



Drug prices: how they are established and existing price control systems

Precios de los medicamentos: cómo se establecen y cuáles son sus sistemas de control

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ABSTRACT Price is one of the main barriers of access to medicines. It is therefore important to understand how prices are formed and what factors determine the amount, as well as what interventions and regulations are the most appropriate considering their effects on access, innovation, local production and other potential objectives of drug policy. Economic analysis has developed a set of market models that can explain the behavior of prices, although actual markets diverge substantially from the theoretical models. Price regulation is justified by the so-called "market failures." Price regulation based on the cost of production, the most traditional form of price control, has fallen into disuse in favor of systems of international reference pricing and value-based pricing.

KEY WORDS Drug Price; Government Regulation; Control.

RESUMEN El precio es una de las principales barreras de acceso a los medicamentos. Por ello es importante conocer cómo se forman los precios y qué factores determinan su cuantía y también qué formas de intervención y regulación son las más adecuadas teniendo en cuenta sus efectos, tanto sobre el acceso, como sobre la innovación, la producción local y otros posibles objetivos de la política de medicamentos. El análisis económico ha desarrollado un conjunto de modelos de mercado que permiten explicar el comportamiento de los precios, aunque los mercados reales divergen sustancialmente de los modelos teóricos. La regulación de precios está justificada por los llamados "fallos de mercado"; la regulación de precios basada en el costo de producción, la modalidad de control de precios más tradicional, ha caído en desuso a favor de los sistemas de precios de referencia internacionales y por la fijación del precio basada en el valor.

PALABRAS CLAVES Precio de Medicamento; Regulación Gubernamental; Control.

INTRODUCTION

Prices have been, for quite a long time, one of the main access barriers to medicines and a growing challenge for the sustainability of the publicly funded universal health systems. Over time, the public debate on this issue has focused on specific cases of drugs or groups of prescription drugs (such as antiretroviral, oncologic, orphan, and biologic, among others), which have treatment prices extending into a five to six figure dollar amount for a year of treatment per person.

The formation of the price of the new drugs, which are usually protected by exclusivity rights, is quite different to the formation of the price of those drugs that have been in the market for many years, whose exclusivity rights have expired and which are, therefore, subject to the actual or potential competition of generic drug providers. Although the lack of access to medicines due to high prices is generally associated with new drugs and the exclusivity rights that protect them against market competition for some time, in many countries, the price is also an important access barrier to the medicines whose exclusivity rights have already expired.^(a)

This is because, although competition may force down the ex-factory price of the product toward a level near the production cost, there are other factors, such as distribution mark-ups or taxes, which might make drugs unaffordable to a substantial part of the society, especially when drugs are not supplied to the population free of charge or at a price partly subsidized by a health system.

Finally, access to drugs depends on factors other than the out-of-pocket cost paid by users, such as access to health services, distance to dispensaries, treatment acceptability, and so on.

But, although access to drugs depends on a broad number of factors, prices are, undoubtedly, a key factor. It is therefore important to understand how drug prices are formed in order to identify or to develop forms of government intervention that could modify these prices in the best way from a social welfare perspective. This intervention should consider the affordability of drugs and the sustainability of the health systems, as well as the preservation of an adequate level and objectives of innovation, and finally, the protection and development of the national industry.

Many of the frequently asked questions that arise on the debate about drug prices include: What are the causes of high prices?⁽¹⁾ Are high prices justified? And more specifically, are high prices an essential condition to ensure research and, ultimately, the innovation desired by the society as stated by the industry?⁽²⁻⁴⁾ Is price regulation a proper mechanism to keep prices at an efficient and affordable level? If so, which kind of regulation is the most adequate?

All these questions are complex and do not have a unique or simple answer. The proper answers vary according to the type of drug, the characteristics of the country, and the drug policy objectives, among other factors. In this article, we will first attempt to describe, from the economic analysis perspective, how drug prices are formed in the absence of regulations and second, the pros and cons of the different regulation types which have been applied or proposed.

