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Drug price regulation experiences in selected countries: lessons for Brazil

Experiências de regulação de preços de medicamentos em países selecionados: lições para o Brasil

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ABSTRACT

Introduction: Price regulation in the pharmaceutical market is common to countries at different levels of development, but the motivation for its implementation differs between developed and developing countries. **Objective:** To discuss the drug price regulation in Brazil and the need for improvements based on experiences and evidence of drug price regulation in selected countries. **Method:** Review of the literature on regulatory models of drug prices in selected countries. **Results:** Based on the systematized literature, an analysis of different types of drug price regulation by group (European and developing countries) was carried out. **Conclusions:** The literature review was used to observe the different drug price regulations among countries, and to identify examples on how to improve the current regulation in Brazil to achieve more desirable results.

KEYWORDS: Government Regulation; Drug Price; Generic Drugs

RESUMO

Introdução: A regulação de preços no mercado farmacêutico é comum aos países de diversos níveis de desenvolvimento, mas a motivação para sua implementação difere entre países desenvolvidos e em desenvolvimento. **Objetivo:** Discutir, com base em outras experiências de regulação de preços de medicamentos em países selecionados, a regulação de preços de medicamentos em vigor no Brasil, de modo a acumular evidências da necessidade de melhorias na regulação em vigor. **Método:** Revisão da literatura sobre modelos regulatórios de preços de medicamentos em países selecionados. **Resultados:** Com a sistematização da literatura, realizou-se a análise dos diferentes tipos de regulação de preços de medicamentos por grupo de países europeus e em desenvolvimento. **Conclusões:** A revisão de literatura serviu para observar as diferenças da regulação de preços dos medicamentos em distintos países em comparação com a brasileira e trazer sugestões de como aperfeiçoar a regulação atual para se alcançar resultados mais desejáveis.

PALAVRAS-CHAVE: Regulamentação Governamental; Preço de Medicamento; Medicamentos Genéricos

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INTRODUCTION

In markets where competitive forces are not present, at least not to a sufficient extent to guarantee efficient prices, as in pharmaceutical markets, there is broad consensus that some form of intervention on the part of the State is necessary, either to promote competition or to regulate drug prices[1].

Price regulation in the pharmaceutical market is common to countries of different levels of development, but the motivation for its implementation differs between developed and developing countries (DC). In countries where a substantial portion of the population is covered by health insurance schemes, price controls are seen as part of the cost containment strategy. In countries where consumers bear most of the cost of medicines, price controls are seen primarily as a way to increase access[2].

This regulation can occur through two perspectives: (i) supply, which can act in two ways, mitigating the problems arising from the functioning of the market (indirect effects on prices) or through active policies on prices and/or profit margins (direct effects of lowering prices); and (ii) that of demand, seeking to strengthen the buyer's bargaining power[2].

As Espin et al.[1] point out, high drug prices are a major concern for governments, policymakers, insurers, and patients as they can make drugs unaffordable, compromise equitable access and threaten the financial sustainability of public health systems. According to Sood et al.[3], regulations tend to restrict drug spending, improving the well-being of the population, but if inadequate, they can also limit research and development (R&D) incentives, delay launch, limit availability, and even competition for new drugs.

In the wave of deregulation that was imposed on developing countries between 1980-1990, Brazil largely deregulated the prices of pharmaceutical products. Prior to that, drug prices were strictly regulated by the Inter-ministerial Price Committee (CIP), which monitored the prices of various products, including drugs and other health-related products[4]. In addition, the Center of Medicines (Ceme), organ of the Presidency of the Republic, intended to promote and organize the supply, at affordable prices, of medicines to those who, due to their economic conditions, could not acquire them, acted as regulator of the production and distribution of medicines by pharmaceutical laboratories[5]. In 1992, when CIP and Ceme were deactivated, prices were only monitored by the government, a task initially assigned to the Administrative Council for Economic Defense and, later, to the Secretary for Economic Oversight of the Ministry of Finance, between 1997-1999[4].

