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Pharmaceutical pricing

The use of external reference pricing

Kai Ruggeri, Ellen Nolte

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The research described in this document was prepared for the Department of Health within the PRP project 'An "On-call" Facility for International Healthcare Comparisons'.

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Preface

In the UK, negotiations are under way that seek to define new arrangements for the pricing of branded (new) medicines from 2014. The pharmaceutical market in the UK only accounts for a small proportion of global sales; however, UK prices are important as many countries reference their prices against those in the UK. Against this background, the Department of Health has identified the need to better understand approaches to pharmaceutical pricing in a select set of high-income countries and, where applicable, the role of reference pricing as a means to determining pharmaceutical prices. This report seeks to contribute to this understanding by reviewing approaches to pharmaceutical pricing in six high-income countries: Canada, France, Germany, Italy, the Netherlands and Spain.

The report was prepared as part of the project ‘An “On-call” Facility for International Healthcare Comparisons’ funded by the Department of Health in England through its Policy Research Programme (grant no. 0510002).

The project comprises a programme of work on international healthcare comparisons that provides intelligence on new developments in other countries, involving a network of experts in a range of countries in the Organisation for Economic Co-operation and Development (OECD) to inform health (care) policy development in England. For more information on the project please see www.international-comparisons.org.uk.

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Summary

External reference pricing, or international price comparison, is a commonly employed instrument to control prices of pharmaceuticals that are protected by intellectual property rights and benefit from a legal monopoly (in-patent drugs). The UK is among those countries that are most widely referenced by other countries in relation to pharmaceutical prices. Therefore, although the UK pharmaceutical market accounts for just over 3 percent of global sales, pharmaceutical prices in the UK likely impact on prices in countries that reference their prices to the UK. As negotiations are under way in the UK that seek to define new arrangements for the pricing of branded (new) medicines from 2014, there is a need to better understand approaches to pharmaceutical pricing in a select set of high-income countries and, where applicable, the role of external reference pricing as a means to determining pharmaceutical prices.

This report seeks to contribute to this understanding by reviewing approaches to pharmaceutical pricing in six high-income countries: Canada, France, Germany, Italy, the Netherlands and Spain. Data collection involved a review of the published and grey literature, complemented by information provided by key informants in the selected countries.

Pricing strategies for patented drugs vary among countries

All countries reviewed use a range of policies, typically involving elements of statutory pricing, external reference pricing, and negotiations and price-volume agreements although the relative weight placed on each varies. Only Germany permits principally free pricing of in-patent drugs by manufacturers and price regulation mainly relates to the way in which medicines are reimbursed. Several countries employ negotiations between government and the pharmaceutical industry to determine the price of new medicinal products considered of high therapeutic value, which may be informed by external reference pricing (France, Italy, Spain) while the Netherlands uses government-set maximum wholesale prices for all outpatient prescription-only medicines. Generics are typically subject to internal reference pricing (Italy, Spain), or price capping (France). Prices of non-prescription drugs are typically not regulated.

Pricing strategies in place in different countries are informed by the value that is attached to a given pharmaceutical product

Most countries use the notion of 'innovation' as a key determinant although the interpretation of what constitutes innovation varies. The degree to which a drug improves health outcomes is considered a core criterion in all countries, whereas cost (effectiveness)

or budget impact is taken into account by a smaller number of countries only (Italy, Netherlands, Spain).

Responsibility for determining value varies across countries, typically involving an organisation or agency independent of (while accountable to) government. In Spain the agency responsible for determining the value of pharmaceutical products is located within the Ministry of Health although the ultimate decision on the price of given (new) medicinal product is taken by an interdepartmental committee. In the Netherlands, although valuation is undertaken by the Pharmaceutical Care Committee outside government, the Ministry of Health takes the ultimate decision on pricing. Canada has set up a special agency, the Patented Medicine Prices Review Board (PMPRB), which is responsible for evaluating and regulating ex-factory prices for patented drugs.

Most countries reviewed use some form of external reference pricing to inform decisions on prices of new (innovative) pharmaceutical products

The relative role of external reference pricing vis-à-vis other pricing strategies varies among countries and so do the actual methods used. Thus, countries differ with regard to the number and composition of countries considered for referencing, ranging from four countries in France and the Netherlands, seven countries in Canada to over twenty countries in Spain. Reference prices are typically applied at market entry and followed up with later revisions. The actual approach to calculating the reference price varies among countries and details of algorithms used often remain unclear.

Experts confirmed that external reference pricing typically forms only one of many aspects to pricing and that the relative weight of approaches used is highly dynamic. For example, in the Netherlands reference pricing presents an important mechanism as it applies to all prescription-only drugs but as generic options become available its role is becoming less important. In France and Spain, external reference pricing was perceived as important in that it forms the basis for price negotiations for new, innovative medicines. It was also noted that the prices used from other countries may not be reliable because of a lack of transparency on pricing mechanisms related to rebates and insurance payments.

Among the countries reviewed, Italy abolished external reference pricing in 2001 because of a perceived lack of evidence of effectiveness in controlling costs. Likewise, Germany does not strictly use a formal system of external reference pricing although since 2011, all newly licenced medicines are subject to a ('early') benefit assessment, which forms the basis for determining the price of the new product.

The variation in the role of external reference pricing as one of many pricing mechanisms makes the assessment of the potential impact of a price change in one country on the price in another country difficult

Our review echoes evidence presented elsewhere about the high variability of external reference pricing across different settings and of the relative importance of this approach in comparison with other pricing strategies.

There is also considerable variation in the terminology and practices used, and understanding the complexities of countries included in reference baskets for external pricing requires considerable semantic clarification. Furthermore, there is considerable overlap between countries that cross-reference, and it remains challenging to estimate the direct, immediate impact on external reference baskets.

Overall, our review suggests that an impact is likely to be minimal or indirect, largely because of the diverse ways in which reference pricing is implemented in the countries examined. The position of this report is to confirm that these are relevant countries, particularly for the United Kingdom, but that understanding the specific influences on drug prices in the scope of external references is unclear.

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1.1 **Background**

Pharmaceutical^a prices differ across high-income countries. There have been attempts to classify countries in ‘high’ and ‘low’ price countries;¹² however, cross-national comparison of pharmaceutical prices is challenging because of differences in the relative level of sales in each country, fluctuations in exchange rates and the proportion and combination of pharmaceutical expenditure, as well as the type of product being compared.³ Furthermore, information on actual prices is often limited.

A recent analysis by the Department of Health in England, comparing ex-factory prices of the top-selling 250 branded products in primary care across OECD countries, found that in 2010 UK prices were lower than in all 12 comparator countries, by between 4 percent in France and 180 percent in the United States.⁴ When examining the five-year average for 2004 to 2010 this picture changed slightly. Thus, while UK prices remained significantly lower than those in the United States (by just over 150 percent) and in seven European comparator countries (by between 3 percent in Italy and 22 percent in Germany), they were somewhat higher than those in Spain, France and Finland (by between 3 percent and 5 percent). However, international price comparisons have to be interpreted with caution given differences in drug usage, market shares – including the relative balance of generic and branded drugs – and distribution costs.¹

Pharmaceutical prices are, to considerable extent, driven by supply and demand, but the nature of the product means that the pharmaceutical market does not always follow the same rules as other markets. Market imperfections arise from both the supply side, as they relate to, for example, patent protection or the regulatory approval process, and the demand side, with various actors involved, including the prescribing physician, the pharmacists and the patient,⁵ alongside third party payers (for example local or national government, health insurers) providing partial or full public subsidy for drugs.¹ In an attempt to correct for market imperfections, and also as a means to curb pharmaceutical spending more generally, governments in Europe and elsewhere have introduced pricing and reimbursement policies to promote the rational use of pharmaceuticals.^{6,7} Policies vary substantially among countries, however, reflecting in considerable part national policy

^a We here use the terms medicinal or pharmaceutical product(s), pharmaceuticals, medicines and drugs interchangeably.

priorities, which may for example place different weights on health policy from those placed on pharmaceutical industry policy.

Within Europe, most countries employ some form of direct price control, which involves the setting of a fixed maximum price of a medicinal product or the use of measures that influence the price, such as statutory pricing, price negotiations or public procurement.⁸ Conversely, free pricing is uncommon, and typically only implemented for specific products such as newly patented pharmaceuticals on launch, such as in Germany and the UK.⁷ Other commonly employed strategies include:

- *International price comparison (or external reference pricing)*: The practice of using the price(s) of a medicinal product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country.⁸
- *Profit controls (or rate of return regulation³)*: Used in the UK; describes a profit framework which is negotiated periodically between the Department of Health and the pharmaceutical industry (Pharmaceutical Price Regulation Scheme, PPRS).^{4,b}
- *Internal reference pricing*: Commonly employed in EU countries as a means to regulate out-of-patent drug prices. Describes the practice of setting the price to be paid by public payers by comparing prices of equivalent or similar products in a chemical, pharmacological or therapeutic group.^c The 'reference price' applies to all pharmaceuticals within the corresponding group of products.

Pricing policies can affect the availability and prices of pharmaceuticals beyond a given country's border, for example, when that policy is taken up by other countries. This is directly relevant to external reference pricing, which we explore in further detail in the following section.

External reference pricing

External reference pricing, or international price comparison, is a commonly employed instrument to control prices of pharmaceuticals that are protected by intellectual property rights and benefit from a legal monopoly (in-patent drugs).^{3,6} By 2011, 24 out of 27 EU Member States had used some form of external reference pricing.⁹ The only exceptions were Denmark, Sweden and the UK, and, until 2011, Germany, which has now begun to consider medicine prices elsewhere for certain new medicines.

External reference pricing typically draws on countries with similar economic background and/or geographic proximity as a benchmark. However, there are exceptions, with countries outside the European Economic Area also employing external price referencing,

^b It is worth noting, however, that in recent PPRS agreements, these profit controls have been supplemented by price reductions. This is a reflection of the difficulty of operating a profit control mechanism in an international environment with complexities arising from, for example, international transfer pricing arrangements.