In fact, most industrialized countries with a publicly funded universal health system, somehow regulate drug prices. For this reason, it is difficult to obtain conclusive evidence, in a strict sense, of how prices would behave in the absence of regulations. It is not easy either to obtain conclusive evidence of the effects of regulations, given that there are no two equal regulatory systems, even under the same name, and this is why the results cannot be generalized to a generic type of regulation.

On the other hand, the actual enforcement of regulatory norms frequently differs a lot from the regulations established under formal legislation. It is also frequent that the regulations are construed in different ways and the decisions made by the regulator are discretionary and highly unpredictable. In addition, the regulatory decisions are not often very transparent. All in all, when trying to analyze the effects of a price regulation system, researchers often do not know precisely which specific mechanisms are being analyzed under a determined official name.

HOW ARE DRUG PRICES SET?

Economic analysis attempts to explain the behavior of markets, that is, which factors account for the prices and the quantities which are exchanged.

In order to do so, the economic analysis has developed a series of theoretical models of market structures which allow to make predictions that can be contrasted with empirical evidence.^(b)

The basic market structures are 1) perfect competition, 2) monopoly, 3) monopsony, 4) oligopoly, and 5) oligopsony. These structures share certain assumptions, such as the rationality of the economic agents; that implies that suppliers and consumers try to maximize the benefits or the profits, respectively, or that they generally behave in a predictable manner subject to the conditions specified by the model.

The main differences among the former structures are the existence of: a) multiple suppliers and consumers (perfect competition), b) one supplier or consumer (monopoly and monopsony), and c) a few suppliers or consumers (oligopoly and oligopsony). In general, market models assume that the real characteristics of all the goods exchanged in the market are the same and, as a result, the goods are homogenous and undistinguishable, which in the case of drugs it would imply that all units have the same quality, efficacy, and safety. Some market models accept the existence of product differentiation, which implies that, although goods are homogeneous, the publicity and the brands manage to make consumers perceive them as different, which can create brand loyalty. The simplified versions of most of the models assume that agents have accurate information of the features and the existing prices of the goods.

Perfect competition

Theory predicts that under perfect competition a single price will exist – the equilibrium price – which enables companies to make normal profits, understood as the normal benefit that encourages entrepreneurs to continue their business. However, it should be noted that, even if there is competition among manufacturers, the price differences paid by consumers in a country may be substantial if there is no competition in the wholesale and retail markets as well.

In the case of drugs, this market structure may be an acceptable representation of the market of a multiple source drug, a drug whose patent has already expired (generic competence), where there is a high

number of manufacturers and consumers and drugs are sold under their International Nonproprietary Name (INN). Initially, in this case, there is no incentives for the companies to advertise their products as the possible effects of advertising would not only benefit the company spending money in publicity, but would spread to all the companies in the market.^(c) In any case, including the name of the manufacturer along with the INN on the drug packaging somehow helps differentiate the product.

Monopolistic competition

If products are differentiated, perfect competition turns into monopolistic competition, i.e., a competitive market for generic drugs of a certain brand – that is, multiple source products of a single drug, each one sold under a fantasy name. This market structure is characterized by the differentiation of products and the likely loyalty of consumers towards a certain brand. In this type of market, the price of the products with identical features may differ substantially. The companies that invest more and in a more effective way in advertising will initially incur in higher costs but, in the end, they might generate higher profits, if publicity sufficiently increases the demand of the product as well as the price these companies can charge in comparison with their competitors.

Monopoly and monopsony

A monopoly may be thought of as the market of an innovative drug during its market exclusivity period, which has no substitutes or therapeutic equivalents equally effective and safe. In this type of market, the supplier can determine the price or the quantity: if the supplier establishes a higher price, the number of products sold will be lower and vice versa. A reasonable entrepreneur would typically not establish the highest possible price but a price that maximizes their benefits. On the other hand, monopolistic entrepreneurs are clearly interested in advertising their products because the profits and the additional benefits derived from the increase of the demand due to publicity are entirely for them. In addition, the brand loyalty that may be obtained during the exclusivity period will

help entrepreneurs keep market power when the period of exclusivity ends.