The abusive increase in the prices of medicines and the sale of pharmaceutical products of dubious quality led, in 1999, to the establishment of the Parliamentary Commission of Inquiry (CPI) on medicines. In the same year, the Brazilian National Health Surveillance Agency (Anvisa) was created, with the institutional mission of protecting the health of the Brazilian population through the sanitary control exercised over products and over the commercialization of medicines[6]. In the subsequent period, as a result of the CPI, the need to reduce the rise in drug prices and realign them to the levels of the previous decade was defined. Due to this, there was exemption from taxation of medicines, through Law No. 10,147, of December 21, 2000, by the Contribution Social Integration Program/Contribution for Social Security Financing (PIS/Cofins), and the de-indexation of drug prices from inflation indexes[7,8].

Also, in 2000, Provisional Measure (MP) No. 2,063, of December 18, defined the regulatory norms for the drug sector in Brazil, instituting the Parametric Formula for Price Readjustment of Medicines and creating the Medicines Chamber. This MP was converted into Law No. 10,213, of March 27, 2001, and later revoked by Law No. 10,742, of October 6, 2003, which led to the creation of the Drug Market Regulation Chamber (CMED) in 2003[6].

Through Law No. 10,742/2003, it was established, in Art. 4, the rules for the adjustment and determination of drug prices, which should be based on a price ceiling model calculated on the basis of an index (Broad Consumer Price Index - IPCA), on a productivity factor (expressed as a percentage, allowing to pass on to consumers projections of company productivity gains), and on an intrasector relative price adjustment factor (calculated on the basis of market power, determined by monopoly/oligopoly power, information asymmetry, and barriers to entry) and across sectors (calculated on the basis of varying input costs, provided that such costs are not recovered by computing the index)[9].

The formula used to calculate the readjustment became:

$$VPP = IPCA - X + Y + Z$$

Where VPP represents the percentage change in the price of the drug; IPCA represents the inflation rate measured by the percentage change in the IPCA; X represents the productivity factor; Y represents the relative price adjustment factor between sectors; and Z represents the intra-sector relative price adjustment factor[10].

Through Resolution No. 2, of March 5, 2004[11], CMED became responsible for controlling the entry prices of medicines, according to specific rules for each type: (i) new products (object of patent and with gain for treatment) - factory price (FP) cannot be higher than the lowest FP practiced in the related countries (Australia, Canada, Spain, United States, France, Greece, Italy, New Zealand, Portugal, and the FP practiced in the country of origin of the product), adding the applicable taxes; (ii) new products not covered by the previous definition – FP is based on the cost of treatment with drugs used for the same therapeutic indication; (iii) new drug presentation already marketed by the company - FP cannot be higher than the arithmetic average of the prices of drug presentations; (iv) not marketed by the company or already marketed in a new pharmaceutical form – FP cannot exceed the average price of the drug presentations available on the market, weighted by the revenue of each presentation;

(v) new pharmaceutical form in the country or new association of active ingredients already existing in the country – FP, in the case of new associations, cannot exceed the sum of the prices of monodrugs, or in the case of new pharmaceutical forms, the cost of treatment with existing drugs in the Brazilian market for the same therapeutic indication; (vi) generics – FP cannot be higher than 65% of the price of the reference drug.

In 2012, the report of Judgment No. 3,016 of the Federal Court of Accounts recommended that the Ministry of Health review the regulatory model provided for in Law No. 10,742/2003, in order to unlink inflation adjustments. After verifying that 86% of the drugs in a sample of drugs with the highest revenue were priced above the international average, with 46% having the highest price in Brazil, it also recommended the periodic review of prices based on criteria such as international comparison, exchange variation, and costs of different treatments. The Judgment gave rise to a public consultation, which culminated in the change of parameters for calculating the Factor Z[8]. It is noteworthy, however, that the regulation defines only positive adjustments, with no possibility of price reduction[7,12].