^c In 2011, 20 of the 27 EU Member States had applied an internal reference price system, that is, a maximum reimbursement amount has been defined for groups of interchangeable pharmaceuticals; the only exceptions were Austria, Cyprus, Ireland, Luxembourg, Malta, Sweden and the UK.

often drawing on European countries for comparison. Examples include Brazil, South Africa, Jordan and Lebanon, which draw, to varying degrees, on selected European countries, alongside Australia, Canada and the United States.¹⁰

Generally, the number and composition of countries ('basket of reference countries') considered for comparison varies. A recent study of 27 EU Member States plus Norway by Leopold et al. (2012) reported the number of countries in a given basket to range from under 5 to over 20 countries.¹¹ Leopold et al. (2012) further noted that among those EU Member States that use external reference pricing, the United Kingdom (n=11/24) was among the most frequently referenced, following Germany (13/24), Spain (13/24) and France (11/24).¹¹ According to the Office for Fair Trading (2007), in 2007, countries which reference pharmaceutical prices to the UK included Belgium, Canada, Finland, France, Hungary, Ireland, Italy, Japan, Poland, the Netherlands, Norway, Poland and Switzerland (Figure 1.1).¹² In 2007, these markets accounted for around 25 percent of world pharmaceutical sales while the UK pharmaceutical market itself accounts for just over 3 percent of global sales only.¹² Therefore, pharmaceutical prices in the UK will likely impact on prices in countries that reference their prices to the UK.

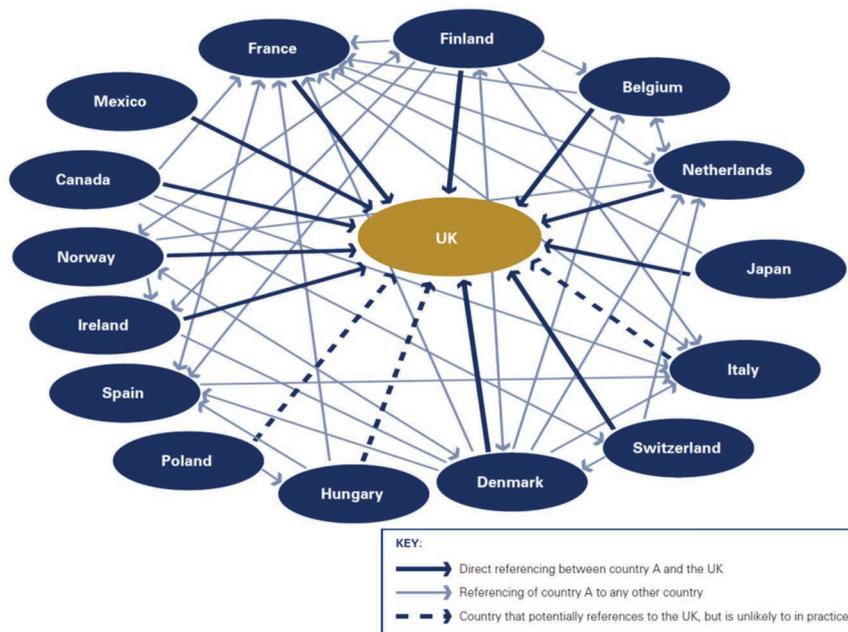


Figure 1.1 Overview of countries that reference to the UK

SOURCE: Office for Fair Trading (2007)¹²

The Office of Fair Trading (2007) further noted that prices in the UK may have further 'ripple' effects as a consequence of countries indirectly referencing the UK.¹² Evidence from Germany, also a country frequently referenced by others as noted above, has illustrated the potential knock-on effects of changes in pharmaceutical prices in Germany among countries that reference Germany.¹³ For example, it showed how, for a given drug that is marketed in all countries that reference Germany, a price reduction in Germany of

€1 would reduce domestic prices by between €0.27–0.29 in the Netherlands, €0.21–0.23 in Ireland and €0.07 in Austria. However, as Austria also references to the Netherlands and Ireland, prices in Austria would fall by an additional €0.08, so the cumulative (direct and indirect) impacts of a price change in Germany would result in a total reduction of €0.15 in the price of that drug in Austria.

However, overall, the impact of external reference pricing on prices elsewhere is not well understood. This is in part because countries not only vary in the number and composition of countries included in the reference basket as mentioned above, they also tend to employ different algorithms to determine the reference price for a given product. Furthermore, typically, external reference pricing forms only one of several strategies to regulate pharmaceutical pricing so its relative importance in determining the price of a given product will vary within and across countries.

In the UK, the current profit framework for pharmaceutical pricing, the Pharmaceutical Price Regulation Scheme described earlier, comes to an end in December 2013.¹⁴ Negotiations are under way between the Department of Health and the British Pharmaceutical Industry (ABPI) that seek to define new arrangements for the pricing of branded (new) medicines, also referred to as value based pricing, from 2014. Given that the UK is among the core countries referenced by others, the Office of Fair Trading (2007) has highlighted how a (revised) UK pharmaceutical pricing scheme should take account of the effect that UK prices may have on global investment incentives.¹² It is against this background that the Department of Health has identified the need to better understand the overarching approach to pharmaceutical pricing in a select set of high-income countries and, where applicable, the role of reference pricing as a means to determining pharmaceutical prices in these countries.

1.2 Aims and objectives

In this report, we seek to contribute to our understanding of overarching approaches to pharmaceutical pricing in a select set of high-income countries, and, specifically, the role of external reference pricing in determining pharmaceutical prices where applicable. We do so through reviewing approaches to pharmaceutical pricing in selected countries. Specifically, the review sought to understand, for each of the countries reviewed:

- the underlying principles of how pharmaceutical pricing policies are developed and applied
- the overarching approach to determining the value of new medicines
- where applicable, the role of external reference pricing as a measure to determine prices.

1.3 Our approach

Data collection involved a review of the published and grey literature as identified from bibliographic databases (PubMed), the world wide web using common search engines (Google Scholar), and governmental and non-governmental agencies and organisations

involved in or analysing pharmaceutical policies in the countries under review and internationally, including the OECD and the World Health Organization.

The report further drew on key informants in five countries identified as expert in pharmaceutical policies to provide information about the role of external reference pricing in particular (see below). Key informants were identified from a network of experts contributing to the work by the OECD on pharmaceutical policies. Experts were invited to complete a detailed questionnaire (see Appendix). The questionnaire collected data on the overarching principles of how pharmaceutical prices are developed in the country under review, the strategies that are being used to determine the price of pharmaceuticals, the range of stakeholders involved, approaches to determining the value of a given medicinal product, and the role of and approaches to external reference pricing (where applicable) and its importance in determining the price of pharmaceuticals in the country under review.

Selection of countries

The selection of countries reviewed in this report was determined in consultation with the Department of Health. The selection of countries was not designed to be representative of different approaches to healthcare financing and organisation; instead, countries were selected on the basis of the size of the pharmaceutical market in Europe. On this basis, we reviewed France (17.8 percent of pharmaceutical sales among 31 European countries in 2010), Germany (17.6 percent), Italy (13.0 percent) and Spain (9.7 percent) (the UK had the fifth largest market, at 8.9 percent).¹⁵ We also included the Netherlands, which, while having a comparatively small European pharmaceutical sales market (at just over 3 percent in 2010), includes the UK as an important core reference country. For the same reason, we also included Canada.

1.4 About this report

This report is structured as follows. Following this introduction of the topic in Chapter 1, Chapter 2 provides an overview of approaches to pharmaceutical policies in six countries, focusing on the role of external reference pricing in particular, and discusses the overall findings of the review. Chapter 3 provides profiles for each of the six countries reviewed; the country profiles follow a similar structure, beginning with a brief introduction to the health system context and then describing the principles and strategies to pharmaceutical pricing policies in place, approaches to determining the value of medicines, and, where applicable, approaches to and role of external reference pricing as a means to determine pharmaceutical prices.

This chapter provides an overview of the review of pharmaceutical pricing policies in Canada, France, Germany, Italy, the Netherlands and Spain. We begin with a brief overview of the key characteristics of healthcare financing and expenditure in the six countries under review. We then provide a summary assessment of the principles of pharmaceutical pricing policies in place in each of the countries, and discuss how countries determine the value of medicinal products in particular. Four out of the six countries under review use external reference pricing, and Germany has recently introduced a form of international benchmarking; we then discuss approaches to, and the role of, external reference pricing as a tool in more detail. We close with a discussion of observed findings and their relevance to the UK context. Further detail on each of the countries reviewed here is presented in Chapter 3.

As illustrated in Table 2.1, countries reviewed here present different forms of healthcare financing, with social security schemes – mandatory social health insurance the major source of healthcare financing in France, Germany and the Netherlands. Conversely, Canada, Italy and Spain operate mainly tax-funded systems. In 2010, overall health expenditure varied from 9.3 percent in Italy and 9.6 percent in Spain, to over 11 percent in Canada, France and Germany, and up to 12 percent in the Netherlands (UK: 9.6 percent).¹⁶ This variation is further reflected in per capita health expenditure, ranging from a low of US\$2,964 purchasing power parity in Italy to US\$5,056 in the Netherlands (UK: US\$3,433). Per capita spending on pharmaceuticals shows a slightly different ‘ranking’ order, ranging from a low of US\$481.2 purchasing power parity in the Netherlands, US\$510.8 in Italy and US\$580.2 in Spain, to US\$740.7 in Canada (UK 2008: US\$ 369.4).