The markets of those drugs undergoing a period of exclusivity which are offered by a sole provider are potentially monopolistic markets. However, the degree of market power held by the drug owner depends on the existence or non-existence of other drugs, known as "Me-too" drugs, prescribed for the same conditions, which are good substitutes and competitors of the drug having exclusivity. In any case, the experience seems to show that drugs prescribed for the same conditions and having similar effects, which are protected by exclusivity rights, do not usually compete in price as much as in publicity and advertising in order to achieve the best possible differentiation of the products.

The past situation of the statins or the Angiotensin Converting Enzyme inhibitors (ACE inhibitors) and, in general, the markets of Me-too drugs, in which all or most of the molecules have patent protection, conforms quite well with the oligopoly structure with product differentiation which, in practice, can coexist with little differences in the real characteristics of the products. As the exclusivity of several molecules expire and they enter the market of the competitors, the market structure turns into a combination of oligopoly, monopolistic competition, and perfect competition.⁽⁷⁾

The economic theory states that the price of those drugs under patent, without substitutes or close competitors, which are then in a monopolistic situation, will be established at a level that helps maximize the benefits, which is normally a price much higher than the direct production cost. On the other hand, the theory states that if the monopolist entrepreneur can divide and isolate the markets of their products, the entrepreneur will adopt the strategy employed by the discriminatory monopolist, which consists in establishing for each market the price that maximizes the profits. This may lead to the existence of different prices in each market segment within the same country.

In the US, the public sector is legally entitled to pay the lowest market prices. The most important private health insurers also obtain remarkable discounts in relation to the catalog of drug prices of the firm while individuals, who have a lower income, cannot afford a private health insurance, and are not entitled to a public insurance, are frequently the ones paying the highest prices.

At an international scale, high-income countries which have the financially strongest health systems would initially be expected to be the countries paying the highest prices. However, this prediction is not supported by evidence, nor even theoretically substantiated; in low-income countries there is often a great inequality in the distribution of personal income and a very poor health system. In this case, the monopolist entrepreneur may find it more beneficial to sell the products at very high prices in low-income countries, these prices being even higher than the prices in high income countries. These products will be affordable only for a minority with high purchasing power but not for the majority of the population nor for the health systems of the country.

A national health system with a single centralized purchasing mechanism would be a clear example of monopsony: the consumer would have a strong potential market power to the extent that, in many cases, the consumer may temporarily impose prices which are lower to production costs and generate losses to several companies. It is clear that this type of situation may not be sustained for a lot of time given that companies would end up leaving the market and problems such as lack of availability or shortage of drugs would come up.

Theoretical market models and actual markets

There is large theoretical consensus regarding the market behavior and more specifically, the price formation expected for a set of basic market structures: perfect competition, monopolistic competition, monopoly, and monopsony. For instance, it is accepted that perfect competition results in a single price for all the market. However, there is far less consensus in the case of oligopolies, composite market structures (monopoly-monopsony, for instance), and in general, models in which simplifying assumptions are left aside in order to make them more similar to the characteristics of the actual markets, for instance, markets models with limited transparency, which do not comply with the condition of perfect information that characterizes the theoretical model of perfect competition.

On the contrary, the behavior of actual markets often differs significantly from the theoretical market models which attempt to characterize them, and specially, from the basic versions described in standard economy manuals. In drug markets, the differences are especially visible due to certain particularities of the sector: for instance, in the case of prescription drugs, it is not the consumer who decides or selects which drug to take, but the physician on behalf of the consumer.

This legal regulation is justified by the limited information that consumers have about their "necessities" (health status and diagnostic) as well as the characteristics (efficacy and safety) of the drugs available to meet such necessities.

However, the level of information that the prescribing physician has is also far from perfect. There is an obvious asymmetry of information between prescribing physicians and pharmaceutical companies. In the end, pharmaceutical companies generate and spread the information about the efficacy and safety of drugs, which comes, to a great extent, from the research studies on drugs done by these companies. Due to the lack of information, buyers frequently believe that the higher the price of the drug, the better the quality. This behavior, which the economic theory defines as irrational and which has no place in the standard models, frequently happens in real life. Another peculiar characteristic of this sector is the high level of public financing, which frequently causes both the prescribing physician and the consumer to be insensitive to prices when they decide to use a drug.

