



Access to High-priced Medicines in Hospital Settings in Europe

A Study in Four European Countries

Research Report



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Abstract

Background: The demand for new medicines is constantly rising—and alongside that demand are increasing prices on patented pharmaceuticals. Significant disparities regarding access to medicines are emerging across the European Union (EU). However, only limited data is available on the price difference of medicines used in hospitals across the EU. The aim of this paper is to assess access to patented, high-priced medicines used in hospitals in different EU Member States.

Methods: Four EU Member States (Austria, France, Spain and Latvia) were selected for study. Hospital prices of five medicines in three key therapeutic areas (cancer, rheumatic diseases and hepatitis C) were collected. Official list prices for hospital procurement were compared and unit prices were related to annual gross domestic product (GDP) per capita. Additionally, 14 semi-structured interviews with key informants were conducted to gather information on access to the medicines for the inpatient sector.

Results: The hospital prices of medicines are disconnected from the GDP per capita of a country. Latvia and Spain have higher prices for the studied medicines compared to Austria and France, despite having lower GDPs per capita. Latvia has the lowest annual GDP per capita, but the price of the selected medicines in Latvia is the highest of all four countries.

Conclusions and Recommendations: This study presents evidence of price inequalities of high-priced medicines in the hospital sector in Europe. Several policy recommendations are presented to address this challenge.

I. INTRODUCTION

The recent inclusion of high-priced, patented cancer and hepatitis C medicines on the World Health Organization (WHO) Model List of Essential Medicines (EML) has changed the approach for access to essential medicines as a human right. Not since the inclusion of on-patent medicines for HIV/AIDS on the EML, which identifies medicines that satisfy the global priority health care needs, has the list undergone such a radical change. However, even wealthy governments are struggling to provide their populations with access to new medicines that are now recognised as essential for all people, but are simply unaffordable. The most recent illustration of this problem is the introduction of sofosbuvir, a breakthrough hepatitis C treatment that entered the United States (US) market with a list price of \$84,000 per person for a course of treatment [1].

While European Union (EU) governments and the EU itself repeatedly express commitment to universal and equitable access to healthcare [2], [3], the current model of ensuring that access for patients across the EU does not seem to be effective. In fact, significant disparities in access to medicines across the EU are emerging as prices of new, needed medicines threaten to overwhelm the healthcare budgets of many EU Members [4]–[7].

Pharmaceutical expenditure as percentage of gross domestic product (GDP) has increased in every EU Member State [4] over the last decade. In parallel to this rise in expenditure, the demand for medicines is growing as a consequence of an aging population, the increased burden of chronic diseases and the availability of new and novel treatment options [8].

Pharmaceutical spending represents the third most important component of health care budgets of EU Member States after inpatient and outpatient care [5], [9]. Austerity and cost-cutting interventions were implemented during the global economic crisis to reduce pharmaceutical expenditure, particularly in Eastern and Southern Europe [10]. Increased co-payments for patients, de-listing of reimbursable medication and higher value-added tax (VAT) on medicines are among the most commonly applied interventions [10]. While it has been argued that these measures have had a major effect on health equity and access to medicines in the EU, few studies exist that assess their impact on gaps in access to medicines in Europe [11], [12].

Opacity of the actual prices of medicines across the EU makes it challenging to assess price equity and affordability [8]. It is impossible to access data on the true prices of medicines after negotiation with the manufacturer. The paucity of cross-country analysis regarding medicines pricing policy sparked an increasing number of publications on national pharmaceutical systems in recent years [5], [13]–[15]. Despite these efforts, evidence on the impact of price and reimbursement policies on access to medicines between EU countries remains scarce. Furthermore, the majority of studies have focused

on the outpatient sector; only limited data is available on pharmaceutical expenditure and prices of medicines used in hospitals [4].

Information on hospital procurement prices is regarded as a ‘black-box’ since the amount hospitals pay for medicines remains unknown and often confidential [8], [16], yet hospital physicians are the primary prescribers of high-priced medicines in many countries [5], [16]. The introduction of high-priced medicines to hospital formularies has led to a disproportional increase of pharmaceutical expenditure in hospitals in recent years [17]. Despite the rising impact of high-priced medicines on health care and hospital budgets, little data on what hospitals pay for medicines and, in particular, differences in those costs across EU Member States, is available.

To accurately assess equity in terms of universal access to health care within the EU, more data on access to high-priced medicines used in the inpatient sector is urgently needed. The objective of this exploratory study is to assess access to high-priced and on-patent medicines used in a sample of hospitals in four selected EU countries (Spain, France, Austria and Latvia). In particular, we compared list prices of five medicines in key therapeutic areas where treatment costs are known to have increased in recent years, and which represent a high burden of disease: cancer, rheumatic diseases and hepatitis C [6].

Key concepts

Access to medicine

‘Access’ is defined as the ability of patients to get medicine and medical care when they need it [18]. Several frameworks exist to describe determinants of access to medicines [18]–[20]. While these frameworks have different purposes and perspectives in defining access to medicines, they all agree that affordability and availability are essential components of the access equation.

Affordability

‘Affordability’ usually describes the out-of-pocket payments made by patients for all or part of the cost of a medicine. It has a significant impact on patients’ access to medicines. Here, we are concerned with the ability of nation states to afford essential medicines and the extent to which national health budgets are able to cover the costs of patients’ medical needs.

In the context of this study, affordability is defined by a ratio between the monthly cost of a regimen and GDP per capita. This indicator can be used as a reference point for cross-country comparisons to analyse how expensive a treatment option is for different Member States [21]. If the price of a medicine is too high for a government, the medicine can be considered unaffordable to the national health budget.

Availability

‘Availability’ usually refers to a medicine’s presence in a given facility ‘off the shelf’ at the point of delivery. Supply-side factors that influence availability depend on the overall pharmaceutical expenditure of a country, the price of a medicine, and other determinants such as supply chain mark-ups, supply chain efficiency, market structure and procurement

and regulatory policies. Demand-side factors are influenced by disease burden, the level of a medicine's use and aspects regarding the medical culture of a country [5].

In this study, which is assessing high-cost medicines, we define availability in the context of high-income countries where the government and/or a social insurance scheme is primarily responsible for the cost of treatment and might deem the medicine 'unaffordable'. If it is deemed unaffordable and access is limited as a result, its availability is affected.