Table 2.1 Key characteristics of healthcare financing and spending in six countries

	Canada	France	Germany	Italy	Netherlands	Spain
Healthcare financing (2010) (%of health expenditure)						
Taxation	68.8	3.9	6.7	77.9 ^(a)	8.5	69.2
Social security schemes	1.4	73.7	70.5	0.2	77.2	4.6
Private health insurance	13.2	14.2	9.6	1.0	5.2	5.7
Out-of-pocket payments	15.0	7.6	12.4	19.7	5.5	20.2
Other	1.6	0.7	0.8	1.2	3.6	0.3
Total expenditure on health as % of GDP	11.4	11.6	11.6	9.3	12.0	9.6
Total expenditure on health per capita, (US\$ purchasing power parity)	4,445	3,974	4,338	2,964	5,056	3,076
Public expenditure on health as % total health expenditure	71.1	77.0	76.8	79.6	85.7	73.6
Pharmaceutical expenditure (2010)						
Total expenditure on pharmaceuticals as % total health expenditure	16.7	16.0	14.8	17.2	9.5	18.9
Total expenditure on pharmaceuticals per capita (US\$ purchasing power parity)	740.7	634.5	640.0	510.8	481.2	580.2
Cost-sharing arrangements						
Pharmaceuticals	Yes	Yes	Yes	Yes	Yes	Yes

Source: OECD (2012)¹⁶Note: ^(a)Healthcare financing data for Italy are for 2009.

2.1 Principles of pharmaceutical pricing

Table 2.2 provides an overview of the principles of pharmaceutical pricing in the six countries reviewed. We find that pricing strategies for patented drugs vary among countries reviewed, although all countries use a range of policies, typically involving elements of statutory pricing, external reference pricing, and negotiations and price-volume agreements although the relative weight placed on each varies. Among countries reviewed, only Germany permits principally free pricing of in-patent drugs by manufacturers and price regulation mainly relates to the way in which medicines are reimbursed. Here, a number of mechanisms are being used (see Section 2.3).

External reference pricing forms the basis for negotiations between government and the pharmaceutical industry for new medicinal products considered of high therapeutic value in France and Spain. Likewise, in Canada, for new patented drugs that are considered as breakthrough, significant improvement or moderate improvement, a median international price comparison test can be applied to determine (ex-factory) prices. Price negotiations also form the basis for price setting for new in-patent drugs in Italy. Negotiations may be informed by prices in other countries but this does not form a core criterion for negotiations. In the Netherlands, the government sets maximum wholesale prices for all outpatient prescription-only medicines; the maximum wholesale prices are informed by external reference pricing.

Conversely, generics are typically subject to internal reference pricing (Italy, Spain) or price capping (France). Prices of non-prescription drugs are typically not regulated.

Table 2.2 Principles of pharmaceutical pricing strategies in six countries

Canada	France	Germany	Italy	Netherlands	Spain
<p>The Patented Medicine Prices Review Board (PMPRB) regulates ex-factory prices for prescription and non-prescription patented drugs to ensure that prices of patented medicines sold in Canada are not excessive. Where prices are found to be excessive, public hearings or mandatory price reductions are possible. PMPRB does not regulate prices charged by wholesalers, retailers or pharmacies. Pricing in the generic market is primarily driven by provincial and territorial drug plans.</p>	<p>The key actors involved in pricing policies are the Transparency Commission, which determines the added therapeutic benefit, and the Health Care Products Pricing Committee (CEPS), which determines prices through negotiations with manufacturers. Pricing strategies differ between the ambulatory care and hospital setting but principally involve external reference pricing and price–volume agreements. Outpatient drugs considered as of moderate to high added therapeutic value are subject to price setting through negotiations with the industry based on external reference pricing; prices for generic drugs are determined based on a fixed proportion of the originator price through negotiations with the industry. Price setting in the hospital sector is similar to pricing in the ambulatory care sector; also negotiations between hospital and manufacturers.</p>	<p>The principles of pharmaceutical care are regulated within Social Code Book V. Pharmaceutical prices are principally set freely by manufacturers; from 2011 all newly licenced medicines are subject to a ('early') benefit assessment, overseen by the Federal Joint Committee; this forms the basis for determining the price of the new product. Price regulation mainly relates to the way in which drugs are reimbursed:</p> <ul style="list-style-type: none"> • statutory pricing: applies to prescription drugs and non-prescription drugs that are exceptionally covered under the statutory health insurance (SHI) system at wholesaler and pharmacy levels • mandatory discounts and rebates • discounts or rebates negotiated between manufacturers and retailers and SHI funds or hospitals 	<p>The Italian Medicines Agency (AIFA) is responsible for price setting for in-patient drugs based on negotiations with pharmaceutical companies. Negotiations follow a set of criteria and may also be informed by prices in other European countries. Generic drugs are subject to internal reference pricing, established through AIFA's Transparency List.</p>	<p>The Ministry of Health, Welfare and Sport determines the maximum wholesale price set for all outpatient prescription-only medicines; where manufacturers sell their products to a pharmacy directly, they have to restrict the prices to the maximum wholesale price set by the ministry. The government regulates prices pharmacies may charge through setting of maximum fees. Maximum wholesale prices are set drawing on external reference pricing. Central price setting does not apply to over-the-counter products.</p>	<p>The Ministry of Health, Social Services and Equality is responsible for pricing of drugs. The main mechanisms include external and internal reference pricing as well as price negotiations:</p> <ul style="list-style-type: none"> • <i>external reference pricing</i> applies to new medicines where there is no comparator in the Spanish market • <i>internal reference pricing</i> is used if a comparator exists within Spain (generics) • <i>free pricing</i> for non-reimbursable medicines <p>Price negotiations apply to new innovative medicines while generics are subject to statutory pricing. Cost-plus pricing is not applied as a rule; however, the production costs should be provided by the manufacturer on the pricing application form.</p>

2.2 Determining value of pharmaceuticals

Pricing strategies in place in different countries are informed by the value that is attached to a given pharmaceutical product. ‘Value’ is technically defined as ‘what consumers would be willing to pay or to give up for a good or service’.¹⁷ In the context of pharmaceuticals, value refers to the specific features attributed to a given drug in a particular context, such as its degree of innovation, availability or accessibility, or importance in relation to public health. Therapeutic value has been defined as ‘the effect conveyed on a patient following administration of a pharmaceutical which either restores, corrects or modifies a physiological function(s) for that patient’.⁸

Table 2.3 provides an overview of the range of criteria used in the six countries to determine value of a (new) medicinal product. Most countries use the notion of ‘innovation’ as a key determinant, although the interpretation of what constitutes innovation varies. The G10 High Level Group on Innovation and Provision of Medicines (2002) has defined innovative medicines as those that are ‘either more effective, or cause fewer or milder adverse effects, or are easier to use than existing ones used for the same purpose, although not all commercial innovations have the same therapeutic value’.¹⁸

This definition is to a certain degree reflected in the set of criteria used among countries reviewed here; the degree to which a drug improves health outcomes is considered a core criterion in all countries, whereas cost (effectiveness) or budget impact is taken into account by a smaller number of countries only (Italy, Netherlands, Spain).

In France, medicinal products are grouped according to the added therapeutic value of new drugs when compared with available medicines. The Italian approach involves an algorithm to determine degree of therapeutic innovation based on assessments relating to cost and sustainability of new medicines. The degree of innovation is a core criterion for assessing the value of a given product in Germany; the judgement of whether medicines are ‘innovative’ is based on an assessment of whether the drug has a therapeutic advantage or fewer side-effects. The degree of innovation is also considered in Spain, alongside disease severity, incremental clinical benefit considering cost-effectiveness and budget impact, as well as the availability of alternatives for the treatment of the same condition. A similarly wide range of criteria is employed in the Netherlands, which considers therapeutic value, patient benefit, cost-effectiveness and financial impact on the core basket of services, pharmaceutical and health budgets, the insurance funds and social impact.

Responsibility for determining value varies across countries, typically involving an organisation or agency independent of (while accountable to) government. The only exception among countries reviewed is Spain, where the agency responsible for determining the value of pharmaceutical products is located within the Ministry of Health. However, it is worth noting that in Spain, the ultimate decision on the price of a given (new) medicinal product is taken by an interdepartmental committee (the Interministerial Pricing Committee), which involves representatives from the Ministry of Health, Social Policy and Equality, the Ministry of Industry and the Ministry of Finance. In the Netherlands, although valuation is undertaken by the Pharmaceutical Care Committee (CHF) outside government, the Ministry of Health takes the ultimate decision on pricing, albeit informed by advice from the CFH. Canada has set up a special agency, the Patented

Medicine Prices Review Board (PMPRB), which is responsible for evaluating and regulating ex-factory prices for patented drugs.

Table 2.3 Determining the value of medicinal products in six countries

Canada	France	Germany	Italy	Netherlands	Spain
<p>Primary factors used by PMPRB (given greatest weight):</p> <ul style="list-style-type: none"> • increased efficacy • reduction in grade or incidence of adverse effects <p>Secondary factors:</p> <ul style="list-style-type: none"> • route of administration • patient or caregiver convenience • compliance gain • time to effect • duration of treatment course • success rate • percentage of population treated effectively • disability avoidance 	<p>The Transparency Commission at the National Authority for Health (HAS) assesses all new drugs for added therapeutic value and categorises them in one of five groups (ASMR):</p> <ul style="list-style-type: none"> • major improvement (new therapeutic area, reduction of mortality) • significant improvement in efficacy and/or reduction of side-effects • modest improvement in efficacy and/or reduction of side-effects • minor improvement • no improvement 	<p>Degree of innovation key determinant. Judgement of a drug as 'innovative' as defined by the Federal Joint Committee is based on an assessment of whether the drug has a therapeutic advantage or fewer side-effects. Patient benefit as set out in Social Code Book V should consider:</p> <ul style="list-style-type: none"> • improving health status • reducing length of illness • increasing length of life • reducing side effects • improving quality of life 	<p>Therapeutic innovation of drugs is evaluated by AIFA using a series of algorithms</p> <p>Health technology assessment is used to relate innovation to cost, then used in final evaluation to determine sustainability</p>	<p>Pharmaceutical Care Committee (CHF) at the Health Care Insurance Board (CVZ) determines value therapeutic value, patient benefit, cost impact and budget impact</p> <p>Further criteria include innovative characteristics, availability of therapeutic alternatives, and social, legal and other criteria; economic analyses are undertaken from a societal perspective</p>	<p>The Directorate-General for Pharmacy and Healthcare Products at the Ministry of Health determines the value of new medicines according to:</p> <ul style="list-style-type: none"> • severity of disease • certain patient group need • therapeutic and social value, incremental clinical benefit considering cost-effectiveness • rational pharmaceutical expenditure and budget impact • alternatives availability for the treatment of the same disease, at lower cost • degree of innovation

2.3 External reference pricing

As indicated above, most countries reviewed here use some form of external reference pricing to inform decisions on prices of new (innovative) pharmaceutical products, although the relative role of this strategy vis-à-vis other pricing strategies varies. Among the countries reviewed here, Italy no longer uses external reference pricing; indeed, this strategy was abolished in 2001 because of a perceived lack of evidence of effectiveness in controlling costs. As noted above, the main mechanism to determine prices is through negotiations between the Italian Medicines Agency (AIFA) and pharmaceutical companies, although prices elsewhere may be used to inform decisions. Likewise, Germany does not strictly use a formal system of external reference pricing. Since 2011, all newly licenced medicines are subject to a ('early') benefit assessment, which forms the basis for determining the price of the new product. For medicines that were shown to provide an added benefit, the Federal Association of Statutory Health Insurance (SHI) Funds will negotiate with the relevant manufacturer to agree on a reimbursement level. Where negotiations fail, an arbitration committee will define the reimbursement level based on the European price level.