The cost structure in the pharmaceutical industry

When we analyze how drug prices are formed and which may be the most suitable regulatory mechanisms, we have to take into account all the elements that form the final price for the consumer or for the health system: the manufacturer's price, the wholesale and retail distribution margins, the taxes, among others. The pharmaceutical companies along with the market regulators are directly responsible for the formation of the import prices and the so-called "ex-factory prices."

The large pharmaceutical companies that base their business model on the constant commercialization

of new drugs (big pharma)^{d)} have a cost structure in which the prevailing costs are those associated with Research and Development (R&D), the costs of information, advertising and marketing, and the costs of intellectual property management. These types of costs are not objectively and unequivocally attributable to a specific drug and, by no means, to a drug unit.

For instance, the cost of all R&D activities (including the cost of the projects which end up with a successful market product and the cost of the projects which fail at any stage of the R&D process and never reach the market) has to be recovered through the sales of the commercially successful products. In other words, the price of these products must logically recover the cost of both the successful and the unsuccessful projects. Instead, in the companies that produce generic drugs, especially in those companies in which drugs are sold under INN, the prevailing costs are those derived from direct manufacturing.

Distribution margins are, generally, established by the public regulator and they account for a specific percentage of the ex-factory price. In other cases, the distribution margins are free, they are established as a result of the interaction of consumers and suppliers in the distribution market, in which the competence levels vary a lot among countries.

In a great number of countries, the retail sector – the pharmacies – has changed from its traditional, highly atomized structure of small, independent establishments, experiencing the growth of the largest commercial chains which often integrate the two traditional distribution levels: wholesale and retail. It is common to find the distribution sector divided in two big blocks: the independent pharmacies sector, where the small establishments prevail, and the large chains sector, which is usually bigger in terms of global sales, characterized by a high technical level and a small number of companies hold a major part of the market share. The tendency to the vertical integration in the distribution sector has many positive aspects: it helps rationalize the retail sector and obtain economies of scale by means of improving the logistics and the management systems but, at the same time, it tends to reduce the level of competition in the sector, which is likely to increase the intermediation margins and, consequently, the prices for consumers.

Finally, the indirect taxes on drug prices also have to be considered. For instance, the Value

Added Tax (VAT) is applied to drugs in a few countries while, in other countries, it is not. These taxes are usually regressive, as the majority of indirect taxes, meaning that for the families with lower income level they represent a relatively higher expense and they also exert a higher dissuasive effect over consumption. This is why many experts and scholars of this sector are against the idea of applying these taxes within the drug sector.

DRUG PRICES REGULATION

Is the regulation of drug markets justified?

Most of the countries do not allow pharmaceutical companies to freely set drug prices, in particular, for drugs undergoing a period of exclusivity and which are financed by the country's public healthcare system.^{(e)(8-10)} The main reason for this decision is that actual drug markets do not work in the way the theoretical models have foreseen, especially the perfect competition model, which justifies the superiority of a non-regulated market system.

It is widely accepted that the main goal of price regulation is to bring the price as close as possible to the efficient equilibrium price which characterizes a perfectly competitive market. Nonetheless, this principle can also be balanced by other drug policy objectives, mainly the protection and promotion of the national industry.⁽¹¹⁾

Drug prices depend on the market conditions of the country, as well as on the regulatory mechanisms implemented and on how these mechanisms are applied in the actual market. The capacity to regulate prices is determined by the regulator's bargaining power at two levels: firstly, in relation to other countries and international organizations, concerning the implementation of certain regulations and policies and, secondly, in relation to companies in regard to specific drugs.

