How to Price and to Reimburse Publicly Funded Medicines in Latin America? Lessons Learned from Europe

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Abstract: This paper reviews the main pricing policies in Latin American countries, discussing their shortcomings. It also gives an overview of the most common pricing and reimbursement policies in Europe and describes in detail three well-established approaches — international price referencing, value-based pricing, including setting up of health technology assessment, and generic and biosimilar policies — building on country examples.

Introduction

Pricing and reimbursement of medicines and vaccines are a "hot topic" among policy makers in Latin American countries (LAC), and globally. Partially triggered by the COVID-19 pandemic but more so by the launch of highly specialized medicines with an extremely high price tag which jeopardize the functioning of the whole health care system; examples include gene and cell therapies and further medicines to treat rare and ultra-rare diseases, including cancers. In response, several Latin American countries, such as Chile, Mexico and Peru, are currently discussing draft laws to regulate medicine prices, and in Bolivia, a government committee responsible for medicine pricing was created in 2021.[1]

Traditionally, affordability of medicines was mainly a concern for low- and middle-income countries, but this has changed in the last few years as many high-income countries, including those in Europe, have also reported not being able to pay for new innovations. This has led to national policy reviews as well as to international debates resulting in the adoption of the World Health Assembly resolution WHA72.8 in 2019 on improving the transparency of markets for medicines, vaccines, and other health products.[2] In this article, we take a critical look at how countries in Latin America can move towards regulating pharmaceutical prices and reimbursement by learning from experiences from the European region.

While countries in the Latin American region still struggle with managing a public sector which aims to provide financial protection and universal health coverage for health services including medicines and vaccines,[3] European countries either operate a national health service or a system based on social security contributions or a mix of both, which has made important progress towards universal health coverage. In Latin America many health services including medicines are mostly financed through out-of-pocket expenses,[4] in specific around two thirds of medicine funding come from household incomes.[5] The absence of an operational public system which provides effective, safe and affordable medicines constitutes one of the main challenges with regard to patients' access to medicines.

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In addition to the lack of public funding and provision of medicines, there is limited experience in pricing policies for medicines in Latin American countries, which may be one explanatory factor for the high prices of medicines in Latin America compared to European countries, which leads to higher out of pocket expenses.[6] Huge differences exist between Latin American countries regarding the extent of policy implementation to regulate prices and to reimburse pharmaceuticals; with Brazil and Colombia having the most elaborated systems and having introduced price regulation mechanisms such as external price referencing. Moreover, there are limited experiences, like the ones of Mexico and Chile, in which elements of external price referencing are being used during price negotiations.

The European experience of decades of regulating pharmaceutical prices and assessing medicines as part of their reimbursement decisions is of tremendous value for the Latin American region. Acknowledging that European countries apply a wide variety of different pharmaceutical policies, it is of interest to learn from these policies, both in terms of success factors as well as pitfalls that should be watched out for.

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We will first layout the main pricing and coverage policies in several Latin American countries (Brazil, Chile, Colombia, Ecuador, El Salvador, Nicaragua and Mexico) and discuss their possible shortcomings. This is followed by an overview of the most common pricing and reimbursement policies in Europe, which includes a detailed description of three well-established policies (international price referencing, value-based pricing including setting up of health technology assessment, and generic and biosimilar policies) by giving country examples. The intention of this paper is to inform about different policy options that may be considered for possible follow-up, but it will not give any recommendations for any specific policy and policy design, since it is acknowledged that even if a policy which was effective in one country cannot be easily transferred to another country's context but requires considering country-specific factors.

Methods

The article includes information on relevant pricing and reimbursement policies in Latin American and European countries. The selection of countries from Latin America was based on the decision to discuss countries with the most elaborated pharmaceutical pricing systems as well as countries that provide good practice examples. For Europe, we offer specific overview information on 20 large and middle-size countries; apart from the United Kingdom, all of them are either European Union (EU) Member States or members of the European Free Trade Association (EFTA).

While for the included Latin American countries the overall pricing policy environment is presented, for Europe only a few pharmaceutical policies were selected for in-depth description. The selection of those pharmaceutical policies in the European context was based on recommendations given in the 2020 WHO guideline on country pharmaceutical pricing policies.[7] The recommendations were developed based on a systematic literature review with a ranking of evidence and therefore provide a strong evidence base for this article. An additional key reference for selecting reimbursement policies was the 2022 report published by WHO Europe "Payer policies to support innovation and access to medicines in the WHO region."[8] The final decision of selected policies was guided by comments made in the review process.

To extract policy information from Latin America as well as from Europe, we performed a pragmatic literature search in PubMed as well as in grey literature including from websites of relevant national organizations. The literature search was undertaken in December 2022. The majority of information on the European context was derived from unpublished data, in particular the PPRI indicators[9] (yet unpub-

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lished at the time of drafting of this paper), provided by the Pharmaceutical Pricing and Reimbursement Information (PPRI) Network, a network of competent authorities of 50 countries, mainly in the European region.[10]

Results

Pricing Policies in Latin American Countries

Most Latin American countries (LAC) have not yet well-established pharmaceutical pricing policies. Moreover, in countries where those have been implemented, such as Brazil and Colombia, descriptive and analytic evidence on the impact of these policies is scarce.[11] According to anecdotal reports, it resulted in higher prices of medicines in LAC compared to Europe.[12]

Box 1

Demanding Access to Medicines through Judicialization

Judicialization is understood as the use of right-based litigation to demand access to medicines and medical treatment.[13] According to available data, in no other region of the world is judicialization of health care more widespread than in Latin America.[14] In this regard, Brazil and Colombia are the main exponents, with a growing trend in Chile, Costa Rica and Argentina.[15]

The judicialization of health care in Latin America has two characteristics. First, lawsuits are brought individually rather than collectively. Secondly, judicialization appears to mainly relates to high-cost medicines, i.e., it is a highly "pharmaceuticalized" judicialization.[16] However, some authors emphasize that judicialization would not be homogeneous across Latin America and would also target health interventions that were eligible for reimbursement and procurement but are not available to patients in practice.[17]

Judicialization has become an alternative pathway for the population to gain access to medicines outside the health system's prioritization mechanisms, as favorable court rulings can be achieved rather easily. In addition, some structural factors favour judicialization, such as political and regulatory dysfunctions, lack of or insufficient health coverage, limitations or inequalities in access to health care, and fragmentation of health systems.[18] Judicial intervention in health policies has a budgetary impact that can affect the financial sustainability of health systems. It also has consequences associated with low governance and effects in terms of inefficiency and inequity for the coverage decision system.[19]

Brazil

Brazil, a country with a National Health Service, is one of the first countries that developed price regulation in the region; the price regulation was first established in 2003 as a response to the rising medicine prices. One of the characteristics that distinguishes Brazil from other LA countries is that it is an important medicine producer and there is an industrial development policy for the sector led by the Science, Technology and Innovation Ministry and the Health Ministry.[20]

In Brazil, for a drug to be marketed, it must be authorized by the National Health Surveillance Agency (ANVISA) and have a maximum price set by the Drug Market Regulation Chamber (CMED).[21] CMED is an interministerial organization in charge of price regulation. The price types that are regulated are the ex-factory price, the maximum price for sale to the government and the maximum price to the consumer.[22] There are three stages in the price-setting process: 1) authorization of the maximum price, where CMED determines the price cap for the Brazilian market; 2) inclusion into the public coverage system, where a new price is set (not higher than the price cap); and 3) price negotiation in the public and private markets.[23] For this purpose, a hybrid approach is used that considers elements of health technology assessment (HTA) and the following pricing tools: price cap, value-added tax exemption, mandatory discounting in public procurement and mark-up regulation.[24] (Table 1) One of the distinctive features of the Brazilian case is that the regulatory mechanism depends on the additional therapeutic value of the new drug in relation to existing alternatives and the patent status. The additional therapeutic value analysis is based on HTA information provided by the manufacturer and on evaluations performed by the CMED Secretariat.[25]