Table 2.4 provides an overview of the main features of external reference pricing in the countries under review. Reflecting the variation in the role external reference pricing takes in each of the countries, the actual methods used vary among countries. For example, countries differ with regard to the number and composition of countries considered for referencing, ranging from four countries in France and the Netherlands, seven countries in Canada to over twenty countries in Spain, although Spain does not consider a pre-specified basket of countries for reference but rather refers to a broader grouping of countries located in the Eurozone. Canada uses a basket comprising countries with comparable economic indicators and available evidence on the medicines; it also includes the US in order to balance high and low cost countries in the list.

Most countries reviewed here use external reference pricing when determining the price of innovative medicines, although the Netherlands applies this strategy to all prescription-only medicines, and, more recently, also for high-cost medicines and orphan drugs used in inpatient care. Reference prices are typically applied at market entry and followed up with later revisions. Countries typically use the ex-factory price for deriving external reference prices; among the countries reviewed here the only exception is the Netherlands, which uses pharmacy retail prices.

The actual approach to calculating the reference price varies among countries and details of algorithms used often remain unclear. For example, in France, derivation of the external reference price is based on the stipulation that the initial listing price should not be lower than the lowest price observed in the comparator countries Germany, Italy, Spain and the UK. In the Netherlands, the reference is determined by means of calculating the average price from its comparator countries (Belgium, France, Germany, UK). However, the precise definition of 'average' is not expressed outright and this would clearly be relevant given the limited number of countries; means would easily be influenced by a single outlier whereas a median would be difficult to identify.

Spain uses the lowest available price of Eurozone countries, with country selection varying according to available evidence for new drugs. In Canada, the median price of the seven

reference countries is used to determine the maximum price of the product under review. As all reference countries use a different currency from that in Canada, price calculation also takes account of the average exchange rate of the past 36 months.

Finally, countries also vary in relation to the source(s) they use to determine prices in other countries. The most common method in the countries reviewed was to pay for privately owned data from research firms, with some communication with various national health offices.

Table 2.4 Main features of external reference pricing in six countries

	Canada	France	Germany	Italy	Netherlands	Spain
Countries considered in reference basket ^(a)	7 (France, Germany, Italy, Sweden, Switzerland, UK, USA)	4 (Germany, Italy, Spain, UK)	Not defined	Not defined	4 (Belgium, France, Germany, UK)	22 (potential) Eurozone countries but use varies
'Weight' of external reference pricing in determining price ^(a)	Main criterion	Main criterion	From 2011, prices in other European countries have to be taken into consideration by the arbitration body when determining the price of newly licensed pharmaceuticals	Supportive information	Main criterion	Main criterion
Scope ^(a)	Innovative medicines	Innovative medicines Explicit criterion for products classified as ASMR I-III	Innovative medicines	Reimbursable medicines	Prescription-only medicines High-cost medicines and orphan drugs for inpatient care	Innovative medicines
Price basis ^(a)	Ex-factory	Ex-factory	n/a	Ex-factory	Pharmacy retail	Ex-factory
Calculation of reference price	Reference countries selected on economic and geographic similarities to Canada, including high and low costs for balance Median of reference used as maximum price	Initial listing price should not be lower than the lowest price observed in Germany, Italy, Spain and the UK	Not documented	Not defined	Maximum wholesale price set by reference to average price from Belgium, France, Germany and UK	Lowest available price of Eurozone countries Country selection varies according to available evidence for new drugs
Source of reference price	n/a	Data Finance Services Assurance (DAFSA) – market research company	n/a	n/a	Algemene Pharmaceutische Bond (Belgium) Informationsstelle für Arzneispezialitäten (Germany) Société d'Éditions Médico-pharmaceutiques (France) <i>Dictionary of Medicines and Devices</i>	Euripid (European Price Databank) Manufacturer information

	Canada	France	Germany	Italy	Netherlands	Spain
External reference price application	Reference price determined at product launch Exchange rates based on 36-month average	Price determined prior to market entry	n/a	n/a	(UK) Prices reviewed every six months	First assessment undertaken at market entry with later revisions
Market share of drugs affected by external referencing	n/a	Maximum of 8% of drugs introduced between 2007 and 2011	Since 2011, 12 new pharmaceutical preparations were subject to price negotiations; in one case the arbitration body had to step in	n/a	Value not known; external reference pricing applies to all prescription-only medicines	80% for new molecules 25–40% of total new products (excluding generics)

NOTE: ^(a)Data for France, Italy, Netherlands and Spain derived from Leopold et al. (2012)¹¹ and country profiles (Chapter 3); data for Germany and Canada derived from country profiles (Chapter 3).

Relevance of external reference pricing

There is considerable variation in the market share of pharmaceuticals that are subject to external reference pricing across countries. For example, in France, only 8 percent of drugs introduced between 2007 and 2011 had external reference prices applied. Conversely, as much as 80 percent of new medicines in the Spanish pharmaceutical market have been subject to external reference pricing. In the Netherlands, the precise share of the market subject to reference pricing is not known but it is important to keep in mind that this strategy applies to all prescription-only medicines.

In the context of this report, we sought additional insights from experts in five out of the six countries reviewed, the only exception being Germany. Experts were invited to provide a view on the relative weight of external reference pricing as a strategy relative to other policies that are being applied to determine prices of medicines in their country. This confirmed that external reference pricing typically forms only one of many aspects to pricing and that the relative weight of approaches used is highly dynamic. An illustrative example is provided for the Netherlands, where reference pricing presents an important mechanism as it applies to all prescription-only drugs; however, as generic options become available or as negotiations become more common for setting prices, the impact of external reference pricing becomes less important.

In France, external reference pricing was perceived to be highly important in that it forms the basis for price negotiations for new, innovative medicines. External reference pricing retains some relevance for medicines evaluated as of low or no added benefit although its relative weight may be considered as less important than other pricing strategies, such as internal reference pricing. Similarly, in Spain, external reference pricing plays an important role in relation to innovative medicines only, as a basis for price negotiations. It was also noted that the prices used from other countries are not considered reliable because they lack transparency on pricing mechanisms related to rebates and insurance payments.

2.3.1 Practical understanding of external reference pricing

The previous sections provided a brief overview of external reference pricing strategies as applied in a small number of high income countries. This review echoes evidence presented elsewhere about the high variability of this approach across different settings and of the relative importance of this approach in comparison with other pricing strategies.^{3,11} This variation makes it difficult to assess with certainty the potential impact of a price change in one country on the price in another country.

Where countries use an average from the reference basket, this is often only applied to determine maximum prices or for general comparison.⁷ Thus a change in price elsewhere may only serve as a minor or potential indicator for the final price. Furthermore, there is considerable overlap between countries that cross-reference, and it remains challenging to estimate the direct, immediate impact on external reference baskets.

As noted in the introduction to this report, one study sought to estimate the impact of a price change in Germany on pharmaceutical prices in 15 EU Member States that use external references.¹³ It found that a price reduction of €1 on a given drug in Germany that is also marketed in all countries that reference Germany would reduce prices for the drug in those countries, although the size of the change varied, from €0.15 in Austria to €0.36 in Italy.¹⁹ That analysis illustrates how the size of the impact of external reference pricing

depends on the relative change in price in a given reference country and the relative weight that is given to the reference country in question where it forms part of a larger basket of reference countries. At the same time, the study was only able to estimate potential changes in referencing countries.

Understanding the complexities of countries included in reference baskets for external pricing requires considerable semantic clarification. For example, much of the available evidence on external reference pricing use terms such as ‘average’ without indicating a specific measure of central tendency.²⁰ Likewise, the mechanisms by which individual countries develop their pricing models appear to assume that pharmaceuticals are priced on the same scale at all times, when, in practice, there are known deviations from a standard policy based on type of drug (for example branded vs generic), regular revisions to pricing, and confounds based on preferred supplier costs or profits.¹³ These factors will likely impact the market share of drugs subject to reference pricing. Furthermore, understanding the number of countries accurately would require investigating how different types of drugs have entirely different pricing schemes.

The countries reviewed in this paper comprise a significant level of drug spending at both the EU and global level.⁶ In spite of the complexities of external reference pricing, it should not be implied that prices in each of these countries do not have a major influence on prices elsewhere. However, this review suggests that an impact is likely to be minimal or indirect, largely because of the diverse ways in which reference pricing is implemented in the countries examined. The position of this paper is to confirm that these are relevant countries, particularly for the United Kingdom, but that understanding the specific influences on drug prices in the scope of external references is unclear.