Other factors that affect the availability of medicines in Europe can occur if a company decides to delay market entry in a given country. Pharmaceutical companies might adjust their launch strategies for new medicines based on the price achievable, the risk of that price influencing the price point in other countries, or the risk of parallel importation [5]. Thus, new medicines might enter the market first in countries where high prices can be expected, and where the influence on price elsewhere can be minimised. Perceived risk of parallel importation, in which a product launched in one country is exported to and sold in another without the permission of a patent holder, can also be a factor. However it should be stressed that parallel importation is a mechanism that, among other things, provides a safeguard against a patent holder charging excessively high prices in a particular market by allowing the reintroduction of price competition.

Price

Depending on where medicines are distributed to patients, the 'price' of pharmaceutical products is distinguished by outpatient prices (distribution through pharmacies) and inpatient prices (distribution through hospitals) [22]. This study focused on the official inpatient price (i.e., the official list price that a hospital pays in order to purchase medicines used in a hospital).

To date, there is no internationally or European agreed definition for a 'high-priced' medicine (i.e., the price point at which a medicine can be considered high-priced). A recent report by the WHO defined a medicine as high-priced if the therapy for one patient exceeds €10,000/year to be reimbursed by a public payer [6]. However, price alone is not the only factor that impacts the pharmaceutical expenditure in health budgets.

On-patent medicine

This study focuses on the price of selected patented medicines. A patent gives patent-holders exclusive rights to produce, use and sell that medicine for a period of 20 years, as agreed by EU Member States in the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). Generic competition is inhibited for this period of intellectual property (IP) protection. Due to the market monopoly during the life of the patent, patented products can be expected to demand higher prices.

Hospital only medicine

In some EU countries, a distinction is made between 'hospital only' medicines (HOMs) and a medicine for the outpatient sector. But because the majority of medicines used in hospitals are not considered HOMs, limiting this study to HOMs would not have fully reflected the use of medicines in hospitals. Since the classification and definition of HOMs also differs among countries and is not applied in all countries included in this study, all medicines used in hospitals are taken into account for the selection of the study medicines in order to present the most accurate picture.

In this study, a hospital is defined as a “licensed establishment primarily engaged in providing medical, diagnostic and treatment services that includes physician, nursing and other health services to inpatients and the specialised accommodation services required by inpatients” [23]. The focus is on the price of medicines used in general hospitals, funded by a public institution.

II. METHODOLOGY

This research serves as an exploratory study to assess the contribution of prices on access to patented, high-priced medicines used in hospitals in Europe.

Selection of medicines

Box 1: Criteria for the selection of study medicines

- Proven therapeutic advantage.
- Marketing authorisation in all EU Member States.
- Used to prevent or treat chronic conditions.
- Suitable for hospital use.
- Significant impact on health and hospital budgets.
- Market exclusivity (i.e., patent-protection).
- Used to treat diseases that represent a large burden for both individuals and society.

This study focuses on medicines that account for a large share of health budgets, particularly hospital budgets. Pharmaceutical Health Information System (PHIS) outputs and national reports on pharmaceutical expenditure served as the preliminary basis for the selection of medicines for study [16], after which, proven added therapeutic value was assessed using evaluations from *La Revue Prescrire* [26]–[32]. For inclusion, products must also have been patent-protected, meaning that there is limited or no generic competition on the EU market. Finally, the chosen medicines were expected to hold a valid marketing authorisation in all EU countries through the European Medicines Agency (EMA) [33].

Five medicines from three key therapeutic areas that have recently experienced an increase in costs for treatment due to high medicine prices and high burdens of disease (cancer, rheumatic diseases and hepatitis C) were selected [6]. Three of the selected medicines were recently added to the WHO EML: trastuzumab (Herceptin®), rituximab (MabThera®) and sofosbuvir (Sovaldi®) [24]. Medicines that are part of this list are considered ‘essential’ by the WHO and should therefore be made “*available at all times in adequate amounts and in the appropriate dosage forms, and at a price that individuals and the community can afford*” [25].

Table 1: Selected medicines for data collection

International non-proprietary name (INN)	Brand name	Treatment area	Company
Trastuzumab	Herceptin®	Breast cancer, gastric cancer	Roche
Rituximab	MabThera®	Lymphoma (blood cancer) Rheumatoid arthritis	Roche
Abatacept	Orencia®	Rheumatoid arthritis	AbbVie
Golimumab	Simponi®	Rheumatoid arthritis, Psoriatic arthritis	Janssen Biologics B.V.
Sofosbuvir	Sovaldi®	Hepatitis C	Gilead Sciences

Generally, medicines to treat diseases with a high burden of disease in the EU were selected. Non-communicable diseases, particularly cancers, are the leading cause of death and disability in Europe [6]. Lung, female breast, colorectal, liver and stomach cancers are the most commonly diagnosed and deadliest types [34]. This reinforces our focus on trastuzumab, a widespread treatment for breast cancer, as well as rituximab, a treatment for chronic lymphocytic leukaemia.

According to the National Rheumatoid Arthritis Society, based in the United Kingdom, over 2.9 million people in Europe, many of whom are of working age, have rheumatoid arthritis. On average, every third person with rheumatoid arthritis becomes work-disabled and up to 40 percent leave work completely within five years of diagnosis [35].

Regarding hepatitis C, in 2013 alone, 31,513 cases were reported in 26 EU Member States—a crude rate of 9.6 out of every 100,000 people, according to hepatitis C surveillance in Europe [36].

Selection of countries

Four EU Member States that represent a range of financial situations in the EU (Austria, France, Latvia and Spain) were selected for the study.

Box 2: Criteria for the selection of study countries

- Balanced mix of countries with different GDPs per capita.
- Fair representation of the various sub-regions of Europe and different economic contexts. Different geographical regions are categorised based on the classification of European countries by the United Nations: Northern Europe, Eastern Europe, Southern Europe and Western Europe [53].
- A mix of old and new Member States (year of EU entry prior to, in, or after 2004, respectively).
- A balanced sample of different population sizes.
- Equal numbers of countries with a health insurance system and countries with a national health service.

Semi-structured interviews with key country representatives

To gain further insight into the affordability and availability of the selected medicines, a total of 14 semi-structured interviews with key informants from the four selected countries were conducted. Two categories of key informants were chosen: hospital sector (hospital pharmacists) and pharmaceutical governance sector (representatives from ministries of health, national drug agencies, policymakers and pharmaceutical policy researchers in the field). Interview guides were developed for each category of respondent (see Annex II). To analyse the transcripts, a combination of open coding and structured thematic analysis was applied.

The table below provides an overview of the number of interviews in each category and country, and the specific professions of the interview respondents. To ensure anonymity, the names of hospitals and interview respondents are not declared.