Colombia

In the 2000s Colombia access was ensured to new medicines mainly through judicialization (Box 1), which however resulted in the need to contain health spending. To contain spending a series of policies were implemented including pricing of medicines, promoting their appropriate use and the introduction of health technology assessment.[26] Between 2010 and 2012, a maximum recovery value scheme was established, which consisted of maximum reimbursement values paid by governments to insurers for medications that were not part of the mandatory plan. These maximum values were calculated as 80% of the average wholesale market price. Subsequently, in 2013, a pricing regulation system based on external reference

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prices was established, regulating medicines covered and not covered by the mandatory plan.[27]

The agency in charge of price regulation in Colombia is the National Commission on Drug and Medical Device Prices. It is worth mentioning that there are three types of market authorization for medicines: supervised freedom, regulated freedom and direct price control. Only in the case of drugs classified as directly controlled, markets with high concentration or high financial impact, prices are set at the wholesale level.[28] The pricing methodology has three stages: definition of the relevant market, measurement of its degree of concentration and establishment of an external reference price.[29] (Table 1). In addition, the Drug Price Information System (SISMED) was implemented, which has been key to the operation of price regulation.

Between 2013 and 2020, 2,513 commercial presentations have been regulated.[30] Among the results of price regulation in Colombia, it is estimated that its introduction implied a drop in the prices of regulated medicines of 44% between 2012 and 2015.[31] However, there was also evidence of a significant increase in real spending on medicines in Colombia post implementation, which is explained by an increase in non-regulated prices or portfolio effect and an increase in the quantities sold.[32] In addition, the non-regulation of the margin of pharmacies is criticized, since consumer prices are already on average 23% higher than those set by the maximum selling price at the wholesale point.[33]

Ecuador

In 2014, a price regulation mechanism based on external price referencing was introduced, replacing pricing based on production costs.[34] Three pricing regimes are considered for medicines: regulated regime (new and essential medicines), controlled regime (non-strategic medicines, without price setting) and direct price setting regime (exceptional for sanctioning non-compliance with regulated regime or emergency situations).[35] (Table 1) According to Ecuadorian legislation, essential medicines are defined as those that belong to the Basic Drugs National Frame (similar to National Essential Medicine List). In the 11th revision of this document there are 484 active ingredients registered corresponding to 672 pharmaceutical forms.[36]

In December 2022, there were 1,539 commercial presentations with ceiling price in the regulated regime. However, no impact evaluations of this pricing policy were found.

El Salvador

In 2012 a drug pricing mechanism was established under the responsibility of the National Directorate of Medicines. It regulates the maximum retail price of prescription drugs using external price referencing for originator and a price linked to the originator in the case of generics.[37] (Table 1) The calculation methodology requires a high disaggregation of price information and marketing margins in the reference countries and also a detailed analysis of such information by the National Directorate of Medicines, since prescription drugs were divided into 2,000 homogeneous groups (7,000 pharmaceutical products).[38] After the regulation had been implemented (2013), there was a 36.4% drop in prescription drug prices, maintaining the price over time.[39]

Mexico

In 2005, a maximum retail price was established for patented drugs in which manufacturers participate voluntarily. However, this mechanism presents problems due to its voluntary nature and lack of sanctions for non-compliance, which has led to reforms of the system.[40] External price referencing is used to determine the maximum price (Table 1). However, this mechanism is considered ineffective due to its voluntary nature and lack of sanctions for non-compliance.[41]

Finally, it is worth mentioning the use of price regulation instruments in negotiation experiences in Mexico and Chile for public purchases. In Mexico, between 2008 and 2018 the Coordinating Commission for the Negotiation of Prices of Medicines and Inputs used price information from external markets in its negotiations with the industry.[42] In this regard, a decrease in prices between 40% and 85% is was between 2010 and 2016 for originator cancer medicines in the Mexican public sector with the establishment of the negotiating commission (without attributing direct causality).[43] In Chile, the Financial Protection System for High-Cost Diagnostics and Treatments established in 2015 implemented a pricing mechanism for public purchases of high-cost health technologies included in this regime.[44] This maximum price for government purchases, called Maximum Industrial Price, considers negotiation elements and external and internal reference pricing (Table 1). It is estimated that there is an average 12% decrease in the prices of public purchases of medicines as a result of the operation of this cap price.[45]

Table 1 gives a comprehensive overview of pricing policies in Latin American countries.

Pricing Policies in Europe

There is a variety of pharmaceutical pricing and reimbursement policies which European policy-makers apply, aligned to the particularities of the medicines

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Table 1

Description of Medicine Pricing Policies in Latin American Countries

Country - Year of implementation of current policy	Responsible	Controlled Price Type	Scope of Price Control	Regulatory Details
Brazil - 2003	Drug Market Regulation Chamber (CMED) The CMED is made up of representatives of the Ministries of Health, Justice, Economy and the Chief of Staff.	Ex-factory, Maximum consumer price and maximum government procurement price.	New medicines (innovators, generics and new formulations or API combinations)	• A drug has additional therapeutic value if it has: a) greater efficacy relative to existing drugs for the same therapeutic indication; b) same efficacy with a significant reduction in adverse effects; c) same efficacy with a significant reduction in the overall cost of treatment. • In the case of new drugs with additional therapeutic value, the external reference pricing mechanism (lowest price in a basket of countries) is used to determine the ex-factory price cap. • The basket of countries considered is Australia, Canada, France, Greece, Italy, New Zealand, Portugal, Spain, United States of America and the manufacturer's country of origin. • If there is no therapeutic gain, the price of the medicine will be the lower of the internal reference price (costs of existing drugs for the same condition) and external reference pricing. • For generic drugs the entry price should be 65% of the reference price. • There is an annual price adjustment mechanism that considers inflation and productivity factors. • CMED negotiates with manufacturers a mark-up that is applied to the ex-factory price in order to have maximum consumer prices. On the other hand, in certain government purchases (high-cost drugs and judicializations) there is a mandatory discount on the ex-factory price called Price Adequacy Coefficient, which in 2020 was 21.53%.

Source: Brazil: Ivama-Brummell, et al. (2022), *infra* note 21; Luiza, et al., *infra* note 20; Salha et al., *infra* note 15.
Colombia: Espín Balbino, *infra* note 11; Prada, et al., *infra* note 27.
Ecuador: Durán, Lucio, and Rovira, *infra* note 35; R. Correa Delgado, "Reglamento Para La Fijación de Precios de Medicamentos de Uso y Consumo Humano (Decreto No. 400)," n.d., *available at* <https://www.controlsanitario.gob.ec/wp-content/uploads/downloads/2014/09/D-0400-Reglamento-para-la-Fijaci%C3%B3n-de-Precios-de-Medicamentos-de-Uso-y-Consumo-Humano.pdf> (last visited July 28, 2023).
El Salvador: Rivera, *infra* note 37.
Nicaragua: Reglamento de la Ley N 842. Ley de protección de los derechos de las personas y consumidores, (2013), *available at* <http://legislacion.asamblea.gob.ni/normaweb.nsf/b34f77cd9d23625e06257265005d21fa/bd325486f010cc8206257c24007776d8?OpenDocument> (last visited October 18, 2023)
Chile: Poblete, *infra* note 44.