This chapter provides overviews on pharmaceutical pricing policies in Canada, France, Germany, Italy, the Netherlands and Spain. For each country, we briefly summarise the key features of the health system, then give an overview of the principles of pharmaceutical pricing policies in each. We then describe how pharmaceutical value is determined, and, where applicable, examine external reference pricing strategies in particular. As the use of external referencing often relates to setting of maximum prices, we include a description of how these are determined, where used. Finally, where available, the overall relevance of external referencing within pharmaceutical pricing is described.

3.1 **Canada**

Canada's health system is governed at federal, provincial or territorial and regional levels. Healthcare is a provincial responsibility, and the 13 single-payer, universal schemes (known as Medicare) covering health services in each province or territory as defined by the federal Canada Health Act (1984) are predominantly financed from general federal and provincial taxation.²¹ The provincial responsibilities cover management, organisation and delivery of hospital and physician services and may include supplementary coverage for other medical goods or services, including out-patient prescription drugs. The federal government, through its health department, Health Canada, transfers funds to the provinces to support the provision of healthcare on the condition that the provinces will adhere to the principles of the Canada Health Act.²² The federal government also funds and administers health services for specific groups, such as the armed forces, veterans, immigrants and registered First Nations people, and addresses national health issues by providing grants to the provinces or community groups and by funding health research.²¹

3.1.1 **Principles of pharmaceutical pricing**

Pharmaceutical pricing for innovative medicines in Canada is managed by the Patented Medicine Prices Review Board (PMPRB), an independent quasi-judicial body established by Parliament in 1987 under the Patent Act.²³ The Board is responsible for regulating the ex-factory prices for prescription and non-prescription patented drugs sold in Canada, to wholesalers, hospitals or pharmacies, for human and veterinary use to ensure that they are not excessive. It does this by reviewing the prices that patentees charge for each individual patented drug product in Canadian markets (Box 3.1). If a price is found to be excessive, the Board can hold public hearings and order price reductions and/or the offset of excess revenues. The PMPRB does not have jurisdiction over prices charged by wholesalers or pharmacies, or over pharmacists' professional fees.

Box 3.1 Factors determining 'excessive price' according to the 1987 Patent Act

Section 85 of the Patent Act stipulates five factors that are used for determining whether a drug product is excessively priced:

- the prices at which the medicine has been sold in the relevant market
- the prices at which other medicines in the same therapeutic class have been sold in the relevant market
- the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada
- changes in the Consumer Price Index
- any other factors that may be set out in regulations.

The PMPRB does not cover generics, as the principle focus is to support innovation (R&D) while averting 'excess' prices. This has been noted as an issue, with a 2006 PMPRB review indicating that prices of generic drugs in Canada were between 15 percent and 77 percent higher than in ten developed countries.²⁴ The lack of cost-control in generics reduces the incentive for pharmaceutical companies to invest in innovation while also leading to increased costs for care which can create problems for public health system budgets and reduce access to treatment. Although there have been initiatives at the provincial level to control the costs of generics, there has been little change at a national level.

3.1.2 How value is determined

The level of therapeutic improvement of a given new patented drug is classified as:²⁵

- *breakthrough*: the first one to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication
- *substantial improvement*: offers substantial improvement in therapeutic effects relative to other drug products sold in Canada
- *moderate improvement*: provides moderate improvement in therapeutic effects relative to other drug products sold in Canada
- *slight or no improvement*: offers slight or no improvement in therapeutic effects relative to other drug products sold in Canada.

In recommending the level of therapeutic improvement, the PMPRB considers primary and secondary factors. Primary factors include increased efficacy, a reduction in incidence of the grade of important adverse reactions. Secondary factors consider: route of administration, patient convenience, compliance improvement, caregiver convenience, time required to achieve optimal therapeutic effect, duration of usual treatment course, success rate, percentage of population treated effectively, and disability avoidance or savings. Primary factors are given the greatest weight; these are applied to all four categories of therapeutic improvement. Secondary factors are considered subsequently.

Factors such as the mechanism of action, whether or not the substance presents a new chemical entity or different pharmacokinetic profile will generally not be taken into

account when determining the level of therapeutic improvement of a new patented drug unless these are crucially linked to the primary factors.

3.1.3 External reference pricing

Determining the reference

For newly introduced pharmaceutical products that are categorised as breakthrough, significant improvement or moderate improvement, PMPRB can use the median international price comparison test if it represents the most appropriate price comparison. In this case, the median of the ex-factory prices of the same strength and dosage form of the same patented drug product for each of seven countries (France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States) determines the 'maximum average potential price' for a new patented drug. Where the drug under review is sold in an even number of countries, the median is determined as the simple average of the middle two prices. Where the drug is sold in fewer than five countries at the time it is first sold in Canada, the median international price is calculated on an interim basis; the PMBRB re-determines the median international price after three years and taking account of changes in the consumer price index.

As indicated in Box 3.1, the price ('Average Transaction Price') of a patented drug in Canada is considered excessive if it exceeds the highest price of the same strength and dosage form of the same patented drug for France, Germany, Italy, Sweden, Switzerland, the United Kingdom or the United States. However, where the price of a given patented drug is higher than the highest international price for the same drug product, but there are similar pharmaceuticals (comparable dosage of the same medicine and patentee) also sold in Canada, the product comparison test represents the ceiling price for the new product. Provinces may negotiate lower prices with the manufacturer, although these tend to be private agreements, and therefore not in the public domain.

Application of reference pricing

At the time of product launch in Canada an assessment of the seven specified countries ex-factory prices is determined and the median price becomes the maximum price in Canada. Exchange rates are based on 36-month average exchange rates for each country and are published on the PMPRB website.²⁶

Maximum price

The median international price, when applicable, is the maximum price that can be charged in the Canadian environment. It is based on the average selling price, which is assessed annually. It is therefore possible for manufacturers to charge above this price to certain customers provided it is offset by discounts to others so that the net average price is at or below the maximum. The use of free goods (samples) can also be used to bring the price in line with the maximum price test.

Since manufacturers must report all sales, in principle, they cannot charge higher prices to the private sector unless they sell to the public sector sufficiently below the ceiling to offset these higher prices.

3.2 France

The French health system is based on statutory health insurance (SHI) and provides all legal residents with health coverage, as per the 2000 Universal Health Coverage Act (CMU).²⁷ In 2010, statutory health insurance accounted for 73.4 percent of health expenditure, complemented by out-of-pocket payments, taxation and voluntary health insurance.

The Ministry of Health oversees overall health sector planning and guidance on health policies, while regional health agencies (agences régionales de santé, ARSs), created in 2010, have responsibility for ensuring that healthcare provision meets the needs of the population by improving coordination between ambulatory and hospital care and health and social care services, while respecting national health expenditure objectives.

Health services are delivered through a mix of public and private providers, with generalist and specialist physicians largely working in private practice. Hospitals are public or private (for profit and not for profit), with public hospitals at general, regional or local community level, depending on the size and level of specialisation.

3.2.1 Principles of pharmaceutical pricing

There are three key players involved in pricing policies in France. The Transparency Commission (Commission de la Transparence) at the French National Authority for Health (Haute autorité de santé, HAS) determines the added therapeutic benefit (see below), which forms the basis for price negotiations. The Healthcare Products Pricing Committee (Comité économique des produits de santé, CEPS) determines the price through negotiations with the industry. The committee comprises ten voting members. The third player is the pharmaceutical industry.

Pricing strategies in France differ between the ambulatory care and hospital settings.

Ambulatory care settings

In the ambulatory care setting, drugs considered as of moderate to high added therapeutic value (ASMR categories I–III, see also below) are subject to price setting by government through negotiations with the industry based on external reference pricing. The use of external reference pricing was chosen to ensure a rapid access to innovative drugs.

Drugs considered as of no or low added therapeutic benefit (ASMR categories IV and V) are also subject to price setting by the government, following negotiations with industry based on the price of the most appropriate comparator drug, also drawing on external reference prices. This mechanism was chosen because new drugs without considerable added therapeutic benefit should not lead to higher expenditures for the statutory insurance system.

Prices for generic drugs are determined by government based on a fixed proportion of the originator price through negotiations with the industry. At present, a generic is priced at 40 percent of its originator wholesale price before tax. Where it is not possible to introduce a generic drug at a price of 40 percent of the original drug's wholesale price before tax, because of the restricted size of the market concerned, the formulation of the original drug, or the low price of the original product due to the length of time it has been on the market, a higher proportion of the originator's price may be agreed.

For generics with insufficient penetration into the market an internal reference pricing system applies.

Hospital setting

For hospital drugs that are reimbursed directly by statutory health insurance (la liste des médicaments facturables en sus des prestations d'hospitalisation), the reimbursement tariff is determined by government according to the same process as for drugs in ambulatory care as described above. Prices of hospital drugs that are included in disease-related group (DRG) payments are negotiated between the hospital and the industry and are not subject to government intervention.

3.2.2 **How value is determined**

As noted above, the Transparency Commission at the French National Authority for Health determines the added therapeutic benefit for all new drugs, the amélioration du service médical rendu (ASMR). The Transparency Commission distinguishes five ASMR levels:

- I. major improvement (new therapeutic area, reduction of mortality)
- II. significant improvement in efficacy and/or reduction of side-effects
- III. modest improvement in efficacy and/or reduction of side-effects
- IV. minor improvement
- V. no improvement.

New pharmaceutical products are evaluated according to the following criteria:

- effectiveness and possible side-effects
- position in the therapeutic spectrum relative to other available treatments
- severity of disease or condition
- clinical profile of the drug
- public health impact.

There are no separate schemes for different categories of drugs. All new drugs fall under the same scheme.

3.2.3 **External reference pricing**

Determining the reference

According to an agreement (accord cadre) between the Healthcare Products Pricing Committee (CEPS) and the Association of the Pharmaceutical Industry (Les Entreprises du Médicament, LEEM), CEPS has to accept an initial listing price for pharmaceuticals with an ASMR rating of I, II or III that is consistent with the prices in place in the main EU Member States. This means that the initial listing price should not be lower than the lowest price observed in Germany, Italy, Spain and the United Kingdom.