Table 2: Overview informant interviews

Hospital sector (N = 5)			
Hospital pharmacists	1 Austria	Interview 1:	Chief hospital pharmacist, major university hospital
	1 France	Interview 2:	Hospital pharmacist, public municipality hospital
	2 Latvia	Interview 3:	Clinical pharmacist, major university hospital
		Interview 4:	Hospital pharmacist, major university hospital
	1 Spain	Interview 5:	Chief hospital pharmacist, major university hospital
Governance sector (N = 9)			
Ministries of health, National drug agencies, Policymakers, Researchers		Interview 6:	Medicine commission, Austria
	3 Austria	Interview 7:	Ministry of health, financial management section for inpatient sector
		Interview 8:	National Health Insurance (Österreichischer Hauptverband)
		Interview 9:	Agence technique de l'information sur l'hospitalisation (ATIH)
	1 France	Interview 10:	State medicines pricing and reimbursement agency
	3 Latvia	Interview 11:	Health consultant for the hospital sector
		Interview 12:	Pharmaceutical policy, PhD in social and administrative pharmacy
	2 Spain	Interview 13:	Pharmaceutical policy expert, University of Barcelona
		Interview 14:	Pharmaceutical policy expert, Escuela Andaluza de Salud Pública

Collection of official procurement prices of hospital medicines

Official hospital procurement prices were collected for the four selected countries based on two approaches. First, price data were retrieved from public databases, where available [37]–[39]. Second, the collected price data were checked for correctness by handing out price surveys to the key interview respondents from each country.

The official hospital list price corresponds to the published ex-factory price in France, Spain and Austria [40]. In Latvia, the official hospital price refers to the wholesale or tendered price for hospital medicines and to the maximum reimbursement price set by the government in the case of high-priced medicines.

The actual prices (as opposed to list prices) that hospitals pay following confidential negotiations for discounts and rebates with manufacturers are not published and were not accessible because they are deemed commercially confidential. This is a limitation of the research (see below).

Prices of all available dosages and package sizes of the five selected medicines were surveyed. For subsequent comparison, the unit price of one vial or pill (depending on mode of application) was calculated. All price data was collected in May 2015. Price data was collected in Euros for all countries.

Since the surveyed countries apply different tax levels and systems to reclaim taxes, only net prices were compared to ensure a non-biased comparison [16].

Table 3: Compared price types for medicines referring to official hospital procurement prices

Price type	Austria	France	Latvia	Spain
Official hospital price	Ex-factory price	Ex-factory price	Wholesale price	Ex-factory price
Additions to the hospital price	-	VAT (2.1%)	Wholesale mark-up and VAT (10%)	VAT (4%)
Exemptions for prices of high-priced medicines used in hospitals	-	Supplementary list (<i>liste en sus</i>) for maximum reimbursement price	Maximum reimbursement price for List C medicines	Mandatory discounts by royal decree for patented medicines (7.5% or 15%)
Price types referring to official hospital prices for the study medicines	Ex-factory price	Official hospital purchasing price (maximum reimbursement price)	Official hospital reimbursement price	Official hospital purchasing price (ex-factory price minus mandatory discount)
Source for price data	Price survey data, EKO	ATIH	VMNVD	Bot Plus

Only net prices were used for the price comparison to assess government affordability. Different VATs were disregarded.

EKO = Erstattungskodex; Positive list and maximum reimbursement prices for the outpatient sector

VAT = Value added tax

ATIH = Agence technique de l'information sur l'hospitalisation, information on maximum hospital prices

VMNDVD = Nacionālais veselības dienests

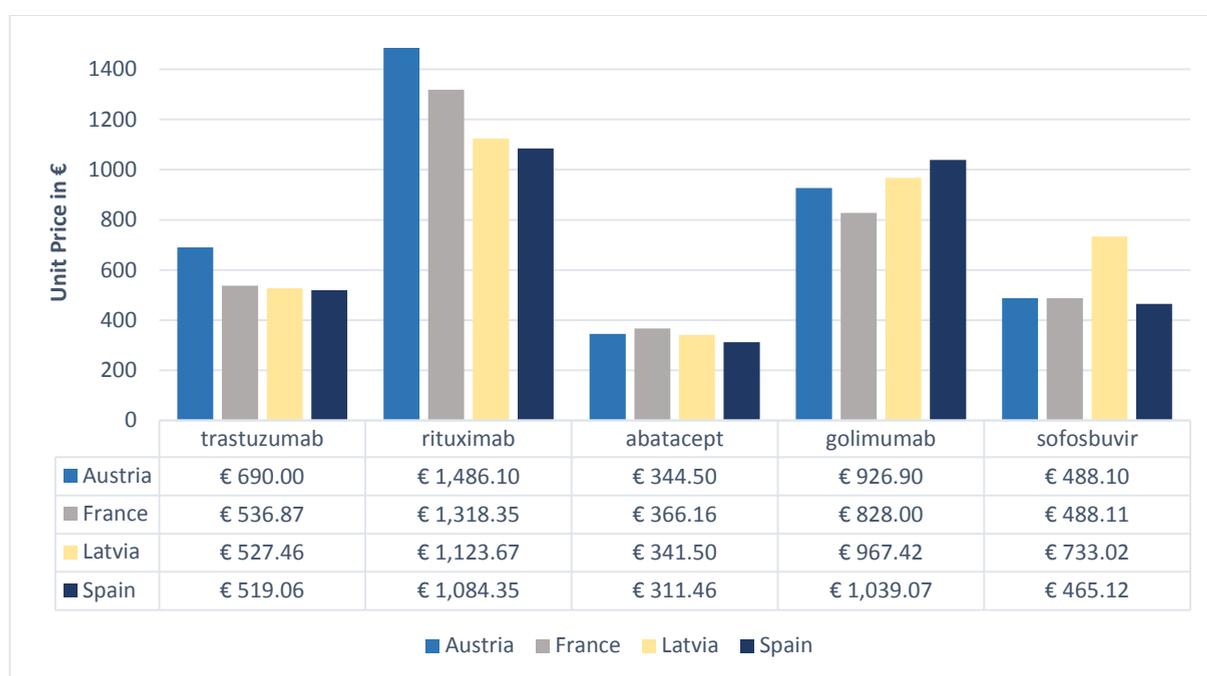
Bot Plus = Access secured information platform on official Spanish hospital prices

Unit prices were related to annual GDP per capita in percent. This ratio was used as a reference point for cross-country comparison to analyse how expensive a treatment option is for different Member States in alignment with previous studies [21], [41]. If the price of a medicine is considered expensive for a government, a medicine might not be affordable within the boundaries of that country’s health budget. Data (from 2013) on annual GDP per capita were retrieved from Eurostat [42].