Globalization of the drug market, more specifically, the standardization of patent regulations and other exclusivity rights achieved through the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) administered by the World Trade Organization, undermined the bargaining power of regulators and consumers especially in developing countries with respect to big pharma. Before the TRIPS agreement,

countries used to independently adopt the patent system they thought to be more convenient for their specific characteristics and their industrial and economic level of development. Under the TRIPS agreement, developing countries are forced to accept minimum criteria, which guarantee the interests of developed countries having a strong pharmaceutical industry. These regulations did not need to be observed by the current developed countries when they had a level of development equal to the present level of current developing countries.⁽¹²⁾

Finally, it should be mentioned that, though the market failures and the pursuit of other political objectives may justify public intervention in drug markets, the regulation may also have equal or bigger failures than those observed in an imperfect market, because regulators may not have the necessary information to do their job well or may not have the knowledge and skills to use such information adequately. Organizations in charge of regulations may be vulnerable to corruption or may be a target to be "captured" by companies persuading regulators to work in favor of their own objectives, instead of working for users or for the society as a whole.⁽¹¹⁾

In view of these market failures, price policy may adopt two non-exclusive but complementary approaches. The first approach consists in replacing the market mechanism through administrative decisions of regulation or price control. The second approach consists in trying to change the market conditions which limit or block competition to make them work in a more competitive and efficient manner.

There are different criteria and strategies applied to the direct regulation of drug prices. There follows a description of some of the most common pricing strategies used.⁽¹¹⁾

Price regulation based on the cost of production (Cost-plus pricing method)

The oldest price regulation strategy, though it has currently fallen into disuse, is the method under which the maximum selling price is fixed according to the cost of production criterion. This strategy consists in identifying the (necessary) costs that a company has to incur to manufacture

a product and adding a maximum mark-up to the production cost. The maximum selling price permitted is determined by doing this addition. Usually, the estimate applied to calculate the maximum selling price of single companies which manufacture (or import) a certain drug is based on the average cost of the industry. In other cases, the estimate is calculated with the costs declared by each company in particular.^(f)

As noted above, most of the costs incurred by companies which develop new drugs cannot be allocated to a specific product. It is clear that, establishing the price of their products using R&D costs incurred for producing this specific product does not make much sense. In order to avoid this issue, until recently, the United Kingdom has applied a regulation system based on global costs of all the drugs a company sells to the National Health Service, to which a markup percentage is added.⁽¹³⁻¹⁶⁾

On the other hand, not all the expenses that a company has to incur are necessary to manufacture a product and, therefore, from a social interest perspective the inclusion of these expenses cannot be justified. In the practice, it is complicated and, to a certain extent, arbitrary to apply a cost of production perspective to determine which of the costs that the company has incurred are necessary and acceptable and which are unnecessary and dispensable so as not to be taken into consideration for estimating costs.^(g)

In view of the characteristics of the costs incurred by pharmaceutical companies, it is clear that the regulation of the price based on the cost of production is not a good option. On top of that, if the cost declared by each single company is taken as reference, the most inefficient companies may be rewarded.

Price regulation based on equal or similar treatments

Other criteria applied to establish the maximum selling price are taken as reference: the price of similar treatments (internal) and adopting international prices as reference (external). The first criterion is quite obvious: the price of a new drug is established according to the price of the drugs currently approved for sale or, in general, to the cost of treatments, which are being prescribed and

which have similar effects to the new drug. This criterion, i.e., not accepting a higher price than the one established for similar available products, is relatively reasonable, nonetheless this principle cannot be applied when the new product has therapeutic advantages that want to be boosted. On the other hand, the criterion applied in France is also reasonable: when a new drug has an equal effect than a product that already exists in the market, to be publicly funded, the launching company has to accept to sell this drug for a price lower than the price fixed for the available drug.