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Table 1 (continued)

Description of Medicine Pricing Policies in Latin American Countries

Country - Year of implementation of current policy	Responsible	Controlled Price Type	Scope of Price Control	Regulatory Details
Colombia - 2013	Medicines and Medical Devices Pricing Commission — Tripartite entity composed of a delegate of the Presidency of the Republic of Colombia, the Minister of Commerce, Industry and Tourism and the Minister of Health and Social Protection.	Wholesale price	• Medicines included in the direct control regime (innovators or generics). • The requirements to consider a drug in a direct control regime are: i) high health or financial impact and ii) high market concentration (less than three suppliers or a Herfindahl-Hirschman Index (HHI) greater than 2,500).	• A relevant market is understood as a set of competing drugs for which there is therapeutic and economic substitution. • External reference price corresponds to the 25th percentile in the basket of reference countries. The external reference countries are Argentina, Brazil, Chile, Ecuador, Mexico, Panama, Peru, Uruguay, Spain, United States, United Kingdom, Australia, Canada, France, Norway, Germany and Portugal. • The internal reference price corresponds to the sales weighted price of pharmaceutical products in the relevant market. • If the internal reference price is higher than the external reference price then prices are regulated using the latter. • The dispensing margin for the institutional market is regulated and varies between 3.5% and 7% depending on the quantity. Thus, the price of drugs through the institutional channel is fully regulated. • A distribution margin of 7% over the ex-factory price is suggested.
Ecuador - 2014	The National Council for Fixation and Revision of Medicines Prices. The council is comprised of the Minister of Public Health, the Minister of Industry and Productivity, the Coordinating Minister of Social Development and the Coordinating Minister of Production, Employment and Competitiveness.	Maximum consumer price	• Medicines included in the regulated regime (innovators or generics). • New and strategic medicines belong to the Regulated Regime. • Strategic medicines are those belonging to the National List of Basic Medicines, medicines for collective health strategies and rare diseases or where there is a lack of competition.	• For new medicines classified as having additional therapeutic benefits, the maximum consumer price is set as the average of the three lowest prices in the basket of reference countries. • The reference basket considers mainly MERCOSUR and ALBA countries. Other countries may be considered if deemed relevant. • In the case of new drugs without therapeutic advantages, a pharmacoeconomic analysis is performed taking into account the existing alternatives to set the cap price. • In the case of strategic medicines (already registered), the cap price is equivalent to the median of the private market retail prices of the medicines participating in the corresponding segment, excluding those prices that are considered atypical.

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Table 1 (continued)

Description of Medicine Pricing Policies in Latin American Countries

Country - Year of implementation of current policy	Responsible	Controlled Price Type	Scope of Price Control	Regulatory Details
El Salvador	National Directorate of Medicines	Maximum consumer price	Prescription only medicines (innovators and generics)	• To determine the maximum consumer price of medicines, homogeneous groups are established, for which an External Reference Price and an average price in Central America are determined. The lower of the two is the maximum consumer price. • A homogeneous group are pharmaceutical products that have the same active ingredient, strength and dosage form. • External Reference Pricing: simple average price of the harmonic average prices of each country for a homogeneous group. The reference countries are from Latin America (excluding Central America and Panama). In addition, a marketing margin is estimated for a sample of countries. • Average price in Central America (including Panama). Simple average price of prices per country, for each homogeneous group. • Generic prices should be between 30% to 40% of the innovator price.
Nicaragua - 2013	Department of Medicines Price Regulation (Ministry of Promotion, Industry and Trade)	Maximum consumer price	New drugs and new presentations must apply for price authorization.	Pricing takes into account the commercial characteristics and the situation of the domestic and Central American markets. No further details on the methodology.
Chile - 2015	Department of Health Technology Assessment – Ministry of Health	Government maximum purchase price (only for High-Cost Financial Protection System)	Health technologies included in the High-Cost Financial Protection System	The maximum price is the lowest price between: (a) Internal reference price. Price of purchases made by the public sector for the same drug in the previous year. (b) External reference price. The lowest price of the purchases made by the public sector in Argentina, Brazil, Colombia, Mexico and Peru. c) Offer made by the laboratory to include the drug in the High-Cost Financial Protection System.
Mexico - 2005	Mexican Ministry of Economy	Maximum consumer price	Patent medicines	Agreement between the Ministry of Economy and the pharmaceutical industry to set a maximum sales price for patented drugs. Participation in this agreement is voluntary. This maximum price cannot exceed an international reference price that considers the average of ex-factory prices of 6 top-selling countries, plus a marketing factor.

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(e.g., specific policies for monopoly medicines and policies for medicines with comparators). As shown in Table 2, some policies are quite common. However, even for policies that are frequently used, the methodological design chosen for implementation can vary across countries. Some of the policies are not mutually exclusive and, in practice, are used in combination for the decision on the price and reimbursement of a medicine.

European countries tend to have a comprehensive reimbursement system to ensure Universal Health Coverage, and an important share of cost-effective medicines are included in a reimbursement list (formulary).[46] The expenses of these medicines are then largely covered by public payers, such as social insurance funds or a national health service; some co-payments such as a fixed prescription fee or a percentage co-payment of the price of a medicine may apply;[47] medicines used in hospitals are fully covered. Most European countries apply price regulation for those medicines which are included in the reimbursement lists, to contain their costs. A few countries (e.g., Belgium, the Netherlands) regulate the prices of all medicines, even those fully paid by the patients to avoid financial burden for the households.[48] Most European countries apply external pricing referencing; this policy is mainly used for new medicines. External price referencing (EPR) is frequently supplemented by a Health Technology Assessment (HTA) to determine the added therapeutic benefits and inform the pricing decision. For medicines with very high price tags, building on information gained through the international price comparison and the HTA, prices are eventually negotiated between the public payers and the companies. For generic and biosimilar medicines, different pricing policies are applied, such as price links, supplemented by demand-side measures.

In the following, EPR, HTA and generic policies as three commonly applied pricing and reimbursement policies are described and discussed.

It should be acknowledged that each European country takes its own decision on how to price and reimburse a medicine. This is also the case for the 27 European Union (EU) member states (such as Germany, France, Italy, Spain, Greece, and Poland), even if the EU countries apply a harmonised procedure for granting marketing authorisation. However, given the challenges to ensure equitable and affordable access in light of new medicines with extremely high price tags, some European countries have started collaborating on policies such as HTA, procurement, or price negotiations to improve the knowledge base and increase the negotiation power.[49]

External Price Referencing

External price referencing (EPR) is applied by 26 EU member states (all but Sweden) and several further European countries, usually for any new medicine.[50] EPR is a typical starting pricing policy. The underlying principle to consider the price information of the same medicine in other countries can be implemented in different variants, as for this pricing policy different methodological approaches, e.g., on the country basket, the calculation of the benchmark price and approaches on how to deal with missing data, can be taken[51] (see Box 2 for the example of a country, which defined several EPR parameters). Studies have highlighted how the design of the EPR methodology can importantly impact the outcomes.[52]

While EPR is a rather technical pricing policy, compared to more priority-based policies such as value-based pricing, it has been wrongfully labelled by some as a simple policy. It requires substantial capacity to correctly conduct the price data collection and comparison. Easy access to price information is needed; however, it is important to understand the context of the price information in databases and to interpret it in a correct manner, based on comprehensive knowledge of the respective pharmaceutical system. Careful selection of suitable price databases is thus key.[53] In this respect, several European countries benefit from the European price database EURIPID for reimbursed medicines.[54] Overall, however, benchmark prices in EPR are misleading and result in overpaying by public purchasers, since for high-cost medicines discounts tend to be negotiated, but the discounted prices remain confidential.