III. RESULTS

Price comparison of study medicines

Figure 1: Unit prices of medicines in absolute values (in €)

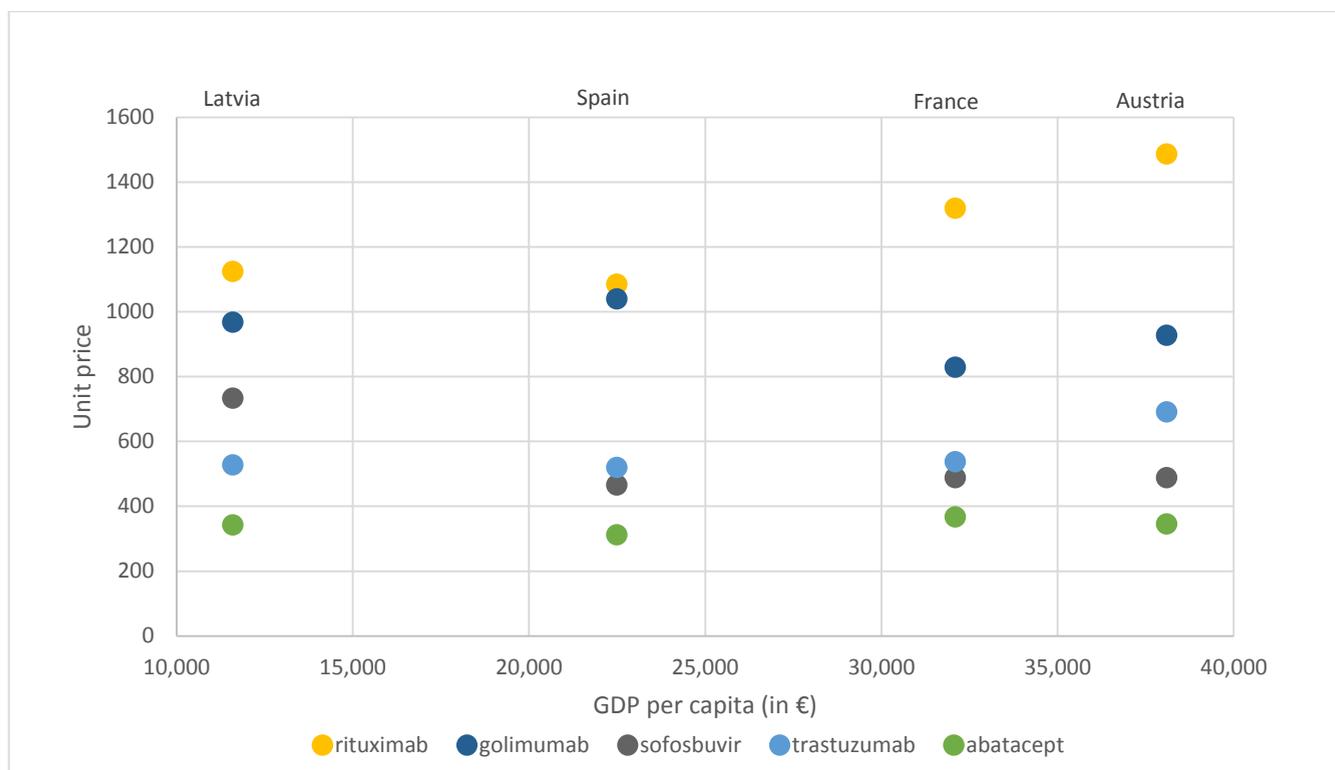


One unit represents the price of one vial for trastuzumab (Herceptin), rituximab (MabThera), abatacept (Orencia), golimumab (Simponi) (intravenous application), and the price for one pill for sofosbuvir (Sovaldi) (oral application). Strengths: Herceptin 150mg, MabThera 500mg/50ml, Orencia 250mg, Simponi 50mg, Sovaldi 400mg

Figure 1 presents the results of the price survey for the studied medicines. Little difference exists between unit prices in the selected countries. However, these differences do not present a clear pattern in terms of which countries have the highest or lowest prices for medicines. While Austria has the highest prices for trastuzumab and rituximab, Latvia, by far, holds the highest price for sofosbuvir. The prices of the other medicines included in the study, abatacept and golimumab, appear to be similar among countries. Considering the economic differences between these countries, the low variance in prices is noteworthy.

Major differences of medicine prices in relation to GDP per capita

Figure 2: Relation of medicine price to GDP (prices and annual GDP per capita in €)