The initial list price for these drugs is fixed for a period of at least five years (starting from their inclusion in the positive list of reimbursable products). After this period, the list price may be renegotiated and external reference pricing is not per definition the main tool used during these negotiations.

However, for drugs with an estimated high budget impact, CEPS may negotiate price discounts mainly based on volume; these discounts are in place during these five years and after.

External reference pricing is mainly used for pharmaceuticals with an ASMR rating of I, II or III. Prices of drugs with an ASMR IV or V are based on the price of the most appropriate comparator drug although, as indicated earlier, external reference prices may also be used as an argument during negotiations with the industry for these drugs.

The price of generics is based on the price of their originator. The basket of countries and the 'formula' (minimum price is lowest price) are not revised regularly.

Sources for external reference prices

The source used by CEPS to determine prices in other countries was originally IMS-Health but has recently changed to Data Finance Services Assurance (DAFSA), a French market research firm. CEPS is in the process of entering a tendering procedure in order to purchase drug price data in four countries.

Application of external reference pricing

External reference pricing is the main tool used for most innovative (ASMR I–III) patented drugs in ambulatory settings. In addition, to set the reimbursement tariff of most innovative (ASMR I–III) hospital drugs that are reimbursed directly by statutory health insurance, external reference pricing is used also.

The use of external reference pricing means that prices of new patented drugs are determined before the drug enters the market. External reference pricing can also be used as an argument to decrease the drug price during later stage negotiations. Prices are derived from the sources described above at all times.

Market share

External reference pricing is important to determine the list price of new patented drugs during their first five years following market entry. Thereafter, the price may be renegotiated and external referencing is not per definition the main tool used during these negotiations. A maximum of about 8 percent of reimbursed drug expenditure in 2011 is related to drugs that were introduced during the period between 2007 and 2011 (last five years) and for which external references were used to set their price.

Maximum prices

There are no maximum prices for drugs in France. However, where costs are above a certain cost per patient per year, CEPS seeks to cap the global level of expenditure for the drug, independent of the number of patients concerned.

3.3 Germany

The German health system is financed mainly from statutory health insurance, complemented by out-of-pocket payments, taxation and voluntary health insurance. About

90 percent of the population is covered by statutory health insurance (SHI), with the remainder covered by substitutive private health insurance.²⁸ Since 2009, all residents have been required to take out health insurance.

In the German federal system, regulation of healthcare is shared between the federal and 16 state governments and corporatist actors. In the SHI system, the Joint Federal Committee (Gemeinsamer Bundesausschuss, G-BA) is the highest decision-making body.

Healthcare services are provided by a mix of public and private providers. Ambulatory care is mainly provided by office-based primary and specialist care physicians who have been granted a monopoly to provide care outside hospital. Hospitals are public (owned by a state, district or city), private for-profit and private not-for-profit (for example, owned by a church-based charitable organisation).

3.3.1 Principles of pharmaceutical pricing

The general principles of pharmaceutical care in Germany are regulated within the Social Code Book V (Sozialgesetzbuch), which sets out the overall framework for the statutory health insurance system (SHI), including coverage and reimbursement of medicines under the statutory system.²⁹ The 1976 Pharmaceutical Act (Arzneimittelgesetz) regulates the safety of medicines, including licensing procedures. Article 78 of the Pharmaceutical Act also touches on pricing to the extent that it authorises the Ministry of Economics and Technology (BMWi) (following approval by the Upper House) to define price ranges for medicines dispensed by pharmacies or wholesalers; the act foresees uniform pricing of prescription drugs dispensed in pharmacies, although this does not apply to non-prescription drugs that are not covered by the statutory system.

Pharmaceutical prices are principally set freely by manufacturers (but see below); however, a complex set of regulations applies along the market chain, which mainly relates to the way in which prices are reimbursed under the statutory health insurance system.³⁰ These include the following:

- *Statutory pricing*: applies to prescription drugs and non-prescription drugs that are exceptionally covered under the SHI system at wholesaler and pharmacy levels. It involves the application of fixed mark-ups on ex-factory prices plus dispensing fee to ensure uniform prices for prescription drugs in all pharmacies in the country as set out in the Pharmaceutical Price Ordinance (Arzneimittelpreisverordnung); non-prescription drugs other than those exceptionally funded under SHI are not subject to this regulation; here wholesalers and pharmacies can set their own prices (based on ex-factory prices).
- *Mandatory discounts and rebates*: Germany uses internal reference pricing, but this scheme is not aimed at regulating pharmaceutical prices directly but to set reimbursement limits under the statutory (SHI) system:⁷
 - Highly innovative drugs are typically not subject to reference pricing (but see below); however, for drugs not subject to reference pricing,

manufacturers are required to provide SHI funds with a rebate on the ex-factory price.^d

- For off-patent, generic prescriptions, manufacturers are required to provide a 10 percent rebate to SHI funds. Where for a given generic drug the manufacturer holds a lower price constant for at least three years (from 2007), the manufacturer may charge the reduced price against the rebate; where the price is reduced by more than 10 percent, the rebate no longer applies (for price reductions introduced after 2007).
- All prescription drugs reimbursed under SHI are subject to a rebate to be provided by pharmacies to SHI funds of currently (2011–12) €2.05 per package.³¹ For non-prescription drugs the rebate is set at 5 percent of the retail price.

Additional mechanisms include discounts or rebates negotiated between manufacturers or retailers and SHI funds, or between manufacturers or retailers and hospitals. To encourage competitive pricing in the off-patent market, since 2004, SHI funds have been able to negotiate further rebate agreements with manufacturers, wholesalers and pharmacies. Since April 2007, pharmacies are required only to dispense prescription drugs for which there is a rebate agreement with the relevant SHI fund in place, unless the prescribing physician explicitly excludes the use of *aut idem* (substitute) preparations.

In the inpatient sector, hospitals may negotiate prices (or rebates on ex-factory prices) with manufacturers and wholesalers. Typically, hospitals enter negotiations as a consortium or purchaser group in order to increase their negotiating power. However, information on the nature and size of prices or rebates is not publicly available.

It is important to note that although the pharmaceutical system in Germany principally allows for free pricing of drugs, manufacturers set the ex-factory prices in consideration of regulatory stipulations in place, including the internal reference pricing system and the statutory rebates (Box 3.2). Overall, only a fairly low proportion of prescription drugs are priced above the reference price. This is largely because the prescribing physician is required, by law, to justify their prescribing decision since all drugs in a given reference pricing group are judged to be similar as defined by the Federal Joint Committee.²¹ Also, all reference prices are determined in a way that at least one drug in each reference pricing group is priced at or below its reference price and so does not require an additional co-payment by the patient.

^d Until 2010, this rebate was 6 percent; it was subsequently increased to 16 percent for the period 1 August 2010 to 31 December 2013, with a price freeze on all prescription drugs imposed for the same period; manufacturers who increase prices are required to provide SHI funds with an additional rebate in line with the rise.

Box 3.2 Impacts of internal reference pricing in Germany

Where manufacturers maintained a higher-than-reference price for a given drug, the market share fell rapidly following introduction of the reference limit. For example, statins became subject to reference pricing in 2005. The statin reference pricing group includes simvastatin, fluvastatin, lovastatin, pravastatin and atorvastatin. Except for atorvastatin, the statin retail prices in 2005 were either already lower than the reference price or they were reduced to the level of the reference price. However, the manufacturer of atorvastatin (Pfizer) had kept the price of its product higher, and its share in the German pharmaceutical market subsequently fell from 40 percent to 5 percent.³² Pfizer challenged the decision by the Federal Joint Committee to group atorvastatin as part of the statin reference group before the courts and only in 2011 did the German Social Court uphold the decision made by the Federal Joint Committee.³³

3.3.2 How value is determined

Judgement of a drug as ‘innovative’ as defined by the Federal Joint Committee is based on an assessment of whether the drug has a therapeutic advantage or fewer side-effects. Patient benefit, as set out in the Social Code Book V, should consider the following: to improve health status, reduce length of illness, increase length of life, reduce side effects, and improve quality of life. Assessment of cost should also consider the appropriateness and acceptability of funding the medicinal product in question under SHI.

3.3.3 External reference pricing

Act on the Reform of the Market for Medicinal Products

Following the 2007 healthcare reform, the Federal Joint Committee was authorised to commission cost-benefit analyses of products and services to be funded under the statutory health insurance system to ensure that prices for innovative pharmaceuticals are appropriate to their effectiveness. The Act on the Reform of the Market for Medicinal Products (ANMOG), passed in November 2010, has taken this further by stipulating that from 2011 all newly licensed medicines are subject to a (‘early’) benefit assessment; this assessment forms the basis for determining the price of the new product. Specifically, the act requires manufacturers to submit evidence (a ‘dossier’) to the Federal Joint Committee on the added benefit to patients of the new drug. Drugs considered are those that have recently been licensed for use or have been licensed for a new therapeutic indication.³³ The Federal Joint Committee can commission the Institute for Quality and Efficiency in Health Care (IQWiG) or third parties to assess the evidence on whether the medicine under review does provide an additional benefit; this assessment has to be completed within three months following the submission of the evidence.

Manufacturers and other stakeholders can comment on the published assessment for a period of three months, following which the Federal Joint Committee issues a decision on the nature of the added benefit of the medicinal product, the recommended patient population, requirements for appropriate use and costs. The decision is also made public and serves as a basis to define the next stages of determining the price of the product. For those products that were shown to have no added benefit, a maximum reimbursement rate is set.

For those medicines shown to provide an added benefit for patients the Federal Association of SHI Funds enters into negotiation with the relevant manufacturer to agree a reimbursement level in the form of a rebate on the ex-factory price. Negotiations have to be concluded within six months. Where the two parties fail to come to an agreement, an

arbitration committee (Schiedskommission) defines the reimbursement level based on the European price level.