While EPR is a national policy, it has major spillover effects across borders, which have been observed in Europe with its wide-spread use of EPR: This pricing policy incentivizes pharmaceutical companies to first launch in countries with high (list) prices (e.g., Germany, Austria), and to delay the market entry of the medicine in lower-priced countries (e.g., Greece, Portugal and Eastern European countries), by months and even years.[55]

EPR has been criticized for not taking into account the potential value of a medicine. A value-oriented approach is pursued through value-based pricing (VBP). Despite being positioned as an important policy for new medicines, VBP lacks an internationally agreed definition.[56] Broadly speaking, VBP implies consideration of the value of a medicine when an authority or payer decides on its price and funding.[57] In particular, it concerns the added (therapeutic) value of the product compared to comparators which is rele-

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Table 2

Overview on Pricing and Reimbursement Policies in European Countries 2022

Countries	EPR	VBP	Generic price link	Biosimilar price link	Reimburse-ment list(s)	RPS	INN prescribing	Generic substitution	Biosimilar substitution
Austria	Yes	Use of VBP elements	Yes	Yes	Yes	No	No	No	No
Belgium	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Czech Republic	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Denmark	Yes	Use of VBP elements	No	No	Yes	Yes	No	Yes	No
Finland	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
France	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	Under implementation
Germany	Yes	Use of VBP elements	No	No	Yes	Yes	Yes	Yes	Under implementation
Greece	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Hungary	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	Yes, for selected biologicals
Ireland	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Italy	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Netherlands	Yes	Use of VBP elements	No	No	Yes	Yes	Yes	Yes	Yes
Norway	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Poland	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Portugal	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Slovakia	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Spain	Yes	Use of VBP elements	Yes	Yes	Yes	Yes	Yes	Yes	No
Sweden	No	Yes, fully-fledged VBP	No	No	Yes	No	No	Yes	No
Switzerland	Yes	Use of VBP elements	Yes	Yes	Yes	No	Yes	Yes	No
United Kingdom	No	Use of VBP elements	No	No	Yes	No	Yes	No	No

Abbreviations: EPR: external price referencing, INN: international non-proprietary name, RPS: reference price system, VBP: value based pricing
Note that the scope of the policies listed is usually limited to defined medicines, e.g., to new medicines in the case of EPR and VBP, to medicines with (generic) competitors for RPS and the generic and biosimilar policies.
Source: "PPRI Indicators" 2023

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vant in pricing and reimbursement decisions whereas therapeutic benefits against placebo to demonstrate effectiveness are considered sufficient for the preceding regulatory decision on marketing authorisation.

Health Technology Assessment

The value assessment is usually supported by a Health Technology Assessment (HTA), which is not a policy per se, but a tool to inform decision-making. In an HTA, different dimensions may be assessed, including clinical effectiveness, safety, costs and economic implications, ethical, social, cultural and legal issues, and organizational and environmental aspects, as well as wider implications for the patient, carers and the population.[63]

Use of HTA for pricing and reimbursement decisions (e.g., systematic use vs. consideration of some components), as well as the type (full HTA vs. rapid assessment) and the methodology vary.[64] This is also linked to the high level of resources and capacity required for conducting an HTA, in particular a full HTA, and lower-resourced countries in Europe have been struggling with installing HTA on a more systematic basis. To address this challenge, European countries have been collaborating on HTA methodologies. This has resulted in the adoption of the 2021 EU Regulation on HTA,[65] which defines the future processes of collaboration on HTA in the EU (see Box 2 for developments on HTA in Europe).

All pricing policies have benefits and limitations, and the limitations of EPR and VBP have become evident when prices for new medicines with high price tags and poor data, such as advanced therapy medicinal products (ATMPs) or other anti-cancer medicines, were to be determined.[66] There is lack of data: price information is missing from those reference countries in which the medicine has not yet been marketed, and uncertainty around clinical performance hinders decision-makers to properly determine the value. Should data be available, an EPR-based benchmark price is likely not affordable for public payers who are the ones to purchase such medicines in European countries. Furthermore, a medicine may be cost-effective following an HTA but still not affordable.

Generic and Biosimilar Policies

European countries have had a long-term experience in pricing, reimbursement and demand-side measures for generic medicines. The policy mix applied is based on the rationale that enhancing use of these medicines through a variety of policy measures contributes to equitable access to high-quality and affordable medi-

Box 2

External Price Referencing in Austria – Methodological Parameters of This Pricing Policy

Since 2004, Austria has been applying an EPR system for new medicines that are reimbursed for outpatient use, and since a legal change in 2017, also, however retrospectively, for those medicines used in hospitals whose sales with social health insurance exceeded an annual threshold of € 750,000.[58] This additional regulation was introduced because pharmaceutical companies of some high-cost medicines tended to use the loophole of an unregulated access to hospitals, where neither EPR nor any other price regulation is applied but the medicines are procured by the hospitals or hospital groups. Austrian prices of high-cost medicines used in hospitals are frequently the highest ones across European countries whereas prices for these medicines in the outpatient sector are in the median and in the upper middle in Europe.[59]

The Austrian EPR basket is a large one, Austria refers to all other 26 EU member states. The benchmark price must not exceed the EU average. The relevant price type considered is the ex-factory price reduced by the statutory manufacturer discount, where applicable. As such, Austria is one of the few countries which considers statutory discounts, i.e., those discounts that are officially published by payers. In case of countries which do not regulate and thus do not publish ex-factory prices (e.g., some Nordic countries), average wholesale margins are used to derive the ex-factory prices. The size of the statutory manufacturer discounts and of the average wholesale margins in the reference countries are reviewed on an annual basis, and they are published on the website of the Austrian Ministry of Health.[60]

Price information is provided by the company as part of the price application. According to Austrian Social Insurance Law, the authority can ask the Austrian National Public Health Institute to review the price data submitted by the company.[61] The institute maintains a pharmaceutical price information service to meet this legal assignment. A price is determined within six months upon receipt of a company's price application. A minimum of price data of two EU member states is required to determine the reference price. Price evaluations are mandatory 18 months after the first time a price was set and 24 months after the second time a price was set; another re-evaluation is possible 18 months after the third time a price was set.[62]

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Box 3

Developments in Health Technology Assessment in Europe

Variation in the use of HTA as part of pricing and reimbursement processes is largely attributable to the resources required. Leading European countries with systematic use of HTA and well-elaborated processes are England, Germany and France.

To support smaller and less-resourced countries, European countries have been collaborating on HTA for nearly two decades. This was done in the framework of the EUnetHTA collaboration of EU member states, with the financial support of the European Commission. EUnetHTA particularly worked on strengthening methodological tools.

To ensure sustainability of this collaboration and to enhance the link between HTA and decision-making, the European Commission published a proposal for a regulation of HTA. The EU Regulation on HTA[67] was adopted after three years of negotiations. It entered into force in January 2022, with a transition period of three years. According to the new legislation, HTA bodies of the EU member states will conduct Joint Clinical Assessments of selected new medicines and high-risk medical devices, thus focusing on the relative clinical effectiveness and relative clinical safety of a new health technology as compared with existing technologies. However, for non-clinical aspects, such as economic, social, ethical and organisational aspects as well as pricing and reimbursement, EU member states will continue to be responsible to conduct their own assessment. With the date of application of the EU legislation in January 2025, cancer medicines will be the first therapeutic group to be subject to joint assessments, followed by assessments for orphan medicines three years later and for all medicines with a centralised marketing authorisation in 2030.[68]

cines by easing the financial burden for patients as well as for the public systems (which tend to pay, at least, partially for most off-patent medicines). Globally, the EU is a leading region with regards to the marketing authorization of biosimilar medicines,[69] and making use of the efficiency gains through biosimilars is an opportunity for European countries to improve access to biologicals.