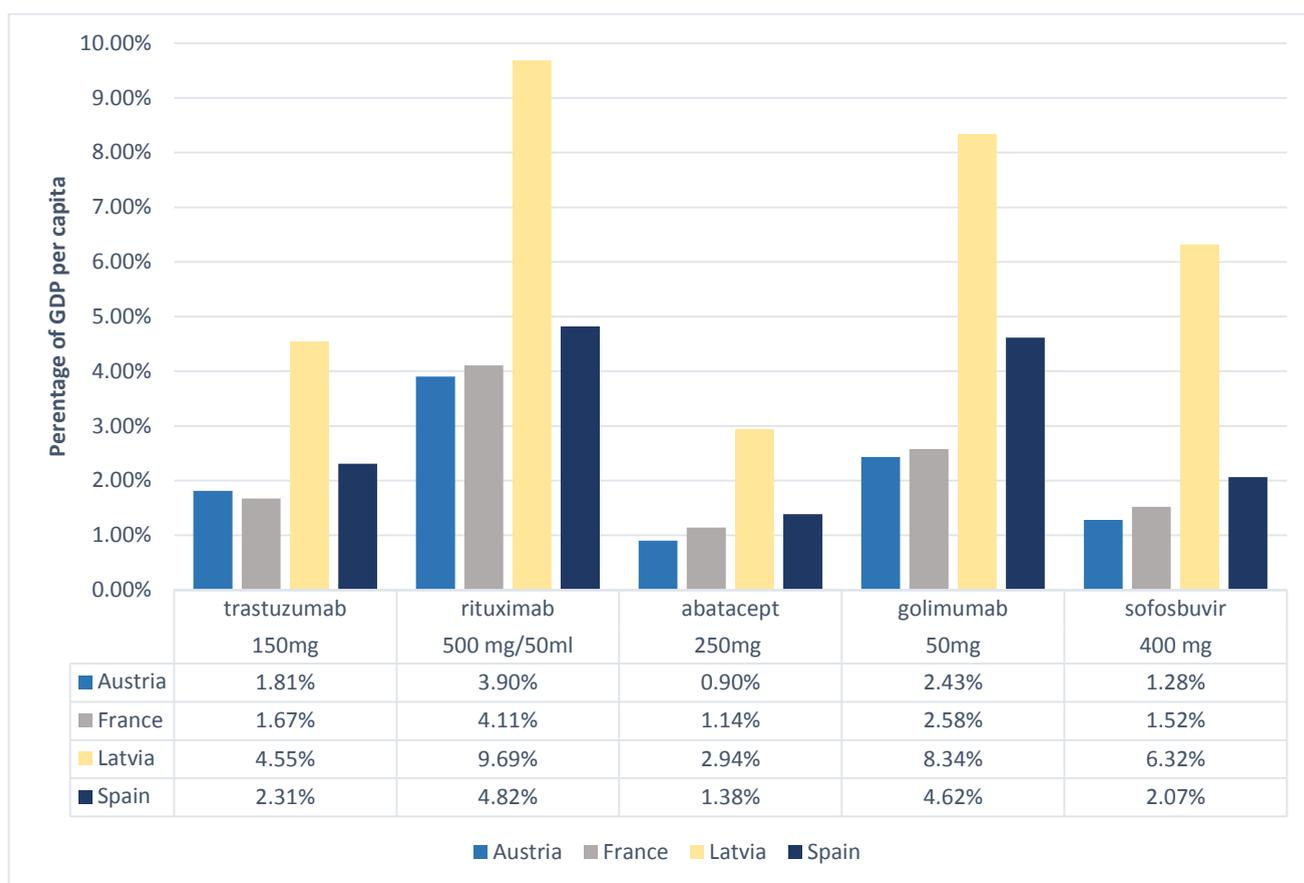


Source: Eurostat, data for annual GDP per capita in 2013 (update 01/06/2015, retrieved 04/06/2015); Price data: Survey by the author, data from May 2015. Strengths: trastuzumab 150mg, rituximab 500mg/50ml, abatacept 250mg, golimumab 50mg, sofosbuvir 400mg.

Figure 2 illustrates the relation of the prices of studied medicines to annual GDP per capita, according to Eurostat data from 2013. Although Latvia has the lowest annual GDP per capita, some products show substantially higher prices compared to the other countries in the sample. In relation to their GDP, both Latvia and Spain pay higher relative prices for the study medicines compared to Austria and France. While Austria has the highest annual GDP in the sample, this is not reflected in the differences in medicine prices. The variances in unit prices are not related to the countries' income levels.

Figure 3, below, depicts the ratio of unit price to GDP per capita, used as a reference point to assess differences in affordability for countries.

Figure 3: Ratio of unit prices to annual GDP per capita



Source: Eurostat, data for annual GDP per capita in 2013 (Update 01/06/2015, retrieved 04/06/2015), Price data: Survey by the author, data from May 2015.

The results show that Austria, France and Spain pay less than 5 percent of their per capita GDPs for a unit of medicine. Latvia, by contrast, has the highest unit price-to-GDP ratio: Latvians are paying up to 8 percent of per capita GDP for golimumab and 10 percent for rituximab. While the ratios for Austria and France show relatively equal values with a difference of about 0.2 percent, the ratio for Spain is noticeably higher for all medicines. In comparison to Austria and France, the price-to-GDP ratio for sofosbuvir is considerably higher in Latvia and Spain. Note that this analysis compares the price of one pill for sofosbuvir, and not the cost of a 12-week regimen of treatment, which also involves additional medicines.

These findings clearly demonstrate that the prices of these medicines are disconnected from the purchasing power of countries in which they are needed.

Different European pricing policies

To date, none of the surveyed countries have a comprehensive definition of high-priced medicines [6]. Yet, in France and Latvia, additional lists for certain high-priced medicines exist, with consequences for pricing and reimbursement. And in Austria and Spain, some government action has occurred in an attempt to rein in spending, particularly for costly treatments.

In France, high-priced medicines used in hospitals are explicitly defined through the list of supplementary medicines ('liste en sus') [37] comprising medicines for treatment areas such as cancer, rheumatoid arthritis, blood products and orphan diseases. These medicines are excluded from the diagnosis-related group system (DRG system, used as synonym of payment rates) and reimbursed separately by health insurance (i.e., directly from the state, rather than from the hospital's budget). The supplementary list for high-priced medicines was established to guarantee equitable access to new medicines in all public hospitals in France by providing government reimbursement to help defray the costs. Prices of these medicines are fixed to a maximum reimbursement price by the Committee for Health Care Products or the Ministry of Health, as the ultimate authority in charge. If hospitals purchase these medicines for a higher price, they must then cover any additional cost from their own hospital budgets. *"Once the price is fixed by the social security, the hospital tries to negotiate it to achieve a lower price,"* explained one hospital pharmacist (Interview 2). That final price, determined by such negotiations, can lead to divergent prices paid for the same medicine by different hospitals throughout the country. The pharmacist elaborated that there is less price divergence for patented medicines since there is limited room for price negotiation when generic alternatives are not available.

In Latvia, medicines are added to the 'List C reimbursement list' if the cost for one patient exceeds €4268.62 per treatment per year. As in France, these medicines are not paid directly by the National Health Service rather than from hospital budgets. The list is published on the Latvian Ministry of Health website and is updated every six months. At the time of the survey conducted for this study, it contained 23 medicines (update December 2015) [39].

More generally, in Latvia, the reimbursement decision is taken on an individual patient basis, with a specific number of patients per year covered. If a patient receives a positive decision for reimbursement, an approval letter is sent to the National Health Service (NHS) which subsequently allows for the purchase of the medicine for the specific patient and on a prescription basis. Clinical eligibility criteria, disease severity, age and life years gained were mentioned as decision criteria (Interview 10).

In Austria, in 2013, a 'medicine commission' was created to develop a definition for high-priced medicines and ensure *"sustainable funding mechanisms and best point-of-care service for cost-intensive medicines,"* according to an expert from the Austrian Ministry of Health (Interview 7). The medicine commission evaluates the following criteria in order to define a medicine as 'cost-intensive': the ex-factory price per defined daily doses; the monthly or yearly treatment costs; and the volume of medicine used in one year.