This regulatory model, apart from the modifications mentioned above, is already 16 years old. According to Dias et al.[8], the longevity of the price adjustment model, without periodic realignment of ceilings to market prices, has generated maximum prices that are disconnected from reality, which increase information asymmetry and may support future abusive increases. The regulatory model in force remains without any realignment, with consequent distortions accumulating between the Maximum Consumer Price (PMC) and prevailing prices. In addition, there is no effective monitoring of drug prices at points of sale by CMED[12].

Thus, given that regulation in Brazil has not led to satisfactory results[8,12] and to the long period without significant changes, we sought to carry out a survey of the international literature on regulatory models applied to drug prices in other countries to seek learning for Brazil. Therefore, the objective of this article was to discuss, based on other experiences of drug price regulation in selected countries, the regulation of drug prices in Brazil, in order to accumulate evidence of the need for improvements in the regulation in force.

METHOD

For the literature review, an electronic search was performed in the Google Scholar and Science Direct databases, which were chosen because they are broader bases and have articles from different areas and countries. The keywords were used in the search: "*medicamentos genéricos*", "generic drug", and "international price comparisons". This research resulted in the selection of 92 texts, from which those that did not mention "price regulation" and that were not articles published in journals were excluded, leaving 34 articles. After reading the abstract of these 34 articles, 12 were selected that presented regulatory models of drug prices in different countries. After a detailed reading of the 12 articles, only the following were used: Brekke et al.[13], Dylst and Simoens[14], Simoens[15], Vogler[16], and Wouters and Kanavos[17]. A new search was performed in Science Direct, using the keyword "*precio de medicamentos*", which resulted in a total of 51 articles. After a brief reading of the title and abstract, four articles were selected that described the way in which drug price regulation works in some DC, of which only the article by Vacca et al.[18] was used. Through the reading of these articles, the selection of referenced articles was carried out, which were inserted in the base. In addition to this systematic search, previously known articles were added. In the end, the base had 17 articles.

This literature review served to observe how the regulation of drug prices occurs in different countries, comparing these regulations with the Brazilian one and leading to evidence of suggestions on how to improve the current Brazilian regulation to achieve more desirable results. The literature was systematized by group of countries, namely European countries and DC.

RESULTS

This section is divided into three parts: the first deals with the regulation of drug prices in European countries, presenting the types of regulation in these countries; the second, with the advantages and disadvantages of these regulations in European countries; and the third, with the regulation of drug prices in DC.

Types of drug price regulation in European countries

In Europe, drug pricing systems tend to adopt: a) a regulated pricing system, with prices being set by a regulatory base; b) a free market approach, where manufacturers are (relatively) free to set prices; or c) a combination of these approaches[15].

Among European countries, only Malta, Denmark, and Germany did not have state control of drug prices in the private sector, being known as "free prices" countries. In Belgium, the Czech Republic, Cyprus, Greece, Latvia, and Luxembourg, all medicines were price controlled. In Bulgaria, the Netherlands, Portugal, and Romania, only the prices of prescription generics were controlled[19]. In Chart 1, it is possible to observe the three main forms of regulation implemented in European countries, a brief description of their methodology, and the countries that apply them.

As for the generic price linkage model, in Austria, the first generic was considered economically efficient if its price was at least 48% below the reference price, and economic efficiency was assumed if the second, and each subsequent follower, offered a sufficiently large price difference from the previously included generic. Furthermore, the price of the reference drug should be reduced by at least 30% within three months after the inclusion of the first generic[19].

For the external reference pricing (ERP), different methods can be adopted to choose or calculate it, taking into account: (i) the basket of reference countries; (ii) the price date (current or at launch); and (iii) the calculation of the reference pricing (lowest price, simple, or weighted average). The resulting value can be

Chart 1. Types of regulations implemented in European countries.