A key prerequisite for successful implementation of generic and biosimilar policies is quality assurance of these medicines,[70] and this is guaranteed through a strong regulatory framework in Europe (biosimilar medicines are centrally authorized by the European Medicines Agency (EMA). Similarly important, health professionals, who prescribe (doctors) and dispense (pharmacists), and patients must have trust into the quality and equivalence of these medicines.[71] To foster this trust, many European countries have been working on capacity-building and awareness-rising campaigns targeted at health professionals and patients. These interventions are supplemented by supportive demand-side measures such as asking doctors to prescribe by the International Non-Proprietary Name (INN) and encouraging pharmacists to dispense the generic instead of the originator, or simply to dispense the lowest-priced medicine out of a group of interchangeable medicines. Most European countries apply prescribing by INN and generic substitution, or at least one of these two policies (Table 2). Usually, these policies have been introduced on a voluntary basis, but some European countries implemented mandatory INN prescribing or mandatory generic substitution. Furthermore, patients in several European countries are incentivized to use lower-priced equivalent generics instead of the originator through the reimbursement policy of a reference price system: for a group of interchangeable medicines a defined price (e.g., the price of the lowest-priced medicine) is funded by the public payers, and should the patient insist on a higher-priced medicine of that group (e.g., a branded generic or the originator), it is only possible against patient payment of the price difference.[72]

Given long-term experience in policies for promoting the use of generics, European countries could build on some lessons learned when biosimilars came into the market. For instance, as shown in Table 2, many European countries that apply a so-called generic price link policy (i.e., setting the price of a generic in relation to the prices of an originator, e.g., at a certain percentage lower than the brand price), also use this policy for biosimilar medicines. The mandated price reductions for the biosimilar medicines are usually lower than for generics.[73] Other countries which do not use the generic and biosimilar price links rather opt for more competitive pricing and procurement mechanisms, such as tendering. For instance, through centralized tenders, Norway achieved price reductions of more than 40% for biosimilars which quickly gained market shares and replaced the biological originator.[74]

Still, in Europe generic policies are more advanced than biosimilar policies.[75] While, for instance, generic substitution, is a standard policy in European coun-

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tries, biosimilar substitution is not yet similarly widespread, though it has been implemented by an increasing number of countries over the years. Despite lack of automatic substitution for biologicals, there are still some other options to explore, in particular through intensive communication with health professionals. Box 4 presents a case study from Denmark reporting on a successful change to a biosimilar.

Discussion

When comparing medicine pricing and reimbursement policies across different regions and countries, caution has to be given to region-/country-specific contexts which might be the reasons for why certain policies are more successful than others.[77] Against this background, several distinct features of medicine pricing systems in LAC can be summarized:

Box 4

Effective Managed Introduction of a Biosimilar in Denmark

Adalimumab originator (Humira®) was a medicine that attributed to a large share of public expenditure, and so patent expiry was eagerly awaited. Denmark used the time to carefully prepare a swift switch from the biological originator to the biosimilar.

In Denmark, adalimumab is provided in public outpatient clinics, and it is bought through national tenders by the centralised hospital procurer Amgros. After patent expiry in October 2018, a tendering process was conducted and three biosimilars were awarded. The biosimilar suppliers were encouraged to deliver as soon as possible. The Danish Medicines Council changed the treatment recommendations to adalimumab biosimilars for all indications following patent expiry. In advent of the expiry, clinical staff was addressed to motivate them to start using the biosimilars as soon as they would be available. A taskforce was established and helped prepare information material for patients and engaged in dialogue with patient organisations.

These activities, including encouraging doctors to switch to biosimilar adalimumab, were important since Danish legislation did not provide for biosimilar substitution. But the preparations, including extensive communication work, proved successful as biosimilars gained a market share of 95% within just six weeks. With biosimilar prices of less than one-fifth of the originator price, Denmark succeeded in gaining savings of 1 million Danish krona (around 150.000 USD) per day, while the total number of patients treated increased.[76]

First, pricing and reimbursement decisions are taken independently from each other in most LACs. This is partially due to health system and institutional structures such as the integration of pricing decisions as part of the marketing authorization process (Brazil) or pricing as part of national public purchases (Chile). While in Europe pricing and reimbursement are also often performed by different institutions, processes are interlinked working towards the goal of providing affordable and accessible publicly funded medicines.

Second, reimbursement decisions are not fully structured in Latin America and health systems are fragmented.[78] In addition, HTA processes and institutions are recent, as in the case of Brazil (CONETEC) and Colombia (IETS).[79] In this sense, Brazil and Ecuador use HTA elements in their pricing, such as whether or not a new drug has additional therapeutic value in relation to existing alternatives. In other words, this is a good starting point with basic HTA elements, but it does not take into account other instruments such as cost-effectiveness studies or budgetary impacts when setting prices.

Third, a distinctive feature of the Latin American reality is the low effective coverage of medicines in health plans, which is reflected in high out-of-pocket spending by households to finance medicines.[80] In practice, this implies that in most cases the price to be regulated is the price sold in pharmacies (Brazil, Ecuador, El Salvador and Nicaragua). The above, with the aim of reducing out-of-pocket spending by means of price fixing. This is a distinctive feature with respect to experiences in developed countries where pricing is linked to the reimbursement decision, as the public payers in those countries cover most of the expenses and thus have the responsibility to secure the overall sustainability of the solidarity-based health care system.

Fourth, a great heterogeneity regarding pricing policies exists in LAC. For example, Brazil uses considerations related to the therapeutic value of drugs, while Colombia places greater emphasis on the concentration and degree of market competition to intervene. Among the similarities is the fact that both countries use instruments related to external and internal reference prices. Another fact, which had already been pointed out by other authors, is that price regulation mechanisms undergo frequent modifications.[81] In fact, in Colombia, a series of modifications to the drug price regulation methodology established in 2013 are currently under consultation.

Taking a closer look at the pricing policies highlighted in the European section, it becomes apparent that implementing pricing policies such as external

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price referencing and HTA requires a lot of upfront investment to set-up the structures as well as continuous resources and knowledge to maintain such systems. But despite these challenges, reported pricing policies used for new medicines in European countries could still be a pathway for LAC, taking into consideration learnings from Europe. In particular, LAC should carefully prepare their implementation by taking into consideration implications of different methodological designs, invest in capacity-building and establish monitoring structures which allow evaluation as a basis for possible adaption.

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In addition, in an important step forward LAC could implement policies that strengthen the uptake of generics and biosimilars such as reference price systems and other demand-side measures such as INN-prescribing. As recommended by the 2020 WHO pricing guidelines and shown by other country examples, investing in generics and biosimilars is a proven way to help carve out money to fund innovations.[82] For example, a review of regulatory pathways and quality of the evidence required for biosimilar approval in Latin American countries highlighted important differences between countries and discrepancies between regulation and practice.[83]

While the Latin American region has many years of experience of collaborating on issues like vaccine procurement through the PAHO Revolving Fund[84] or on health system strengthening issues through the Council of Ministers of Health of Central America and the Dominican Republic (COMISCA),[85] the region could benefit from establishing cross-country pricing and reimbursement collaborations of national authorities. This could either take the form of information sharing amongst public authorities, like the Pharmaceutical Pricing and Reimbursement Information Network (9) or the European Network for Health Technology Assessment (EUnetHTA).[86] The existing collaboration structures could be expanded e.g. beyond immunization and could aim at establishing joint pricing processes such as pooled procurement including performing joint HTAs, price negotiations within pooled procurement for high cost medicines. In Europe, a few similar cross-country collaborations have been established such as the Nordic Pharmaceutical Forum or the Baltic Procurement Initiative.[87]

Conclusions

In conclusion, sparked by the COVID-19 pandemic and the launch of high-priced medicines, many countries in the Latin American region are in the process of establishing pricing and reimbursement bodies within the Ministry of Health or the national marketing authorization agency. This is an exciting time to be thinking of which pharmaceutical policies might be the right fit for the region. For this, we looked at experiences from European countries with their strong reimbursement systems which aim to protect patients from financial hardship. A major learning from the European region is the value of a mix of policies including pricing, reimbursement and demand-side measures and different policies for different types of medicines. In particular, it was shown that policies that boost the use of generic and biosimilar medicines is of key importance. In addition, the European experience of collaboration across countries on different policies and different kind of medicines highlights the value of collaboration and suggests potential of the

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development of cross-country collaborations beyond vaccines.