In Spain, where regional hospital groups and individual hospitals can procure medicines, either by tender or direct negotiations, interviewees pointed out that there are significant price variations among different regions. While pricing and reimbursement is a national responsibility, criteria for reimbursement can differ on a regional level as a measure to

contain costs. This leads to differences in access to certain medicines in Spain’s regions. “There are suspicions that some regions would have better or newer medicine, and there is a felt inequity between regions,” said a health economist from Spain (Interview 13).

According to the existing literature and national surveys, targeted reimbursement procedures or pricing of high-priced medicines in the inpatient sector have not yet been implemented [6]. However, in 2010 the Spanish government introduced a 7.5 or 15 percent mandatory discount by a royal decree on patented medicines as a cost-containment strategy to lower actual prices for medicines in the country. “In the end it is the impact on the budget which is the important thing. A 50 percent difference in price of a very widespread medicine can make a real impact,” noted a policy expert from Spain (Interview 13). This clearly underlines the impact of medicine prices on the overall health budget.

Table 4: Management of hospital procurement outcomes from background analysis and stakeholder interviews

Management of hospital procurement systems		Austria	France	Latvia	Spain
Procurement of hospital medicines	National list		●	●	
	Hospital formulary	●	●	●	●
Purchasing policies	Negotiations	●	●		●
	Tender	○ ¹	●	●	●
Procurement organised	Centralised			○ ²	
	Decentralised	●	●	●	●
Definition of high-priced medicines	Official definition in place	○ ³			
	List of high-priced medicines		●	●	
Funding for high-priced medicines	Within the hospital budget	●			●
	Reimbursed directly by the state	○ ⁴	●	●	

● = occurs in country

○ = applies only to specific medicines, or in specific cases

MoH = Ministry of Health

¹Austrian hospitals use negotiations as the main purchasing strategy; tendering has recently become more important.

²Latvia has a centralised procurement system for specific medicines and vaccines.

³Austria is currently developing a definition.

⁴In two provinces of Austria, Carinthia and Styria, cancer medicines are reimbursed directly by the federal state budget.

Overall, interview respondents emphasised that in addition to price, the overall treatment costs and the burden of disease also contribute to rendering a medicine affordable or less affordable for a health budget.

Hospital pharmacists and government representatives were asked what impact the study medicines have on their hospital budget or national health budget. Overall, study medicines were regarded as expensive or as having a considerable impact on the budget of health insurances and pharmaceutical budgets of hospitals by all informants. In general, the study's therapeutic areas—cancer, rheumatoid arthritis and, especially, hepatitis C—were emphasised to represent a high burden for hospital budgets. In particular, the high costs for the entire treatment with sofosbuvir (Sovaldi®) was highlighted as 'unsustainable' for health budgets, especially by representatives from Spain (Interviews 5, 13 and 14) and Latvia (Interviews 3, 4, 11 and 12).

The specific case of Sovaldi

Sovaldi is an exception regarding its reimbursement status [39], [43]. The product is not part of the reimbursed list in Latvia, so patients must cover costs for the treatment. This is reflected in the Latvian medicines reimbursement system where high-priced medicines are usually reimbursed on a patient-by-patient basis. Before a patient receives a medicine, an approval by a council is required. The council then decides whether the patient is eligible to receive the medicine according to selection criteria. *“A decision is made by at least three doctors, called a council, which take a decision and write an official letter to the NHS regarding the treatment to take for a patient. The NHS then allows the purchase of the medicine through a particular pharmacy. This medicine is purchased only for the specific patient on a prescription basis”* (Interview 12).

Sovaldi is also reimbursed with a restricted procedure in Austria, France and Spain. Patients must fulfil defined country-specific clinical eligibility criteria to be reimbursed for the medicine. As a result, the reimbursement is granted on the basis of the patient's disease severity.

More generally, the high price for the 12-week hepatitis C cure with sofosbuvir was described as 'unsustainable' and 'unaffordable' for health or hospital budgets by the key national informants. *“Hepatitis C medicines—like sofosbuvir—so the new ones, are all not available in Eastern Europe. You can ask in France or in Germany [...] but here no one even [...] they are only dreaming about this [...] because these prices are unaffordable for Latvia,”* said a health consultant from Latvia (Interview 11).

High prices of medicines also an issue for cancer treatment

The other medicines examined for this study, especially cancer treatments, also represent a burden for hospital budgets. A hospital pharmacist from Austria estimated that *“oncology medicines take up to 50 percent of its pharmaceutical hospital budget”* (Interview 1). According to a recent study on actual costs of cancer medicines in 15 European countries, oncology consumes up to 30 percent of total hospital expenditure and the amount spent on high-priced cancer drugs is rising quickly.[44].

It was repeatedly mentioned that total costs for the treatment (i.e., length of the therapy—chronic or acute—and the burden of disease), and not the high price alone, may render a treatment unaffordable.

This finding indicates that high prices of new patented medicines are a relevant issue for countries, regardless of their income level.

IV. DISCUSSION

Price inequalities

The qualitative research here suggests the existence of inequalities regarding access to high-priced medicines within Europe. Previous studies indicate that price levels of medicines in the outpatient sector vary among Member States [45], and that countries with lower income levels pay relatively more than higher-income countries [4]. This study confirms these results for the inpatient sector and, in particular, for high-priced, patented medicines.

Considerable disparities in price levels of official hospital procurement prices exist for the studied medicines. Although Latvia has the lowest annual GDP per capita, some medicines show substantially higher prices compared to the other countries in the sample. As an underlying reason for the price divergence, previous studies suggested the weaker negotiating and market size of small and lower-income countries in price discussions with the pharmaceutical industry [7]. This can also influence market entry of medicines in smaller economies, according to the interviews with key informants.

Both Latvia and Spain were particularly affected by the economic crisis and by the consequent austerity measures which impacted their health systems [11]. We can therefore assume that medicines with a high impact on the health budget pose a barrier for access in these countries.

Echoing previous research [5], this study shows that GDP per capita tends to correlate with access to certain on-patent medicines. In Latvia, access and reimbursement of treatment with high-priced medicines is restricted to a certain number of patients per year. Case-by-case, patients must fulfil pre-defined clinical eligibility criteria to get their treatment reimbursed. As stated in the interviews, this is a result of the limited budget and the high price for the medicines (Interviews 11 and 12).

Lack of price transparency as a barrier

The lack of transparency on actual hospital prices, transaction prices and consumption represents a major obstacle for governments and health systems to respond to rising prices for medicines, according to the representatives from Spain and Austria. This also seems to be a major problem in France, leading to different prices for medicines used in hospitals across the country. Governments and national health services are unable to

estimate how much money is spent on high-priced medicines used in hospitals since both consumption and price data are often kept secret.