Regulation	Methodology	Countries
Generic price linkage	Generic drug prices are set at a percentage below the price of the reference drug.	Czech Republic, Greece, Ireland, Italy and Luxembourg (up to 20% below); Belgium, Cyprus (locally produced medicines); Hungary, Poland, and Portugal (from 20-50% below); France (at least 50% below)[19].
ERP	The practice of using the price of a drug in one or several countries to obtain a reference price for the purpose of setting or negotiating the price in a particular country.	According to Vogler[16], 25 European countries used the ERP to determine drug prices and only Denmark, Sweden, and the United Kingdom did not apply the ERP.
RPR	It implies grouping identical or similar products in so-called reference groups, determining a maximum reimbursement amount to be covered by third parties. The patient pays only the difference between the RPR and the price at the pharmacy.	Belgium, Bulgaria, Denmark, Slovenia, Spain, Estonia, France, Finland, Greece, Italy, Lithuania, Norway, Portugal (ATC 5); Germany, Croatia, Slovakia, Netherlands, Hungary, Latvia, Poland, Czech Republic, Romania (clusters)[16].

Source: Elaborated by the authors, 2020.
ERP: External reference pricing; RPR: Reference pricing for reimbursement.

adjusted by a specific parameter to consider the lower economic capacity of the country in relation to the reference countries. Furthermore, European countries tended to select as reference countries those that shared economic similarities, geographic proximity, or availability of price information. In Estonia, for example, the ERP is used for reimbursed reference medicines and generics, it takes all EU member states as a reference, but explicitly examines the prices of Latvia, Lithuania, and Hungary. Latvia and Lithuania were chosen because they are the closest countries, with similar economic situation, population structure and epidemiological *status*. Hungary was chosen because it has a similar pricing procedure[1].

Policies aimed at controlling sales prices to the consumer may also be subject to control of commercialization margins, the definition of criteria for setting initial sales prices and rules for future price adjustments. In Portugal, the national health system negotiated the price with the laboratory and established the selling price to the consumer, controlling the marketing margins. In addition, prices were revised annually according to the variation of inflation, and there may be years in which the revision was not authorized[20].

Advantages and disadvantages of different types of drug price regulation in European countries

According to Simoens[15], generic FPs varied substantially both between countries and within the same country, which suggested that prices not only reflected underlying production costs but were also influenced by the regulatory environment surrounding registration, pricing, reimbursement, and distribution. Wouters and Kanavos[17] observed that the FP and retail of a generic sample varied greatly across seven European countries. Denmark and Sweden had the lowest prices among the seven countries, while France and Italy had the highest on most weighted indices. The authors found that: (i) the price variation differed between the therapeutic groups and due to differences in the regulation of wholesalers and retailers' margins; and (ii) patients tended to consume more of the drugs that were cheaper in their countries.

It was also observed that countries that did not explicitly require generics to be priced at a certain lower percentage reported considerable price differences from benchmarks (e.g., Netherlands and Slovakia), and attributed this to competition. In addition, generic penetration was more successful in countries with free pricing than with regulation. This was because, in free-market countries, manufacturers of reference drugs could charge higher prices, before and after patent expiration, attracting the entry of generics. Generics, in turn, were able to increase their market share by offering price reductions. The main conclusion was that, if, on the one hand, the price difference between generics and reference tended to be greater in free-price countries due to competition, on the other hand, regulation tended to reduce the price of the reference drug over its life cycle, which discouraged the entry of generics[15,16].

In addition, Dylst and Simoens[14] observed that the highest price levels for generics were in the UK, France, the Netherlands, and Germany, and this was because competition between generic manufacturers took the form of distribution chain discounts. According to the authors, this type of competition is not transparent to market actors and is not fair, as wholesalers and retailers are rewarded for their ability to negotiate discounts on artificial prices, tending to overestimate the price of generics. Because of this, France began to regulate the size of these discounts. On the other hand, the authors observed that generic price competition is transparent to all market actors, ensuring that the prices paid reflect the real value of the product and being able to reduce the prices of reference drugs.