International Reference Pricing (IRP) is the practice of using the price of a drug in a group of countries in order to derive a benchmark for certain country. In practice, a country basket and an algorithm or criterion are established to estimate the regulated price, taking the countries included in the basket as reference: the reference price may be calculated as the average of all the countries, the average from the bottom three countries, the lowest price, and so on. This approach has no logic or economic grounds, apart from trying not to pay much higher prices for the same drug than the average prices set for this drug in the benchmark countries. In fact, the national regulator implicitly decides not to apply a price policy following their own judgment and applies the standard results of the policies – reasonable or arbitrary – followed by the countries included in the basket.⁽¹⁷⁻¹⁹⁾

One of the ostensible issues of the IRP criterion is that it can influence companies to establish a single international price or to, at least, converge in the international prices,⁽²⁰⁾ in order to prevent the “spillover” effects or, in other words, to prevent high income countries adopting the IRP system to include low-income countries when estimating the price. To prevent this effect, companies may react by imposing a higher single price than the price they would accept in the absence of an IRP. Alternatively, they can delay or even stop marketing these new drugs in low-income countries.

Price regulation based on value

Possibly, the most reasonable system and the strategy that, in theory, follows the logic of a common consumer is the implementation of a value-based pricing scheme.⁽²¹⁻²³⁾ One of the traditional modalities of this

approach is the use of an economic evaluation (or pharmacoeconomics) to account for the decisions made when allocating resources in the health sector. To put it simply, an economic evaluation estimates and values the additional health benefits (or effectiveness) and resource effects (costs) of a new drug and compares the resulting incremental cost-effectiveness ratio (ICER) with a fixed threshold. If the ICER found at the price requested falls below this threshold, the requested price is accepted or, alternatively, the drug is accepted for inclusion in the list of essential medicines, or in the positive list, in general, in the drug's public financing scheme granted by the healthcare system. However, this regulation system is quite time consuming, and it requires to be implemented by a regulatory authority with high quality standards and experts able to conduct accurate evaluation studies or to validate the studies submitted by the companies marketing the product.^(24,25)

Other intervention mechanisms affecting prices

Establishing the price of each single product through an administrative decision is just one of the many instruments a country has to influence drug prices. As noted above, authorities may influence prices by changing the market conditions, for example, making the public financing conditional on the drug price, improving the information provided to customers, or giving incentives to users to be sensitive to prices and therefore, make efficient decisions, among other examples. All these measures are not aimed at replacing a poor market operation with regulations, but to make the market function more adequately according to competitive criteria.⁽²⁶⁾ The most important selective financing measures will be explained below.

Positive or negative lists

Granting public financing to a drug implies increasing the demand of the drug above the level it would have if the users were paying directly for the whole price of the drug. Should the authorities not fund the, say, highly expensive or poor cost-effective drugs, they would indeed be applying an

incentive for companies to lower their prices in order to receive public financing. Up to the time being, the United Kingdom has been using a two-stage price setting system. In the first stage, as explained above, regulators do not determine the price of each product, but they set a cap to the benefits or total profits that a pharmaceutical company may reap from its sales to the British National Health Service. In the second stage, the National Institute for Health and Care Excellence (NICE) determines, by conducting evaluation studies, if the cost-effectiveness ratio has acceptable value in respect to the accepted threshold, i.e. between 20,000 and 30,000 pounds per quality-adjusted life year (QALY).

Copayment or partial subsidy

A similar approach to the method explained above is that based on the use of cost-sharing, that is, to divide the drug price between what the user and the health system pay for it. The more expensive the co-payment is (that is, the smaller the subsidy received), the lower the rise in demand produced by the public financing. In France, higher co-payments are actually paid when the therapeutic effect of a drug has low health benefits.⁽²⁷⁾

Internal reference prices

This method can be considered an alternative to co-payment, which is sometimes defined as a voluntary/avoidable co-payment. Under this scheme the health system allows companies to establish at will the selling price for each drug but limits the public financing this drug will receive to a fixed value: the reference price.^(b) This value is obtained by grouping drugs according to a criterion of therapeutic equivalence and establishing the subsidy proportion they received from the health system using the lowest prices of the group of products as reference. The public financing, for example, can be fixed as 30% of the lower price units. When a company decides to fix the price of a drug above the reference price, users will have to pay the difference between the reference price and the price fixed by the company, or to accept the cheaper, therapeutically equivalent, substitute. Under this system, most of the companies tend to fix their prices on the reference price, as they fear that consumers will

refuse to pay the difference and decide to buy the products without a co-payment.⁽²⁸⁾