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References
1. Senado, "Proyecto de Ley: Modifica El Código Sanitario Para Regular Los Medicamentos Bioequivalentes Genéricos y Evitar La Integración Vertical de Laboratorios y Farmacias," 2015, *available at* <https://www.senado.cl/appsenado/templates/tramitacion/index.php?boletin_ini=9914-11> (last visited July 26, 2023); "Proyecto de Ley 5311," 2020, *available at* <https://leyes.congreso.gob.pe/Documentos/2016_2021/Proyectos_de_Ley_y_de_Resoluciones_Legislativas/PL05311-20200521.pdf> (last visited July 26, 2023); Decreto supremo N° 4452, "Estado Plurinacional de Bolivia," 2020, *available at* <https://www.agemed.gob.bo/resoluciones/DS_4452_2021.pdf> (last visited July 26, 2023).
2. WHA72.8 - Improving the Transparency of Markets for Medicines, Vaccines, and Other Health Products," n.d. World Health Assembly, *available at* <https://www.who.int/publications/m/item/wha72.8> (last visited July 26, 2023).
3. R.E. Gilardino, P. Valanzasca, and S.B. Rifkin, "Has Latin America Achieved Universal Health Coverage Yet? Lessons from Four Countries," *Archives of Public Health = Archives Belges de Sante Publique* 80, no. 1 (2022).
4. A. Wagstaff, P. Eozenou, and M. Smitz, "Out-of-Pocket Expenditures on Health: A Global Stocktake," *The World Bank Research Observer* 35, 1no. 2 (2022): 123–57; C. Cid, G. Flores, A. Del Riego, and J. Fitzgerald, "[Sustainable Development Goals: Impact of Lack of Financial Protection in Health in Latin American and Caribbean CountriesObjetivos de Desenvolvimento Sustentável: Impacto Da Falta de Proteção Financeira Em Saúde Nos Países Da América Latina e Do Caribe]," *Revista Panamericana de Salud Publica = Pan American Journal of Public Health* 45 (2021).
5. F. Tobar and E. Martich, "Economic Tools for Ensuring Access to Medicines in Latin American Countries," *Pharmaceuticals Policy and Law* 16, nos. 3–4 (2014): 207–224.
6. D. Moye-Holz and S. Vogler, "Comparison of Prices and Affordability of Cancer Medicines in 16 Countries in Europe and Latin America," *Applied Health Economics and Health Policy* 20, no. 1 (2022): 67–77.
7. "WHO Guideline on Country Pharmaceutical Pricing Policies," WHO, 2020, *available at* <https://www.who.int/publications/i/item/9789240011878> (last visited July 26, 2023).
8. S. Vogler, "Payer Policies to Support Innovation and Access to Medicines in the WHO European Region," Copenhagen, 2022, *available at* <https://www.who.int/europe/publications/i/item/9789289058247> (last visited July 28, 2023).
9. "PPRI Indicators," Vienna, *available at* <https://ppri.goeg.at/sites/ppri.goeg.at/files/inline-files/List_PPRI_Indicators_1.pdf> (last visited July 26, 2023.
10. S. Vogler, C. Leopold, N. Zimmermann, C. Habl, and K. de Joncheere, "The Pharmaceutical Pricing and Reimbursement Information (PPRI) Initiative-Experiences from Engaging with Pharmaceutical Policy Makers," *Health Policy and Technology* 3, no. 2 (2014); S. Vogler and N. Zimmermann, "Improving Medicines Access in Brazil through Collaboration in the PPRI Network," *Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde* 13, no. 2 (2022): 677–677.
11. J. Espin Balbino, J. Rovira Forns, and C. Vaca González, "Chapter 2.4 - Medicine Prices in Latin American Countries," *Medicine Price Surveys, Analyses and Comparisons* 61–83 (2019).
12. Moye-Holz and Vogler, *supra* note 6.
13. Martínez Estay and R.A. Poyanco Bugueño, "El Derecho a La Vida En La Jurisprudencia de La Corte Suprema Sobre Medicamentos de Alto Costo," *Estudios Constitucionales* 20, no. 2 (2022): 2–40; T.S. Andia and E. Lamprea, "Is the Judicialization of Health Care Bad for Equity? A Scoping Review," *International Journal for Equity in Health* 18, no. 1 (2019).
14. A.E. Yamin, A. Andrés Pichon-Riviere, and P. Bergallo, "Unique Challenges for Health Equity in Latin America: Situating the Roles of Priority-Setting and Judicial Enforcement," *International Journal for Equity in Health* 18, no. 1 (2019).
15. C.M. Vargas-Pelaez, M. Raijche Mattozo Rover, L. Soares, C. Raquel Blatt, A.K. Mantel-Teeuwisse, Francisco Augusto Rossi, Luis Guillermo Restrepo, et al., "Judicialization of Access to Medicines in Four Latin American Countries: A Comparative Qualitative Analysis." *International Journal for Equity in Health* 18, no. 1 (2019); L.A. Salha, Leila, F. Costa Reis, R. Moreira Gonçalves, J. Horácio da Silva Lima, N. Abou Salha, R. Pereira Pinto, J. Elmo de Menezes, E. Perez Oliveira, P. Lopes Ferreira, and M. Alves Barbosa, "Judicialization of Health: Profile of Demands for Oncological Medicines in a State in the Central Region of Brazil," *International Journal for Equity in Health* 21, no. 1 (2022).
16. Andia and Lamprea, *supra* note 13; A. Freiberg and J. Espin, "Towards a Taxonomy of Judicialisation for Access to Medicines in Latin America," *Global Public Health* 17, no. 6 (2022): 912–25.
17. *Id.*
18. C.E. Pinzón-Flórez, E. Chapman, L. Cubillos, and L. Reveiz, "Priorización de Estrategias Para El Abordaje de La Judicialización En Salud En América Latina y El Caribe," *Revista de Saude Publica* 50 (2016); Vargas-Pelaez et al., *supra* note 15; A. Acosta, M.Z. Falcão, F.M.A. Aith, and C. Vance, "Judicialización Del Acceso a Medicamentos En El Contexto Suramericano," *Revista De Direito Sanitário* (2019), *available at* <https://www.saludyfarmacos.org/lang/es/boletin-farmacos/boletines/feb202002/05_ju/> (last visited July 27, 2023).
19. F.R. Floriano, F. Raynal, L. Boeira, C. de Agostino Biella, V. Cássia Pereira, M. Carvalho, J. Otávio Maia Barreto, and S. Maria do Valle Leone de Oliveira, "Strategies to Approach the Judicialization of Health in Brazil: An Evidence Brief," *Ciencia & Saude Coletiva* 28, no. 1 (2023): 181-96; Martínez Estay and Poyanco Bugueño, *supra* note 13; Freiberg and Espin, *supra* note 16.
20. V.L. Luiza, M. Auxiliadora Oliveira, G. Costa Chaves, M.B. Flynn, and J.A. Zepeda Bermudez, "Pharmaceutical Policy in Brazil," *Pharmaceutical Policy in Countries with Developing Healthcare Systems* (January 2017): 123-49.
21. A.M. Ivama-Brummell, F.L. Marciniuk, A.K. Wagner, C.G.S. Osorio-de-Castro, S. Vogler, E. Mossialos, C.L. Tavares-de-Andrade, and H. Naci, "Marketing Authorisation and Pricing of FDA-Approved Cancer Drugs in Brazil: A Retrospective Analysis," *Lancet Regional Health - Americas* 22 (June 2023): 100506; A.M. Ivama-Brummell, D. Pingret-Kipman, P.G. Louly, and R.R. Andrade, "Medicines Regulation, Pricing and Reimbursement in Brazil," *Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde* 13, no. 1 (2022): 769-769.
22. Luiza, et al., *supra* note 20.
23. Banco Interamericano de Desarrollo, "Acceso, desarrollo y regulación económica del mercado de medicamentos de Brasil," 2022, Breve 25, *avalaible at* <https://publications.iadb.org/es/breve-25-acceso-desarrollo-y-regulacion-economica-del-mercado-de-medicamentos-de-brasil> (last visited July 28, 2023).
24. Ivama-Brummell, et al., *supra* note 21.