As for the problems regarding the use of the ERP, it was noted that, in Germany, some companies had decided to keep the prices of some medicines high, despite the lower domestic reference pricing (DRP) which led to a subsequent loss of market share. This was because companies knew that prices in this country would later become benchmarks for other countries. Thus, by keeping prices high in Germany, companies were able to obtain higher prices in other countries. Therefore, a consequence of the ERP is to pressure selected countries as a reference to maintain high prices[1].

Regarding the use of the reference pricing for reimbursement (RPR), Brekke et al.[13] observed that, in Norway, this mechanism

was able to significantly reduce the prices of branded and generic drugs in the reference group, as this mechanism aims to stimulate competition and thus make the demand for drugs more elastic. Meanwhile, with the price-cap (PC), which was mandatory only for branded drugs, a large price reduction was observed in generics, while branded ones only obtained reductions below the ceiling. With this, Brekke et al.[13] suggested that RPR was more effective than PC in reducing prices.

Price regulation in developing countries: Latin America, Africa, and Asia

In this section, regulatory models of drug pricing in DC are discussed. In these countries, spending on medicines represents 25-66% of total public and private spending on health and, therefore, represents the largest family expenditure after food[21]. Most of the population in these countries does not have health plans and depends on the public system for access to medicines. The reimbursement mechanism heavily used in European systems, when the public sector bears the expense or part of it (co-payment), is both an efficient price regulator and a stimulator of increasing the share of generics in the market. The absence of these mechanisms in the DCs, or in part of them, shows the importance of regulating drug prices.

However, as highlighted by Kaplan et al.[19] and Ali and Yahia[22], published studies of how governments in developing countries regulate drug prices are relatively scarce. Chart 2 presents some regulation models that are in force in DC.

As shown in Chart 2, in Colombia, three regimes are established: (a) Supervised Freedom, which accepts the price established by the manufacturer with the commitment to report variations and the determination of prices to the *Comisión Nacional de Precios de Medicamentos* (entity that determines the regimen in which a medicine enters); (b) Regulated Freedom Regime (RFG), in which drugs that serve to protect public health enter, with high market concentration or without substitutes upon entering the market. The ERP (average of the three lowest prices of the same drugs produced by the same parent company in the reference countries and at the same level of the distribution chain) is calculated, and established as a maximum price. In 2010, the countries taken as a reference were: Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Panama, Peru, and Uruguay; (c) If a drug in the RFG exceeds the price limit, it passes to Direct Control, in which a limit is directly defined for the maximum selling price to the consumer (PMVP) based on ERP[18].

In Mexico, maximum price regulation is administered by the Ministry of Economy, with the characteristics shown in Chart 2. Generics are exempt from this regulation, as it is argued that competition eliminates the logic of regulation[23]. However, although the supply of generics in the country increased significantly in the 2000s, its share remained low compared to other

Chart 2. Models of drug price regulation in developing countries (DC).