Risk-sharing agreements (RSA)

Risk-sharing agreements are agreements between the health system and a single company under which the price that is actually paid by the health system is not fixed but depends on factors that will come up after selling the drug. For instance, the price accepted can be influenced by a maximum number of units sold. If eventually the number of units sold is higher than the number foreseen, the price – and therefore the total payment – will be cut down according to a rule fixed before. Under other more sophisticated RSAs, payment may depend on the clinical effectiveness the drug has on each patient; for instance, the health system only pays when the treatment has a positive effect on the patient consistent with certain pre-established parameters.⁽²⁹⁾

This scheme can be considered an alternative or a complement to the price based on the value, and it was originally applied when a new drug ICER fell above the cost-effectiveness threshold established. The RSA entails, in its usual application, an opaque real pricing reduction, without changing the official price. This characteristic makes this scheme highly valued for companies as, in this way, they can avoid the effects a reduction in price can bring about in other countries which apply IRP. Nonetheless, the confidential nature that goes with these agreements entails a serious issue, given that it prevents the price transparency, and consequently, it limits the market competition and the explanations that regulators and promoters may give.

Bidding and auction mechanisms

These mechanisms force price competition among bidders (drug suppliers). Under the more sophisticated versions of these mechanisms, biddings do not compel the health system to acquire fixed units of drugs, but the winner or winners become obligatory or preferred suppliers for the health system units. A potential issue of this approach is the need of ensuring the quality of the product and supplier that is awarded the contract (usually, at the lowest price) and that the supply meets the system needs

and demands in order to prevent shortage situations. One of the restrictions of these mechanisms is that it requires the participation of many independent bidders and, therefore, it cannot be applied to drugs under market exclusivity.

Generic drugs policies

These policies are a group of supply and demand measures that intend to boost the use of generic drugs, especially those which are marketed under International Non-proprietary Name (INN) or generic name, rather than the original and generic brand products, which are usually more expensive than the non-proprietary products. The measures adopted under a generic policy scheme include: giving generic drugs priority during the registration proceedings and the public financing allocation, encouraging physicians prescribing of generic drugs, replacing brand name drugs in retail pharmacies, providing reliable education and information to physicians, pharmacists, and users, and developing an adequate administration of intellectual property which help the drugs to enter the generic market as soon as possible, including the possibility to issue obligatory licenses. As in the previous system, all these measures try to guarantee a more competitive market.

GLOBALIZATION OF DRUG MARKETS AND THE INTERNATIONAL STRUCTURE OF PRICES

The pharmaceutical market is one of the most globalized markets, where a small number of multinational companies that bring together the global production and sales and, especially, the development of new drugs, co-exist with a huge number of small national companies. The development of new drugs is the key task undertaken from a global perspective.

In the past, drug markets were segmented, and multinational companies independently established an usually different price for the same drug in each country; in fact, the prices fixed for the same drug substantially varied from one country to another. Currently, markets are becoming increasingly interdependent and prices tend to converge in one price. Several facts contributed to this trend,

such as the innovation which is a global public good, the progressive reduction in fees and other barriers to the international trade, and the global unification of healthcare practice standards and intellectual property regulation. Another fact that contributes to the convergence of international prices is the international reference price mechanism which is adopted by more and more countries every day: companies fear, with good reason, that if they lower their prices for poorer countries, richer countries may claim the same price for them.

Given that innovation in drugs and healthcare technologies in general – as any other form of information and human knowledge – is a public good, it could be more efficient and fair for all the countries to ensure the access to this innovation and to contribute to the financing of the relevant R&D according to each country's economic capabilities, as it is handled in the United Nations Organization (UNO). For that fair access to be possible under the current system of incentives to innovation based on monopolistic intellectual property rights, an equitable price system that respects differences in purchasing capacity would be necessary. In other words, it would be necessary to have a scheme of different prices for the same drug, whose amount would depend on an agreed purchasing power indicator (for example, per capita income). However, this possible solution clashes with the globalization of markets and the single world price trend.