The Journal of Law, Medicine & Ethics, 51 S1 (2023): 76-91. © 2023 The Author(s)

25. *Id.*
26. T. Andia, "El 'Efecto Portafolio' de La Regulación de Precios de Medicamentos: La Respuesta de La Industria Farmacéutica a La Regulación de Precios de Medicamentos En Colombia," September 2018.
27. S.I. Prada, V.E. Soto, T.S. Andia, C.P. Vaca, Á.A. Morales, S.R. Márquez, and A. Gaviria, "Higher Pharmaceutical Public Expenditure after Direct Price Control: Improved Access or Induced Demand? The Colombian Case," *Cost Effectiveness and Resource Allocation: C/E* 16, no. 1 (2018).
28. *Id.*
29. T. Andia, A. Gaviria, C. Gomez, L.F. Jaramillo, S. Marquez, I. Rodríguez, and C. Vaca, "First Evaluation Of Colombian's External Reference Pricing System," *Value in Health* 17, no. 3 (2014): A15.
30. Dirección de Medicamentos y Tecnologías En Salud, *Boletín Gasto de Bolsillo en Medicamentos*, 2022.
31. Prada, et al., *supra* note 27.
32. Andia, *supra* note 26.
33. Dirección de Medicamentos y Tecnologías en Salud, *supra* note 30.
34. C.E. Durán, R. Lucio, and J. Rovira, "Pharmaceutical Policy in Ecuador," *Pharmaceutical Policy in Countries with Developing Healthcare Systems* (2017): 221-236.
35. *Id.*
36. "Cuadro Nacional de Medicamentos Básico CNMB – Ministerio de Salud Pública," n.d., *available at* <https://www.salud.gob.ec/cuadro-nacional-de-medicamentos-basico-cnmb/> (last visited July 28, 2023).
37. L. Rivera, "The Pharmaceutical Price Regulation in El Salvador," 2022, *available at* <https://publications.iadb.org/en/breve-24-pharmaceutical-price-regulation-el-salvador> (last visited July 28, 2023).
38. *Id.*
39. G. Hamilton and F. Tobar, "Experiencias internacionales en la regulación del precio de los medicamentos," in E. Lifschitz, Esteban, ed., *Agencia de Evaluación de Tecnologías Sanitarias en Argentina: Por qué, Para qué y cómo* (Buenos Aires: Fundación Sanatorio Guemes, 2018); Rivera, *supra* note 37.
40. E. González-Pier and M. Barraza-Lloréns, "Trabajando Por La Salud de La Población: Propuestas de Política Para El Sector Farmacéutico," Mexico, 2011, *available at* <https://funsalud.org.mx/wp-content/uploads/2019/11/Doc-PolPublSFarm-vF-Digital-060511.pdf> (last visited July 28, 2023).
41. Cid, et al., *supra* note 4.
42. Moye-Holz and Vogler, *supra* note 6; F. Bañuelos F. 2016. "Mexico's Coordinating Commission for Negotiating the Price of Medicines and Other Health Inputs," *available at* <https://publications.iadb.org/en/breve-14-mexicos-coordinating-commission-negotiating-price-medicines-and-other-health-inputs> (last visited July 28, 2023); O. Gómez-Dantés, V.J. Wirtz, M.R. Reich, P. Terrazas, and M. Ortiz, "A New Entity for the Negotiation of Public Procurement Prices for Patented Medicines in Mexico." *Bulletin of the World Health Organization* 90, no. 10 (2012): 788.
43. Moye-Holz and Vogler, *supra* note 6.
44. S. Poblete, "Precio Máximo Industrial: Instrumento Para La Negociación y La Regulación de Los Precios de Medicamentos de Alto Costo En Chile," *Revista Chilena de Salud Pública* 26, no. 1 (2022): 67–77.
45. "Ley 20850 Crea Un Sistema de Protección Financiera Para Diagnósticos y Tratamientos de Alto Costo," n.d. Ministerio de Salud, *available at* <https://www.bcn.cl/leychile/navegar?idNorma=1078148> (last visited July 28, 2023); *Id.* (Poblete).
46. S. Vogler, M.A. Haasis, G. Dedet, J. Lam, and H. Bak Pedersen, "Medicines Reimbursement Policies in Europe," Copenhagen, 2018, *available at* <https://www.who.int/europe/publications/i/item/9789289053365> (last visited July 28, 2023).
47. S. Vogler, G. Dedet, and H. Bak Pedersen, "Financial Burden of Prescribed Medicines Included in Outpatient Benefits Package Schemes: Comparative Analysis of Co-Payments for Reimbursable Medicines in European Countries," *Applied Health Economics and Health Policy* 17, no. 6 (2019): 803-816.
48. S. Vogler, N. Zimmermann, and M.A. Haasis, "PPRI Report 2018 - Pharmaceutical Pricing and Reimbursement Policies in 47 PPRI Network Member Countries," WHO Collaborating Centre for Pricing and Reimbursement Policies, 2019, a*vailable at* <https://jasmin.goeg.at/1068/> (last visited October 18, 2023) .
49. S. Vogler, M.A. Haasis, R. van den Ham, T. Humbert, S. Garner, and F. Suleman, "European Collaborations on Medicine and Vaccine Procurement," *Bulletin of the World Health Organization* 99, no. 10 (2021): 715-21, *available at* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8477421/pdf/BLT.21.285761.pdf> (last visited July 28, 2023); S. Vogler, M. Salcher-Konrad, and K. Habimana, "Study on Best Practices in the Public Procurement of Medicines: Final Report," Brussels, 2022, *available at* <https://data.europa.eu/doi/10.2925/044781> (last visited July 28, 2023); S. Vogler, M.A. Haasis, R. van den Ham, F. Suleman, T. Humbert, and S. Garner, "Cross-Country Collaborations to Improve Access to Medicines and Vaccines in the WHO European Region," Copenhagen, 2020, *available at* <https://ppri.goeg.at/sites/ppri.goeg.at/files/inline-files/Cross-country%20collaborations_final.pdf> (last visited July 28, 2023).
50. C. Leopold, S. Vogler, A.K. Mantel-Teeuwisse, K. de Joncheere, H. G.M. Leufkens, and R. Laing, "Differences in External Price Referencing in Europe: A Descriptive Overview," *Health Policy (Amsterdam, Netherlands)* 104, no. 1 (2012): 50-60; S. Vogler and P. Schneider, "Assessing Data Sources for Medicine Price Studies," *International Journal of Technology Assessment in Health Care* 35, no. 2 (2019): 106-15.
51. S. Vogler, L. Lepuschütz, P. Schneider, and and V. Stühlinger, "Study on Enhanced Cross-Country Coordination in the Area of Pharmaceutical Product Pricing - Publications Office of the EU," Publications Office of the European Union, 2016, *available at* <https://op.europa.eu/en/publication-detail/-/publication/b1565784-9a9c-11e6-9bca-01aa75ed71a1/language-en> (last visited July 28, 2023); S. Vogler, N. Zimmermann, and M.A. Haasis, "PPRI Report 2018 - Pharmaceutical Pricing and Reimbursement Policies in 47 PPRI Network Member Countries," WHO Collaborating Centre for Pricing and Reimbursement Policies, 2019, *available at* <https://jasmin.goeg.at/1068/> (last visited July 28, 2023).
52. S. Vogler, P. Schneider, and L. Lepuschütz, "Impact of Changes in the Methodology of External Price Referencing on Medicine Prices: Discrete-Event Simulation," *Cost Effectiveness and Resource Allocation: C/E* 18, no. 1 (2020); M. Toumi, C. Rémuzat, A.-L. Vataire, and D. Urbinati, "External Reference Pricing of Medicinal Products: Simulation-Based Considerations for Cross-Country Coordination Final Report Written by European Commission External Reference Pricing of Medicinal Products: Simulation-Based Considerations for Cross-Country Coordination 2/113 European Commission External Reference Pricing of Medicinal Products: Simulation-Based Considerations for Cross-Country Coordination," 2013.
53. Vogler and Schneider, *supra* note 50.
54. Vogler, et al., *supra* note 51.
55. E. Webb, E. Richardson, S. Vogler, and D. Panteli, "What Are the Implications of Policies Increasing Transparency of Prices Paid for Pharmaceuticals?" Copenhagen, 2022, *available at* <https://eurohealthobservatory.who.int/publications/i/what-are-the-implications-of-policies-increasing-transparency-of-prices-paid-for-pharmaceuticals#:~:text=Increasing%20transparency%20in%20the%20pharmaceutical,maintaining%20access%2C%20innovation%20and%20sustainability> (last visited July 28, 2023); S. Vogler, P. Schneider, and N. Zimmermann, "Evolution of Average European Medicine Prices: Implications for the Methodology of External Price Referencing," *PharmacoEconomics - Open* 3, no. 3 (2019): 303-309; M.K. Kyle, "Pharmaceutical Price Controls and Entry Strategies," *The Review of Economics and Statistics* 89 , no. 1 (2007): 88-99.