Country	Regulation model
Colombia	Since 2006, three regimes have been established: (a) Supervised Freedom Regime; (b) RFG; (c) Direct Control Regime. In addition to ERP, a cost minimization analysis methodology is also used, selecting comparable drugs and evaluating treatment costs[18].
Mexico	Since 2004, ceiling price regulation: (a) applies only to patent-protected drugs sold in the private sector; (b) has voluntary participation from manufacturers; (c) uses the ERP to set the threshold for the PMVP; (d) for new products without comparators, allows the manufacturer to set the price, subject to reassessment after three months; and (e) exempt from the regulation of generic and reference medicines whose patents have expired[23].
South Africa	In 1996, it developed a National Medicines Policy, which later led to measures to control manufacturers' prices, including the so-called "single exit price", as well as a single fixed rate of distribution or dispensing. The use of biddings is limited to the public sector[24].
Sudan	In 2009, the law that regulates the prices of medicines became known as the "Medicines and Poisons Act". Before marketing, a drug must be registered with the NMPB, which approves a C&F price. Based on total C&F, the NMPB sets maximum mark-up percentages (margin to cover fixed costs and profit) for all drugs in two distribution steps: wholesaler, 15% of total costs, and retailer, 20% of the wholesaler price[22].
China	According to Tang et al. apud Kaplan et al.[19], in 2006, the mechanism for setting the maximum retail price was based on: i) production cost; ii) government-set wholesale price spread; and iii) prices of comparable products in the market. However, prices are set at the level desired by manufacturers.
Philippines	In 2008, the drug price control policy was signed, defining a maximum retail price for a list of drugs that fall under the Universally Accessible Cheaper and Quality Medicine Act of 2008. Branded drugs under patent were the main target of price control laws[19].
India	In 2012, India passed a new pricing policy designed to increase the number of essential medicines with price controls. The legislation is designed to lower the prices of branded drugs. Under the new policy, a DRP system, the ceiling price of a particular drug is calculated by averaging the prices of all brands with more than 1% market share[19]. Furthermore, the prices of medicines that are not under price control are also regulated to a certain extent, where the government ensures that prices do not increase by more than 10% in a year[25].
Thailand	It employs some policies to indirectly control drug prices and expenditures in the public sector, such as: the implementation of the National Drug List, the National Health Insurance Schemes, and the use of the Drug Related Group to reimburse the hospitalization expenses of government employees[26].

Source: Elaborated by the authors, 2020.
ERP: External reference pricing; RFG: Regulated Freedom Regime; C&F: cost and freight; PMVP: Maximum selling price to the consumer; NMPB: National Medicines and Poisons Board; DRP: Domestic reference pricing.

countries, in part due to high prices[27]. In addition, three prices are defined: (i) the ERP, calculated as the weighted average of the FP of the previous quarter in the six countries where the product has the highest sales penetration. The manufacturer must submit the PRE to the Ministry of Economy each year, which is subject to annual verification by an external auditor; (ii) the reference selling price to the consumer (PRVP), resulting from the multiplication of the PRE by 1.72, and converted into pesos using the average exchange rate calculated by the Central Bank of Mexico corresponding to the period in which the ERP was calculated; (iii) PMVP, price allowed for a drug under patent defined by the manufacturer and printed on the product label. If the PMVP or proposed increases result in a PMVP greater than the PRVP, the former must adjust downwards relative to the PRVP. The *Procuraduría Federal del Consumidor* is responsible for ensuring compliance with the established maximum prices and monitoring the adherence of pharmacies to the law[23].

In South Africa, as mentioned in Chart 2, from the National Medicines Policy, a multifaceted series of interventions was signaled to reduce drug prices and improve prescribing and distribution practices. The single exit price is the only price at which manufacturers can sell the drug to any entity other than the State, and a single flat rate of distribution or dispensing was intended to control costs in the distribution chain[24].

In Sudan, in addition to the information in Chart 2, the drug certificate was valid for five years, with changes in prices being permitted in response to changes in economic circumstances, such as exchange rate fluctuations and inflation adjustments. The government taxed 1.5% of purchase prices in the case of retailers and levied a 15.0% mark-up tax to be paid by importers. Importers were required to stamp the price on the packaging. In the public sector, purchases were made by Central Medical Supplies Public Corporation (CMSPC), the cost and freight (C&F) price being determined by the Tender Committee. CMSPC products were sold to public and private healthcare institutions with a 20.0% mark-up and 12.0% to Revolving Medicine Funds at the state levels. Each level added its mark-up before the drugs were sold to consumers[22].

According to Tang et al. apud Kaplan et al.[19], in 2006, in China, hospitals had a monopoly on the purchase of medicines and their finances depended heavily on the sale of medicines. To alleviate the burden of medical expenses and ensure implementation of the medical insurance plan, retail prices of drugs eligible for the program were regulated and included in the National Basic Medical Insurance Scheme Drug Catalog.