3.4 Italy

In Italy, healthcare is provided through the National Health Service (Servizio Sanitario Nazionale, SSN).³⁴ Established in 1978, the SSN guarantees universal provision of comprehensive care throughout the country. The Italian healthcare system is funded through a combination of national and regional taxation.

Responsibility for healthcare governance is shared between the central government and the 19 regions and two autonomous provinces. The central government provides the legislative framework for healthcare and defines the basic principles and objectives within which the SSN operates. It defines the basic benefits package and standard of health services provided by the regions, with the state-regions joint commission (Conferenza Stato Regioniet Unificata) playing an increasingly important role in priority setting and determining resource allocation criteria.

Health care services are provided primarily through public providers, with some private involvement. Primary care doctors operate under a national contract, complemented by regional agreements. Specialist care is provided by public and private providers in hospital outpatient departments, clinics and doctors' offices.

3.4.1 Principles of pharmaceutical pricing

The Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA) was established in 2004 by Law 326/2003 and is responsible for price setting of those drugs reimbursed by the SSN. AIFA is operated independently with direction from the Ministry of Health and the Ministry of Economics and Finance.

The process of price setting is based on negotiations between pharmaceutical companies and AIFA. Before 2004, an average of European prices was used. However, at present, the negotiation procedure is conducted following a set of criteria, including: product therapeutic value (see below), pharmaco-vigilance data, price of similar products within the same pharmaco-therapeutic group, internal market forecasts of the number of potential patients, and therapeutic innovation.

Negotiations with companies are managed by AIFA's Pricing and Reimbursement Unit with support from the Committee for Pricing and Reimbursement (Comitato Prezzi e Rimborso, CPR). Pricing and reimbursement decisions are made concurrently, with price negotiations following reimbursement evaluation. If no agreement is reached through negotiations, drugs are classified as non-reimbursable. Negotiations are based on criteria that are used for valuation; they may also draw on average European prices, although the latter is no longer a specific criterion for determining the price.

A ceiling for out-patient drug costs is established under law 45/2001. Such spending cannot exceed 13 percent of total health expenditure at regional or national levels. Overall pharmaceutical spending cannot exceed 16 percent of health expenditure. If expenditure exceeds the ceiling, the list of reimbursed drugs is amended and profit controls are extended to reduce spending.

For generic drugs, a system of internal reference pricing applies, which is established through the publication by AIFA of the Transparency List. The mechanism of internal reference pricing is to determine the maximum price to be reimbursed by the SSN, with any remainder charged to the patient. Reference prices apply to all pharmaceuticals within the corresponding group of products.

Where there is uncertainty about the efficacy or safety profiles of drugs, there are programmes in place to ensure access to medicines and outcome monitoring. These include the AIFA Monitoring Registry, managed entry agreements and the AIFA Notes for Prescription, among others.

3.4.2 **How value is determined**

The value of pharmaceuticals is assessed by AIFA through its Technical and Scientific Committee according to the application of a series of sequential algorithms. These algorithms evaluate the degree of innovation and create a class and a numerical score based on innovativeness, precise evaluation of the treated population, the 'endpoints' (primary and/or secondary) and the type of treatment and comparison of the duration of therapeutic effect. The algorithm also takes into account health technology assessment, which relates innovation to the costs that are important in the final evaluation in the Italian context for the sustainability of any potential innovation for the SNS.

To validate the value of particular product it is possible to establish a specific monitoring registry. A managed entry agreement may then be established together with a monitoring registry in order to evaluate the clinical performance of the drug.

3.4.3 **External reference pricing**

External reference pricing was abolished in Italy in 2001 because it was not considered to be effective at controlling costs.³⁵ However, price negotiations may still take account of reference prices adopted by other European countries even if it is not the key criterion on which the price definition is based.

3.5 **The Netherlands**

The Dutch health system underwent a major restructuring process following the Health Insurance Act (2006) (*Zorgverzekeringswet, ZVW*), which made health insurance compulsory for all residents.³⁶ Under the new framework, all residents are entitled to the same comprehensive core basket of health services, which they purchase from private health insurers. The core health basket includes all acute care provided by hospitals, general practitioners and specialists as well as all drug and devices costs. Residents can take out voluntary health insurance to cover additional services.

Health services are generally delivered through private providers in both the ambulatory and hospital sector. Hospitals have traditionally been owned and operated by private not-for-profit organisations. Office-based general practitioners act as gatekeepers to secondary (hospital) care. Insurers purchase services from providers and are free to contract with any hospital individually (selective contracting). However, negotiations of price and quality are regulated, with only a limited number of hospital services subject to price negotiation; these account for about one-third of hospital revenues.

3.5.1 Principles of pharmaceutical pricing

In the Netherlands, the legal basis of setting medicine prices is the 1996 Price of Drugs Act (Wet Geneesmiddelprijzen, WGP).³⁷ It applies to all prescription-only medicines that are dispensed by pharmacies and dispensing doctors. The WGP sets out that the Ministry of Health, Welfare and Sport has to set the maximum wholesale price of all prescription-only medicines. Where manufacturers sell their products to a pharmacy directly, the manufacturer has to restrict the prices to the maximum wholesale price set by the ministry. The government further regulates prices pharmacies may charge through setting of maximum fees.

Maximum wholesale prices are set drawing on external reference pricing (see below). Prices are revised every six months, taking into account changes in the prices of medicines in reference countries and fluctuations in the exchange rates. The maximum prices are published twice a year in the official bulletin. Manufacturers may appeal against decisions on the maximum price of a medicine.

Price setting does not apply to over-the-counter products, with prices set by pharmacies typically following the so-called tax, a list that provides recommended pharmacy retail prices for all available pharmaceutical products on the Dutch market.³⁷

Before 2008, maximum prices only applied to outpatient drugs, but since then a small but increasing number of inpatient drugs is being covered under the Price of Drugs Act.

Low-cost pharmaceutical prices are determined under the preference policy, involving a tendering procedure between manufacturers and health insurers to establish reimbursement prices. Preference policies allow insurers to select the basket of medicines they will provide within a cluster of drugs provided by manufacturers. It is typically used for generics and medicines with a high cost to the insurance. Insurers are not mandated to have preference policies.

3.5.2 How value is determined

The therapeutic value of a medicine is primarily determined by the balance between the intended and unintended effects of the medicine in relation to those of the standard or usual treatment. Other considerations include applicability, experience and ease of use. Effectiveness is determined using intention-to-treat analysis and expressed in natural units, for example life-years gained or quality-adjusted life years (QALYs). Ease of use and comfort may be taken into consideration, as well as applicability or feasibility.

The Health Care Insurance Board's (CVZ's) Pharmaceutical Care Committee (CFH) evaluates therapeutic value, patient benefit, cost-effectiveness and financial impact on the core basket of services, pharmaceutical and health budgets, insurance funds and Dutch society.^{37,38} The Committee also takes into consideration pharmaceutical and/or innovative characteristics, the availability of therapeutic alternatives and social, ethical and other legal criteria. The economic analysis is undertaken from a societal perspective.²¹ The CVZ and CHF evaluation informs the Ministry of Health, Welfare and Sports, which is responsible for the final decision on whether or not a given medicinal product will be reimbursed under the statutory system.

Explicit methods are used to calculate cost-effectiveness, but there is no explicit weighting for the value factors considered such as for severity, unmet need or therapeutic

improvements. Products are not rated on the bases of added value, but if the therapeutic value of the pharmaceutical product is evaluated as too low, it will not be eligible for reimbursement.³⁷ The government may remove certain drugs from the core health services basket where pharmaceutical products are considered ineffective or obsolete, high cost or at risk of inappropriate use.³⁹

3.5.3 External reference pricing

Determining the reference

A maximum wholesale price is set for all prescription-only medicines in the outpatient sector by reference to the average wholesale price of similar medicinal products in Belgium, France, Germany and the United Kingdom.³⁷ ‘Similar’ refers to a product with ‘the same active ingredient, the same strength and the same pharmaceutical form (including generics)’.³⁷

Sources for external reference prices

A maximum price is defined if the product is available in at least two comparator countries. Prices of medicines in these four countries are acquired from the following organisations: the Algemene Pharmaceutische Bond (Belgium), Informationsstelle für Arzneispezialitäten (Germany) and the Société d’Éditions Médico-pharmaceutiques (France); and the Dictionary of Medicines and Devices (United Kingdom).

Application of reference pricing

All prices are reviewed every six months in order to account for price changes in the reference countries as well as fluctuations in exchange rates. External reference prices are applied to all outpatient drugs, including branded and generic drugs, and high-cost medicines and orphans drugs for inpatient care. Only where the price of a pharmaceutical product is lower than the calculated maximum price, no maximum price is set for that pharmaceutical.

Market share

It is not possible to identify a specific market share of drugs covered by external reference pricing. All reimbursed outpatient drugs and some inpatient drugs are covered by external reference pricing, but there are no published data available on the precise figures. External reference pricing is considered very important for new medicines, particularly as a guide for understanding pharmaceutical expenditure, although the Netherlands has also recently begun negotiating prices on a small scale. However, as soon as generic competition becomes available, prices typically fall to a level which makes any reference price irrelevant.

Maximum prices

All price referencing in the Netherlands relates back to setting maximum prices for drugs, which ultimately establish the competitive market in the Netherlands.

3.6 Spain

The Spanish National Health System (Sistema Nacional de Salud, SNS) offers universal coverage for all residents and provides publicly funded and delivered health services, mainly financed through national taxation.⁴⁰ Services are free at the point of use; the only exception is specific non-refundable co-payments for prescription drugs.

National legislation sets out the principles of the SNS, such as the principles of universal coverage (including equal access to care) and of solidarity of public financing. Most funding for publicly financed health care is centrally allocated, through the central tax agency (Agencia Tributaria). Since 2001, regions are permitted to levy additional regional taxes for health care, for example through a regional ‘health cent’ on petrol. However, their contribution to public health care financing is small.