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56. *Id.* (Kyle).
57. Vogler, *supra* note 8.
58. S. Vogler, M.A. Haasis, and N. Zimmermann, "Brief Pharma Report Austria," Vienna, 2019, *available at* <https://ppri.goeg.at/Brief_AT> (last visited July 28, 2023).
59. S. Vogler, "International Comparison of Medicine Prices," *Medicine Price Surveys, Analyses and Comparisons: Evidence and Methodology Guidance* (January 9-10, 2018).
60. *EU-Durchschnittspreise Laut ASVG*, Vienna: BMSGPK, 2022, *available at* <https://www.sozialministerium.at/Themen/Gesundheit/Medizin-und-Gesundheitsberufe/Medizin/Arzneimittel/Arzneimittelpreise/EU-Durchschnittspreise-laut-ASVG.html>.
61. *Id.*
62. *Id.*
63. V. Paris and A. Belloni, "Value in Pharmaceutical Pricing: OECD Health Working Papers," OECD, 2013, *available at* <https://www.oecd-ilibrary.org/social-issues-migration-health/value-in-pharmaceutical-pricing_5k43jc9v6knx-en> (last visited July 28, 2023).
64. Vogler, et al., *supra* note 51; B. O'Rourke, W. Oortwijn, and T. Schuller, "The New Definition of Health Technology Assessment: A Milestone in International Collaboration," *International Journal of Technology Assessment in Health Care* 36, no. 3 (2020): 187-90; A. Angelis, A. Lange, and P. Kanavos, "Using Health Technology Assessment to Assess the Value of New Medicines: Results of a Systematic Review and Expert Consultation across Eight European Countries," *The European Journal of Health Economics: HEPAC : Health Economics in Prevention and Care* 19, no. 1 (2018): 123-52.
65. S. Vogler, et al., "Medicines Reimbursement Policies in Europe," WHO Europe, Copenhagen, 2018, *available at* <https://apps.who.int/iris/handle/10665/342220> (last visited July 28, 2023); *Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on Health Technology Assessment and Amending Directive 2011/24/EU*, 2021, Brussels: European Parliament and of the Council, *available at* <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32021R2282> (last visited July 28, 2023).
66. S. Vogler, *Medicines Pricing: Limitations of Existing Policies and New Models* (Singapore: Palgrave Macmillan, 2020).
67. See *supra* note 65.
68. *Id.*
69. J. O'Callaghan, S.P. Barry, M. Bermingham, J.M. Morris, and B.T. Griffin, "Regulation of Biosimilar Medicines and Current Perspectives on Interchangeability and Policy," *European Journal of Clinical Pharmacology* 75, no. 1 (2019): 1-11.
70. WHO Guideline, *supra* note 7.
71. W. Kaplan, V. Wirtz, and R. Laing, "Policy Options for Promoting the Use of Generic Medicines in Low-and Middle-Income Countries " 2016; A. Ferrario, G. Dedet, T. Humbert, S. Vogler, F. Suleman, and H. Bak Pedersen, "Strategies to Achieve Fairer Prices for Generic and Biosimilar Medicines," *BMJ* 368 (January 2010).
72. A. Acosta, A. Ciapponi, M Aaserud, V. Vietto, A. Austvoll-Dahlgren, J.P. Kösters, C. Vacca, M. Machado, D. Hazbeydy Diaz Ayala, and A.D. Oxman, "Pharmaceutical Policies: Effects of Reference Pricing, Other Pricing, and Purchasing Policies," *The Cochrane Database of Systematic Reviews* 2014, no. 10 (2014).
73. S. Vogler, D. Panteli, N. Zimmermann, and R. Busse, "Überblick Über Maßnahmen Zur Förderung Des Einsatzes von Biosimilars in Europäischen Ländern," *Arzneiverordnungs-Report* (2022): 57-81.
74. D.M. Dalen, S. Strøm, and M. Locatelli, "Biosimilar Bidding in Centralized Tenders in Norway," *Nordic Journal of Health Economics* 9, no. 1 (2021): 11–23.
75. S. Vogler, P. Schneider, M. Zuba, R. Busse, and D. Panteli, "Policies to Encourage the Use of Biosimilars in European Countries and Their Potential Impact on Pharmaceutical Expenditure," *Frontiers in Pharmacology* 12 (2021): 1479.
76. "New International Record for Switch to Biosimilar," n.d., Amgros, available at <https://amgros.dk/en/knowledge-and-analyses/articles/new-international-record-for-switch-to-biosimilar/?report=reader> (last visited Ju*ly 28, 2023); T.B. Jensen, S.C. Kim, E. Jimenez-Solem, D. Bartels, H. Rolighed Christensen, and J. Trærup Andersen, "Shift from Adalimumab Originator to Biosimilars in Den*mark." JAMA Internal Medicine 180, no. 6 (2020): 902-903.
77. T. Bossert, N. Blanchet, S. Sheetz, D.M. Pinto, J. Cali, and R. Pérez-Cuevas, "Comparative Review of Health System Integration in Selected Countries in Latin America," 2014, *available at* <https://www.semanticscholar.org/paper/Comparative-Review-of-Health-System-Integration-in-Bossert-Blanchet/d4293e5e720da2802b628a9e60e2af65f5928819> (last visited July 28, 2023).
78. *Id.*
79. N. Justo, M.A. Espinoza, B. Ratto, M. Nicholson, D. Rosselli, O. Ovcinnikova, S. García Martí, M.B. Ferraz, M. Langsam, and M.F. Drummond, "Real-World Evidence in Healthcare Decision Making: Global Trends and Case Studies from Latin America," *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research* 22, no. 6 (2019): 739-749; A. Pichon-Riviere, F. Augustovski, S.García Martí, V. Alfie, and L. Sampietro-Colom, "The Link between Health Technology Assessment and Decision Making for the Allocation of Health Resources in Latin America," *International Journal of Technology Assessment in Health Care* 36, no. 2 (2020): 173-178.
80. I.C. Martins Emmerick, V.L. Luiza, L.A. Bastos Camacho, C. Vialle-Valentin, and D. Ross-Degnan, "Barriers in Household Access to Medicines for Chronic Conditions in Three Latin American Countries," *International Journal for Equity in Health* 14, no. 1 (2015).
81. Espin Balbino, et al., *supra* note 12; Tobar and Martich, *supra* note 5.
82. WHO Guideline, *supra* note 7.
83. V.F. Azevedo, A. Babini, C.V. Caballero-Uribe, G. Castañeda-a-Hernández, C. Borlenghi, and H.E. Jones, "Practical Guidance on Biosimilars, with a Focus on Latin America: What Do Rheumatologists Need to Know?" *Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases* 25, no. 2 (2019): 91-100.
84. PAHO Revolving Fund ,n.d., Pan American Health Organization, *available at* <https://www.paho.org/en/revolving-fund> (last visited July 28, 2023).
85. SE-COMISCA: Consejo de Ministros de Salud de Centroamérica y República Dominicana, n.d., *available at* <https://comisca.net/> (last visited July 28, 2023).
86. EUnetHTA, n.d., *available at* <https://www.eunethta.eu/> (last visited July 28, 2023).
87. Vogler, et al., *supra* note 49.

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