In 2012, India approved, as mentioned in Chart 2, the National Pharmaceuticals Pricing Policy. Of the new drugs included in this policy, 348 are defined as essential. With the prerogative of encouraging investment, this policy establishes that medicines patented under the Indian Patents Act of 1970, and which are the result of endogenous products or processes, are exempt from price controls for a period of five years, as well as a formulation that involves a new delivery system developed through endogenous R&D[19,28].

In Thailand, in 2006, about 60% of medicines in the country were imported. Furthermore, the acquisition of public hospitals took place through group purchasing mechanisms, and the retail prices established were not controlled by the government, but companies notified the authorities of price increases. Mark-ups on generics were considerably higher than on branded drugs, however, the prices of branded drugs were more than four times higher than generics[26].

DISCUSSION

The analysis of drug price regulation in Brazil, in perspective with the international literature, provides some examples and points for reflection that can generate improvements in the regulation in force. For example, while in Brazil there is no distinction in the regulation of prices for innovative products developed in-house, India, as shown above, exempts endogenously developed products or processes from price controls for a period of five years and the same occurs for formulations with a new delivery system developed through endogenous R&D[19,28]. This shows that the current regulation of drug prices in Brazil does not generate incentives for innovative efforts to be carried out in the country. Thus, India's example shows that Brazilian price regulation misses the opportunity to stimulate the entry of innovative medicines, especially those that are introduced by Brazilian companies with incremental innovations.

Another international example that brings reflections on Brazilian regulation concerns the regulation of prices of generic drugs. In Austria, for each subsequent generic follower, there should be a sufficiently large price difference from the previously included generic and, in addition, the price of the reference drug should also be reduced[19]. In this way, the regulation in force in Brazil could achieve more desirable results, in relation to the price of generics, if the differential in the entry price of these drugs, in relation to the reference drug, was greater than 35% and if the reduction of the price of subsequent generics by regulation was encouraged.

The two previous paragraphs show that Brazilian regulation is not aligned with public policies for generics and incentives for innovation, as found in some countries. Therefore, price regulation is not achieving the objectives listed by Espin et al.[1], which indicate that an optimal price regulation system must: (i) be aligned with previously agreed policy objectives; (ii) guarantee accessibility, financial sustainability, and product quality; (iii) be directed to achieve lower prices than those that would otherwise prevail; (iv) be able to improve innovation, availability, and domestic production; and (v) be easy, objective, transparent, predictable, and not too expensive to administer.

The Brazilian regulation of drug prices seems to have been inspired by those that were already in force in European countries when the CMED was created. However, some recommendations have been proposed so that, together with price regulation,

Chart 3. Recommendations to expand the generics market in Europe.

Country	Policy recommendations	
Bulgaria	Avoid, or at least optimize, price binding for generics (the price ratio with the reference drug is 30%, suggesting that this percentage be reduced).	Avoid, or optimize, the use of ERP for generics.
France	Avoid price reductions for generics (which receive 60% of the price of the reference drug before the patent expires).	Avoid, or optimize, the use of ERP for generics.
Portugal	Limit the price reduction of new generics to 65% of the price of the reference drug.	Abolish the annual generic price review.

Source: Elaborated by the authors, according to *Medicines for Europe*[30], 2020.
ERP: External reference pricing.

or through its modification, European countries with a low share of generics can expand their use and ensure better efficiency in their markets. Some recommendations are also valid for the Brazilian case, such as those listed in the Medicines for Europe study, summarized in Chart 3.

A great concern was observed in the study by *Medicines for Europe*[30] so that the reduction in generic prices does not lead to shortages of medicines, and there must be a balance between availability and price. This does not seem to be the case in Brazil, especially considering the large number of suppliers operating in the retail market[29]. In addition, both the linking of the price of generics to the reference drugs and the margin administered in Brazil were recommended to other countries. For some European countries it was recommended to reduce the margin.