Limited access to consumption and price data seems to hinder governments from assessing the impact of high-priced medicines for hospital budgets. *“Governments should at least measure the consumption of medicines used in hospitals. For now, we can only estimate how much they pay for the medicines and how many medicines are actually used in hospitals,”* said a government representative from Austria (Interview 6).

In countries where hospitals must accommodate the costs of high-priced medicines within their budgets, such as Spain and Austria, discounts and rebates for the medicines used in hospitals can lead to shifting costs from the inpatient to the outpatient sector and vice-versa. Because hospitals have to accommodate for high-prices within their budgets, they welcome discounts and rebates of various kinds. This can have consequences on the prescription behaviour in the outpatient sector and lead to greater spending on medicines in general, according to an Austrian government representative (Interview 7).

V. STUDY LIMITATIONS

Pilot study

The exploratory design of this study aimed to yield insight into a field where prior research is scarce. Since its exploratory nature required a small sample of countries, the study cannot be considered representative for the entire hospital sector in the EU. Its objective was rather to give an appraisal of the current situation of access in four European Member States, and to draw conclusions for further research, methodological refinement and, subsequently, policy recommendations.

Differences in each pricing and reimbursement policy

National differences in terms of pricing and reimbursement policies make price comparisons of medicines complex. It is essential to address and explore country-specific aspects to get a better understanding of the effects of national policies on access to medicines. Furthermore, understanding the hospital procurement systems and differences in hospital prices is a prerequisite for allowing a meaningful price comparison.

No access to the actual price data

Limited transparency and accessibility of price data for the inpatient sector was a major barrier for this research. Existing medicine databases in the EU are either only accessible for public authorities of EU Member States, such as the Euripid [8], [46], or offer fee-for-service information, such as the Pharmaceutical Price Information (PPI) service from the Austrian Health Institute [47]. However, these databases do not provide data on hospital prices. Hence, the sources of information for this study were national sources and databases, such as national lists for hospital medicine prices. These lists usually have different structures and formats, are incomplete, vary in level of detail and are published in

the national language, with the national specifications for price levels [8]. Thus, this direct search for price data was only possible in an explorative way with a small-scale study sample, while ensuring accuracy and comparability of price data. Due to the lack of access to data on actual prices paid, only the maximum purchasing price, as the official hospital procurement price, could be assessed. As Richard Bergström, EFPIA Director General, has confirmed, actual prices will never be public since countries are (or think they are) getting better prices, which is poor logic since they do not know what others may be paying.

Price per unit is only one of the components to consider

Price per unit is one of many components that contribute to the affordability of a treatment option for a country. Looking at the cost of a full course of treatment can demonstrate more dramatically the consequences of price per unit changes. For example, while the full cost of a 12-week treatment course to cure hepatitis C with sofosbuvir [48], [49] is priced around €41,000 in France, it is approximately €70,000 in Austria and Spain.

Such a price comparison, however, is only possible if a standardised treatment regimen exists. This is not the case for all the study medicines, as cancer medicines usually have a personalised treatment regime, and thus a comparison of unit prices was applied. It should be noted, however, that a seemingly small difference in unit prices can have a bigger impact on health budgets once treatment costs and burden of disease are taken into account. This could be especially true with diseases, such as many cancers, that require long-term treatment and that affect a significant proportion of the population.

Notwithstanding its limitations, this research provides knowledge on an unexplored field of pharmaceutical policy and presents initial evidence of differences in access to high-priced and hospital medicines in Europe. While previous studies and surveys on medicine prices have largely focused on prices in the outpatient sector [13], [50]–[53], this study can be considered as a starting point to uncover the situation of pricing and access in the inpatient sector. Further research is needed to extend this knowledge on a pan-European level and shed light into the pricing and reimbursement policies in the inpatient sector.

VI. CONCLUSIONS

The study presents evidence for inequalities of prices of high-priced medicines in the hospital sector in Europe. The results show that the list prices of medicines are not related to the national income of European Member States. The price inequalities do not respond to any rationale according to the financial constraint of the health systems since the Member State with the highest procurement prices (Latvia) has the lowest GDP per capita.

From the outcomes of the interviews, we can conclude that national strategies to lower prices for medicines were perceived as insufficient and not tackling core issues, such as

the need to increase price transparency and improve cooperation in the management of hospital procurement. The inpatient sector still represents a ‘black-box’ for policy-makers since it remains unknown what hospitals pay for the medicines they purchase.

The lack of transparency on hospital prices, actual transaction prices and consumption can increase difficulties for governments in responding appropriately to increasing prices for medicines and to the public health needs of their populations. To challenge this situation—which is expected to be no different in low- and middle- income countries—increased transparency on prices of medicines in the inpatient sector, including transparency on actual prices paid, as well as official asking prices, is highly recommended. This information can help governments re-establish their bargaining power with the pharmaceutical industry in order to get medicine prices that reflect their capacity to pay.

Immediate action must be taken to guarantee high-quality patient care today and sustainable European health systems in the future.

VII. RECOMMENDATIONS

In order to address unequal access to medicines in Europe, HAI suggests the key following recommendations for policy-makers at both European and national levels.

1) Transparency on the price of medicines in the inpatient sector is needed

There is a clear lack of transparency in the hospital sector in all the Member States studied. This can consequently reduce competition among suppliers of products used in the hospital sector and result in artificially higher medicine prices. In terms of strategies to lower prices, fair generic competition is the most effective way of reducing medicine prices and overall expenditure of medicines.

More transparency in medicine prices would allow governments to compare, evaluate and adapt their medicine pricing policies in order to provide more affordable needed medicines to their citizens.

The EU should ensure full transparency and public access to information about prices across EU Member States (e.g., procurement prices, reimbursement prices, retail prices) and oblige Member States to publish secret discounts and rebates through a publicly accessible EU database that contains annually updated information on the actual prices of medicines.

2) Hospitals’ pharmaceutical expenditures and consumption at national and international levels should be surveyed

Without transparency and access to comprehensive data of both real expenditure and consumption of medicines in each hospital, it is impossible to evaluate the pharmaceutical expenditure in hospitals as part the national healthcare budget. Policymakers and

governments should gather this information in order to effectively respond to increasing prices and demand for medicines, particularly for medicines that account for a large share of the health budget.

3) National and EU strategies to ensure equal access to high-priced medicines should be developed

To date there is no united definition of access to medicines or high-priced medicines in Europe. Such a common definition would allow the establishment of common standards as a basis for further policy recommendations.