Responsibility for organising publicly funded health care largely rests with the 17 regions (autonomous communities). Regions have their own basic law (Statute of Autonomy), parliaments and governments, and develop regional legislation.

3.6.1 Principles of pharmaceutical pricing

Pharmaceutical policies in Spain (including approval, pricing and reimbursement decisions) are one of the few policy areas which have remained centralised. According to Act 29/2006, the Ministry of Health, Social Services and Equality is responsible for pricing and reimbursement of medicines as defined in articles 89 and 90 of the Act, alongside the Ministry of Economy and Finance and the Ministry of Industry, Tourism and Trade.⁴¹ The Interministerial Pricing Committee (IPC) is responsible for setting maximum ex-factory prices of pharmaceuticals and healthcare products that are to be reimbursed under the SNS.

The main mechanisms to determine the price of medicines include external and internal reference pricing as well as negotiations. Price negotiations apply to new (innovative) medicines while generics and copy-products are subject to statutory pricing:⁴¹

- *External reference pricing* is used for new (innovative) drugs, for which there is no similar comparator on the Spanish market, for example when the medicine covers an unmet medical need or brings a major therapeutic benefit over an existing comparator.
- *Internal reference pricing* is used when there is a similar comparator in the Spanish market. There can be a premium price for the new medicine if the ratio of benefit to risk (incremental added therapeutic value or clinical benefit) of its efficacy or safety improves.
- *Cost-plus pricing* refers to setting the price on the basis of the production costs plus granting a profit margin. This mechanism is not applied as a rule, but the production costs should be provided by the manufacturer on the pricing application form. Cost-plus pricing mechanisms are regulated in RD 271/1990 on medicines pricing regulation.

There is free pricing for medicines included in the list of non-reimbursable medicines. Annual reviews are carried out for medicines with high socio-economic impact. Rebates and discounts are set up as cost-containment measures.

3.6.2 How value is determined

In Spain, the Directorate-General for Pharmacy and Healthcare Products at the Ministry of Health determines the value of new medicines according to:

- severity of disease
- needs of certain groups of patients

- therapeutic and social value; incremental clinical benefit considering cost-effectiveness
- rational pharmaceutical expenditure and budget impact
- availability of alternatives for the treatment of the same disease, at lower cost
- degree of innovation.

These criteria are developed in more detail in the form of an algorithm to inform decisions. Dental drugs are not included in the medicines pricing and reimbursement procedure.

Generic medicines undergo a simplified scheme or process and are priced 40 percent below original costs. They are not assessed by the IPC. However, the scheme or process, and the total number of generic medicines approved, are reviewed in every meeting about new generic medicines being priced and approved for reimbursement. New dosages or different pack sizes do not undergo a total process of value assessment.

3.6.3 External reference pricing

Determining the reference

The price of the medicine in other European Union countries is an important criterion in the price negotiation for innovative medicines for which there is no therapeutic comparator on the Spanish market; examples include orphan medicinal products and other medicines that cover an unmet medical need. The basket of countries considered is not specified, with comparisons typically using the lowest available price in countries of the Eurozone. The price in Spain should also be lower than the lowest price in Eurozone countries if the cost-effectiveness ratio is not favourable and the budget impact is high.

As a rule, innovative medicines with a therapeutic competitor in the Spanish market may receive a percentage price premium. To attain this, they must have evidence-based added therapeutic value regarding an improvement of the benefit–risk relationship, either on efficacy or on safety. If the drug is evaluated as not having demonstrated added value for endpoints, morbidity or other relevant factors, the drug's price is set at the price of the therapeutic comparator available on the market – either daily treatment cost or overall treatment cost. The choice of comparator is preferably based on one used in a head-to-head clinical trial, or one considered as the standard of care using an indirect comparison or meta-analysis in such a case. When a basket of brand names or generics is available, the cheapest product or the average price of different products could be chosen instead.

Notwithstanding the aforementioned paragraph, the price criterion could be the external reference price (the lowest) if the price of competitor is too low and the negotiation for a premium price over this one does not succeed.

Sources for reference prices

Manufacturer information is considered for price data. In some cases, databases from countries as provided by the network of competent authorities on pricing and reimbursement are consulted. A voluntary European database Euripid is also consulted routinely. Fixed prices in Spain are ex-factory prices. For this reason, the information may not be particularly useful when the price of reference is not ex-factory but pharmacy purchasing price (list price) and margins are unknown.

Application of reference pricing

External reference prices in Spain are applied at two stages depending on the type of assessment: the first assessment at market entry and the second assessment at periodic revision. A third assessment is made in some cases. The sources of prices are the same as those used at the first assessment.

External reference pricing is the main tool used for determining the price of patented medicines as well as most innovative medicines without a similar comparator or competitor in the Spanish market. In the case of patented or innovative medicines with a similar comparator or competitor in the Spanish market, the main tool for determining the price is internal reference pricing. Nevertheless, it is sometimes difficult to compare the new drug with the old comparator because of the low price of this one. In these cases, external referencing is also applied. These products are usually new molecules.

Market share

With new molecules, the market share of products using external referencing is approximately 80 percent. Drugs subject to external reference pricing account for approximately 25–40 percent of the market share of the total number of new products (excluding generics).

Maximum prices

There is no absolute maximum fixed price in Spain although there is an indication that maximum fixed prices may be considered in the future as a measure to control costs. Where the price is extremely high, there are some considerations which may be taken into account for deciding on a possible reimbursement amount for a new medicine, including cost-effectiveness analyses and budget impact analyses. Some mechanisms for reimbursement are in place which may be used by the Directorate-General for Pharmacy and Healthcare Products at the Ministry of Health, including:

- inspections and review to certify outpatient medicine compliance
- dispensing limits for certain medicines to outpatients through hospital pharmacy services
- establishing therapeutic algorithms or national guidelines in order to identify patients who achieve maximum benefit from the treatment
- annual review of price and sales.

Currently, the maximum external reference prices used in Spain are among the lowest prices in Europe.

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APPENDICES

Appendix 1 Country questionnaire

An 'on-call' facility for international healthcare comparisons

Pharmaceutical pricing

Pharmaceutical prices differ across high-income countries. They can affect the availability and prices of pharmaceuticals beyond a given country. Countries are using a range of policies to determine pharmaceutical prices with external price referencing, or international price benchmarking, a commonly employed instrument to determine prices of pharmaceuticals considered for reimbursement.

This project seeks to better understand the role of external reference pricing compared with other strategies to influence pharmaceutical pricing in a select set of countries. We here define external reference pricing as 'the practice of using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country'.⁵ We have developed a set of questions to help us assess the more salient features of pharmaceutical pricing strategies used in your country.

For the purposes of this work we distinguish the *price* from the *value* placed on a given drug. While price refers to the monetary amount with which a given drug is exchanged on the market, the term value as used here refers to specific features attributed to a given drug in a particular context, such as its degree of innovation, availability or accessibility, or importance in relation to public health.

In considering these questions, please reflect on the various stakeholders who are directly or indirectly involved in price setting. Where possible and appropriate, please provide relevant references such as (non-) governmental or industry documents or reports, research papers or any other reference you deem important (e.g. news articles).

1. What are the overarching principles of how drug prices are developed in your country?
Examples may include ensuring maximum access to drugs for the population, limit national health spending, etc.

⁵ Folino-Gallo P, Muscolo L, Vogler S, Morak S. PHIS Glossary: Glossary for pharmaceutical policies/systems developed in the Pharmaceutical Health Information System (PHIS) Project. Issued 2009, updated 2010 and 2011.

2. What strategies are used in your country to determine the price of pharmaceuticals and why have these been selected?
Examples may include external reference pricing, internal price referencing, price fixing, free pricing and/or other direct or indirect controls.
3. Who is involved in determining the price of pharmaceuticals in your country?
Please list all stakeholders that are involved, directly or indirectly, in this process. If possible, please provide a flow-chart overviewing the key stakeholders and processes involved.
4. How does your country determine the value of a drug?
Some countries have specific criteria to assess value. Examples may include therapeutic benefit, the degree of innovation, the burden of disease targeted, etc. We would like to understand how this informs decisions on value and thus pricing.
5. How does value differ across types of drugs?
Examples may include separate schemes for general medicines and dental drugs, having unique pricing schemes based on type of drug, etc.
6. How is external reference pricing implemented in your country?
Please provide information on the basket of countries referenced, variations by type of drug, frequency of revisions to the country basket/formula, criteria for application (e.g. new drugs only, drugs without generic option, drugs with alternative options) or any other elements that you consider relevant in this context.
7. Which sources do you use to determine prices used in the countries included in your external reference pricing system?
Source of prices may include companies or national reimbursement authorities; prices may be manufacturer's posted price (ex-factory), pharmacy purchasing price, other; please also describe the process of applying exchange rates, and any other information you consider relevant.
8. Please describe at what stage of market availability external reference prices are applied. How are the prices for those points in other countries obtained?
Examples include at market entry, after market entry or periodic revisions. Please indicate whether the source of prices that are applied (see also question 7) at these different stages differ and how.
9. For which types of products is external reference pricing the main tool used for determining the price?
Examples may include patented/not patented, brand/generics, hospital/ambulatory, most innovative, etc.
10. What is the market share (in %) that is affected by external reference pricing?

Please indicate if the proportion of market share refers to GDP, pharmaceutical spend, healthcare spend or another aspect of the health economy.

11. Is there a maximum price for drugs in your country?

Please describe whether a maximum or fixed price is used at all times or whether it is possible for purchasers or suppliers to get a different price.

12. If maximum prices are used, how these are determined?

Please describe the process by which maximum prices are derived and to what extent this draws on external reference pricing. Please also describe how the maximum price is calculated. Examples may include an average of comparators, median of reference basket, minimum of reference basket, etc.

13. How important a tool is external reference pricing in determining drug prices in your country? Please indicate on a scale of 1 (not used or irrelevant) to 10 (consistent application across a large number of drugs). Please explain your reasoning.