dispensed in the community pharmacies the purchase is made by pharmacies who then submit the invoice to the regional health service for reimbursement according to the prices set by the central government.

Lately, there are many experiences that are being carried out, both by hospitals and at regional level, of different and innovative models of purchasing with the objective of obtaining better prices or to introduce the concept of value in the acquisition. Specifically, we highlight the auction system in the field of prescription drugs and the models of aggregated purchase, purchase by results, purchase of complete processes and innovative public purchase for hospital drugs.

Drug auctions on prescription drugs

Drug auctions consist of adjudicating the supply of prescription drugs through a public tender. With the auctions the best offer is selected, thus setting the price to pay for a drug by the health service to the pharmacy offices, regardless of the prescribed brand. Thus, the laboratory that offers the lowest price takes the grant of a certain active principle.

This system has been implemented by the region of Andalusia that periodically publishes an auction in which it includes all the medicines that have generic. This system that seeks to achieve price reductions in those medicines that by the traditional system would not go down in price.

This mechanism, although foreseen in the Spanish Law under the heading of “selected prices”, has not yet been developed at the central level. The auction model has reported price reductions on some drugs, generally not exempt of some controversy with some pharmaceutical companies as well as Farmaindustria (National Trade Association of the Spanish based Pharmaceutical Industry).

Aggregated purchases

There are several experiences of aggregated purchasing in our country, both at the central level and at regional level. Many regions like in Madrid, Galicia, Andalusia, Bask Country, etc. have a central purchasing office for tendering for all hospitals. Recently the central government has also set up a purchasing center to which some regions have joined. In some regions, there are several platforms of purchasing which recently are also conducting tenders jointly for all hospitals, like the joint platform of the Catalan Health Institute (ICS) and the Catalan Health and Social Care Consortium (CSC) in Catalonia.

Usually, tenders are addressed to pharmaceutical product but there are some experiences where the tender is by therapeutic indication. These tenders consider that the products are similar for the same indication and do not have, objectively, differences among them.

Purchase of complete processes

In some cases, such as for oxygen therapy or dialysis, there are tenders not just for drugs but for the entire service, including administration devices, tracking and monitoring mechanisms, distribution and home delivery services.

Payment by results

In some hospitals, payment by results is being introduced into the purchase contracts. That is, to pay to the pharmaceutical companies based on the results obtained instead of on the units sold. In that cases, only those units of product that have achieved the therapeutic goal previously agreed are paid. At regional level this is generally given in Catalonia where drugs for the treatment in some oncological indications like lung and colon cancer, among others, are already paid in this way.

The payment linked to results, apart from the difficulties inherent to its implementation, have proved to be a good way to align the objectives of public sector, mainly hospitals, and pharma companies in favor of health outcomes, while reducing costs to pay from the hospitals and accelerates the development of programs for registration and measurement of outcomes as a key and pivotal element of a health system. Measuring outcomes in real life settings may justify that the resources used and drug costs are an investment and have a clear return in the form of improvements in the health of the people.

Public Innovative Purchasing (PIP)

The PIP is a contract that is put out to tender for a solution for an existing problem or unmet need. In consequence, the product or system that does not exist at that time, but can probably be developed in a reasonable period. That is, the tender requests the devel-

opment of new or improved technology to be able to meet the requirements demanded by the buyer.

Most of the existing experiences have been made with medical devices and services where what is bought is not an existing product but a system that responds to a health goal.

Although there is little experience in this type of procedure and it seems that drugs are not candidates for a PIP (due to its regulation through controlled clinical trials and authorizations related to them), they will surely be involved in this type of tenders in which there is a global solution that does not exist in which the drug can be a part of it.

6.6 Look-out for Near Future

The evolution of scientific knowledge especially in the health field is opening an exciting new era in this area. This will allow changes that will transform the rules of standard care moving towards more personalized and targeted drug technologies therefore enabling improvements in patients. Moreover, a change in the model of care is now necessary. The current health systems were designed to save lives and to treat acute diseases. At present the real challenge is to adapt new models due to patients live longer with chronic or degenerative conditions. So, we should design new future models that should consider this new condition of patients, chronification of pathologies, and not only based on acute situations. This implies that there will be a problem for the public system because they should face these new situations not only related to medicines or technologies but also to a new approach. It is necessary to treat or cure patients maintaining the sustainability and the affordability of public systems and providing early access of these innovations to patients.

The main characteristics of new models should:

1. **Guarantee sustainability and affordability.** These new models should ensure both principles through efficient allocation of resources and should stimulate at the same time innovation and promote a competitive environment.
2. **Provide Add value.** These new approaches should encourage the innovation of new medicines and technologies that really change the evolution of the diseases.
3. **Promote the Access.** These new proposals should make sure that patients get timely and equitable access to new medicines and technologies to obtain the benefits from these new therapies.
4. **Be Flexible.** These new proposed models should be designed with sufficient flexibility to reach new future challenges which mean that changes can be performed in the current models.
5. **Have different perspectives.** New approaches are needed to be done not only based on price and budget impact but on added value of medicines or technologies including a more holistic health and social care systems approach.

Traditional models are based on economic results, (rebates, price/volume agreement, etc.) without considering health outcomes. Now the perspective is changing and we are designing new agreement models which consider these health outcomes (partial response

or total response, rebates for sub-optimal responses, reimbursement if clinically significant improvement is achieved etc.).

However, different and more efficient models will be needed in the future improving the existing ones. These models must include different perspectives by all the stakeholders and should be robust and with at least 3-5 years' perspective.

The future situation in Spain looks very complex. Our regulation on P&R was designed in the early nineties and the government has made two attempts in the last three years to pass a new one.

This new legislation should promote new principles in P&R procedures, transparency, robust assessment and multidisciplinary approach to this process. The system should be updated and adapted to the XXI century challenges.

We need to establish clear procedures to assess these new technologies with an appropriate methodology and to promote clear criteria for decision making. This new approach must include the regional perspective because Regional Governments are the real payers of these innovations. On the other hand, early dialogue with the different stakeholders are needed to have some predictability in the decision-making process. It is essential to harmonize all these criteria and the type of assessment at European level either by EUnetHTA or by the EMA to have the same European principles.

In conclusion, a holistic value-based approach is required. There is a need to change the current systems based only on price to systems based on health results and added value. The governance of this procedure at the UE level is very relevant and should be clarified in future. In Spain, the regulation should be reviewed, updated and aligned with the European principles. All these changes are to be based on two basic principles, to assure the sustainability of the systems guaranteeing the access of the innovation to patients.

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