The creation of joint procurement groups within and across Member States could improve the bargaining power position of some countries in price negotiations and lead to the lowering of prices. According to the interviewed hospital pharmacists, group purchasing can achieve better prices for expensive medicines. Indeed, we see the emergence of this strategy in Europe by Belgium, the Netherlands and Luxembourg in one group, and by Bulgaria and Romania in another, which have jointly negotiated lower prices for new patented medicines [54].

Furthermore, the exchange of Member States' best practices in pricing policies and an evaluation of the added therapeutic value and cost-effectiveness of new medicines would be beneficial on a European level.

The researchers support the Council of Europe 2015 recommendations that suggest Member States consider limiting reimbursement to only those medicines with a proven added therapeutic value as compared to existing alternatives [55].

4) Further research in the pharmaceutical inpatient sector is needed

Pharmaceutical policies that specifically focus on the inpatient sector are scarce and their impact remains to be evaluated [8]. Member States should gather more data on the micro level to assess access inequality, or the lack of access to needed medicines, in their countries. Before implementing new policy measures, independent impact assessments on health should be performed to ensure evidence-based policy making.

Overall, this study illustrates the need to gather more data to develop evidence-based policies in the hospital sector.

Abbreviations

DRG, T2A	Diagnosis-related group system, tarification à l'activité
BMG	Bundesministerium für Gesundheit, Austrian Ministry of Health
CEPS	Comité économique des produits de santé, Committee for Health Care Products
EFPIA	European Federation of Pharmaceutical Industries and Associations
EKO	Erstattungskodex, positive list for reimbursement in the outpatient sector
EMA	European Medicines Agency
EML	Essential Medicines List
ERP	External reference pricing
EU	European Union
GDP	Gross domestic product
HOM	Hospital-only medicine
INN	International Non-proprietary Name
IP	Intellectual property
IPC	Interministerial Pricing Committee
MEAs	Medicine entry agreements
MS	Member State
MoH	Ministry of Health
NHS	National Health Service
OECD	Organisation for Economic Co-operation and Development
PHIS	Pharmaceutical Health Information System
PPRI	Pharmaceutical Pricing and Reimbursement Information
PPI	Pharmaceutical Price Information Service
TRIPS	Trade-Related Aspects of Intellectual Property Rights
VAT	Value-added tax
WHO	World Health Organization
WTO	World Trade Organization

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Annex I

Selection of medicines: Strengths, package sizes and application

INN	ATC	Available dosages	Available package sizes	Mode of application	Available pharmaceutical form
trastuzumab	L01XC03	150 mg	1	parenteral	powder for solution for IV injection
		600mg/5ml	1	parenteral	
rituximab	L01XC02	100mg/ 10ML	1 or 2	parenteral	solution in a single-use vial
		500mg/50 ml	1	parenteral	solution in a single-use vial
abatacept	L04AA24	250 mg	1 or 2	parenteral	powder for solution for IV injection
		125 mg	1 or 4	parenteral	SC injection, prefilled syringe
golimumab	L04AB06	50mg/0.5ml	1	parenteral	solution for SC injection

Annex II

Interview guide 1: Hospital sector

A. General information on the study medicines

1. Looking at the study medicines, are you buying these medicines for your hospital? What is the procurement process?
2. Who determines the price for these medicines?
3. Is the price that your hospital pays to purchase the medicines publicly available?
4. Do you consider them 'expensive' for the pharmaceutical budget? Is there a category or list of high-priced medicines?
5. Are you required to buy products where the government has set the price, or can you also procure the medicines from other countries (i.e., parallel-import)?

B. Affordability of high-priced medicines for hospitals

6. Does your hospital have a fixed annual budget for medicines?
7. How do you prioritise or rationalise the use of high price medicine? (Take the sample of medicines as examples.)
8. Are you able to provide these medicines to all patients who suffer from the related diseases?
9. Are there any policy changes in recent years that have impacted the prices your hospital is paying for these medicines?
10. Are there any quotas in terms of volume or maximum procurement prices set for procurement of high priced medicines for hospitals?
11. Are there risk sharing agreements for the procurement of a high-priced medicine?
12. Are there price volume agreements for the procurement of a high-priced medicine?
13. Do you know if other hospitals are using the same procurement system as yours?

C. Availability of medicines

14. Are all medicines of the sample available in your hospital?
15. Are you aware of any shortages or problems with the supply of these medicines in your hospital (*or heard of problems from other hospitals*)?
16. Have you perceived problems with availability of high-priced alternatives in the same therapeutic areas (i.e., cancer, rheumatic diseases, hepatitis C)?

D. Reimbursement of medicines

17. Are all study medicines reimbursed?
18. If yes, is your hospital fully or partially reimbursed?
19. Is every patient who has the disease eligible to get the treatment reimbursed?
20. Are you aware of changes in the reimbursement or eligibility criteria for high priced therapeutics in recent years (e.g. de-listing)?

Interview guide 2: Pharmaceutical governance sector

A. General information on the sample medicines of the study

1. Looking at the sample of medicines I sent you, are you familiar with them?
2. What is the process of setting the price for these medicines?
3. Do you consider them 'expensive' for hospitals (*and for the pharmaceutical budget in general*)?

B. Management of expensive medicines

4. How do national authorities define a 'high-priced medicine'? Is there a category as such?
5. Who determines the price for (high-priced) medicines used in hospitals in your country?
6. Do you know how different the price the government sets and the price the hospital pay is?
7. Does the procurement process differ for high-priced medicines?
8. Is the price the government sets or negotiates publicly available?

C. Pricing policies for hospital procurement

5. What policy changes have been implemented to contain pharmaceutical costs for the inpatient sector?
6. Are there risk sharing agreements for high-priced medicines for hospitals?
7. Are there price volume agreements for procurement of high-priced medicines?

D. Reimbursement for high priced medicines

8. Are all sample medicines from this study reimbursed by the national health care system?
9. If yes, are they completely reimbursed or are there cost-sharing agreements or co-payments?
10. Is every patient who has this disease eligible to get the treatment reimbursed?
11. Are you aware of changes in the reimbursement or eligibility criteria for the study medicines in recent years (e.g., de-listing)? (If yes, can you name the reasons?)

E. Availability of high-priced medicines

12. Do you perceive delays in market entry of expensive medicines after they have been centrally authorised by the EMA (e.g., hepatitis C medicines)?
13. Are you aware of any shortages in supply of high-priced medicines?
14. Have you seen examples where hospitals undertake parallel importing because they could get lower prices?