In Mexico, for example, it was believed that generic prices could be set by competition, without the need for regulation[23]. However, the consequence of this was a low generic market in the country due to high prices[27], a situation different from European countries, perhaps due to differences in markets and forms of regulation. Criticisms were also observed regarding the application of the annual price adjustment for generics, in which it is assumed that the price of generics is already linked to the price of the reference drug. Thus, as long as there is an annual price adjustment method for the reference drug, any change in the price of the reference drug will already affect the price of the respective generic[30].

Brekke et al.[13] showed that, in Norway, when the PC was in force (compulsory only for the reference drug), the price of the reference drug tended to fluctuate close to the ceiling, while the price of the generic was greatly reduced. PC is used in Brazil to adjust the prices of generic and reference drugs. However, reference drugs have kept their prices closer to the ceiling than generics, which tend to detach their prices from the PMC[29]. In this way, the review of prices for generics per PC in Brazil may be leading to the ineffectiveness of the current regulation.

Other criticisms of the annual price adjustment model in Brazil were observed, mainly regarding the determination of factors and the lack of clarity in the way they are calculated. As Dias et al.[8] showed, in the determination of Factor X, the lower the estimated productivity, the greater the increase allowed. This can be a problem, because, in a way, the regulation is not encouraging companies to increase their productivity, in order to obtain greater readjustments. In determining Factor Y, negative values are accumulated and discounted at future times of increase in production costs. For generics, production costs tend to decrease over time, which may be contributing to the determination of higher PMC. There may still be other factors contributing to the decrease in costs, which are being accumulated and not discounted, leading to, once again, the detachment of the PMC from the prices practiced in the market.

In addition, as already mentioned, there is no monitoring of prices at points of sale by CMED[12] to check these detachments, and it is only up to the consumer protection and defense agency to inspect consumer relations[31]. However, the inspection process tends to occur only when there is a complaint from consumers[31].

The main criticism, in Brazil's case, of the use of the ERP is regarding the selection of countries used as a reference. All of them have a higher income level, and neither geographic proximity nor economic, sanitary, and disbursement similarities are considered, not reflecting the dynamics of the national market. Discussions on this point make clear the need to accept the particularities of each country in determining drug prices. Colombia, for example, in 2010, already used as a reference country with greater geographical proximity and economic similarities[18], and this point should be reviewed in the regulation in force in Brazil. In addition, in 2013, Colombia carried out a technical project to propose changes to the regulation in force[32], showing the importance of carrying out studies aimed at verifying the effectiveness of the regulatory model and modifying factors that prevent this greater effectiveness.

Finally, there are criticisms of the competition model for discounts in the distribution chain, showing that these lead to higher prices than those that would prevail in price competition[14]. In Brazil, this is the type of competition that has been observed for generics. However, in view of the criticisms about the lack of clarity of real prices when this type of competition is in force, it should be observed how this may be hindering the growth of the participation of generics in the national market and even leading to the practice of higher prices. There should be greater control by the regulatory agency regarding this point and, perhaps, some type of regulation should be established for these discounts in the distribution chain.

CONCLUSIONS

The regulatory model for drug pricing in Brazil has been in place for 16 years without any significant changes. As a result, it has been observed the determination of maximum prices totally unrelated to the prices practiced in the market[8,12,29] and no monitoring of prices at points of sale by CMED[12], producing unsatisfactory results.

The review of the international literature served to observe how the regulation of drug prices occurs in different countries, comparing these regulations with the Brazilian one and leading to evidence of suggestions on how the current regulation could be improved to achieve more desirable results.

Thus, there is a need for deeper analysis of the characteristics of the markets studied to identify the possibilities of application of such measures in the Brazilian market. This article opens the discussion on the need for debate, reflections, and evaluations on the regulation of drug prices in Brazil and indicates paths for future studies on regulatory models that are more effective than the current one.

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Author's Contributions

Miranda C - Conception, planning (study design), acquisition, analysis, data interpretation, and writing of the work. Paranhos J, Hasenclever L – Conception, planning (study design), and writing of the work. All authors approved the final version of the work.

Conflict of Interests

The authors inform that there is no potential conflict of interest with peers and institutions, politicians, or financial in this study.