FINAL COMMENTS

Drug prices are one of the main access barriers to drugs and imply a challenge to the economic sustainability of the healthcare systems. One of the factors that limits the competition in the drug markets is the public financing of drugs, aimed at ensuring an equitable access to medicines and healthcare consumption. Public or private financing by a third party or insurer enables consumers of medicines to make consumption decisions without budget restrictions. Another factor that limits competition is the system of incentives to innovation, based on patents and other exclusivity rights or privileges, which easily turn the drug markets into actual monopolies.

Health authorities may deal with the issue of highly expensive prices following two strategies that are complementary: applying measures to make the actual markets more competitive or substituting the market mechanisms for an administrative regulation of prices.

Drug markets have different characteristics. On the contrary, drug policy objectives also differ from one country to another. Therefore, there is not a unique approach or solution to all of them. First, it is necessary to differentiate single-source markets from multiple-source markets. In single-source markets, it is usually possible and advisable to promote competition policies from the supply side and from the demand side perspective.⁽²⁶⁾

Instead, in markets under exclusivity it is difficult to promote competition from the suppliers side, except if radical measures are adopted, such as establishing compulsory licenses, which let competitor products enter the market. In any case, in markets with a single supplier, supply policies of a pro-competitive nature, such as providing better information to users and physicians, giving them incentives to make users and physicians sensitive to drug prices, or establishing selective financing mechanisms based on the therapeutic value or the cost-effectiveness ratio of treatments can indeed be applied.

In any case, to curb the prices of drugs subject to market exclusivity, it is probably indispensable to apply administrative regulation of prices. Currently, the two main options to achieve this goal are the IRP system and value-based pricing. Apparently, the IRP system can be adopted more easily, as its main requirement to the regulator is to have access to an adequate basket of international prices and to apply the algorithm or rule to calculate the national price. The IRP system does not have any economic logic nor a theoretical foundation. On the other hand, it is becoming progressively difficult to have access to real international transaction prices in most countries because of the confidential nature of discounts and other selling agreements which are imposed to healthcare systems by the pharmaceutical companies as a condition to negotiate some discounts. Value-based pricing has a clearer theoretical foundation – to pay more for medicines which as defined as having a higher value to patients and society; it also enables a more transparent and predictable

price regulation. Though at the beginning it might seem to bring about heavy workload for the regulator – or for the agencies in charge of conducting the relevant studies for evaluating health technologies – in practice, the necessary effort is embraceable, due to the fact that regulators may need to decide to conduct evaluation studies, to assist pricing and reimbursement decisions, only on drugs that make a substantial contribution to people's health. Furthermore, companies could be asked to conduct and submit evaluations justifying the contribution and effectiveness of the new medicines, as well as the prices of better treatments for existing therapies. Regulators, with the collaboration of agencies in charge of evaluating technologies, could limit their job to develop the required methodology to conduct these evaluations and to validate the evaluations the companies submit before them.

For a country with limited experience and resources a pragmatic combination of approaches may consist in sequentially adopting both mechanisms, first the IRP system and later conducting – or request the product owner to conduct – an economic evaluation study for those drugs that entail a high additional cost and a limited or unknown therapeutic contribution.

Another feasible approach, which indeed merges both perspectives, would be to establish an international reference price based on the

prices of a country basket which has adopted a transparent and explicit value-based pricing. Then, the initial reference price obtained could be adjusted to the country's purchasing capacity using a relative wealth index, such as the purchasing power parity. Furthermore, the studies conducted in the reference countries in the basket could be gradually replicated using local information and making the necessary adjustments, or even conducting original evaluations for that country.

In any case, an efficient and fair solution, at a global level, for setting drug prices is something that could hardly be achieved through the regulation of prices independently conducted by national authorities. In my opinion, a satisfactory long-term solution requires, in the first place, a coordinated action undertaken by the consumers at an international level, in a way that the global supply formed by multinational companies faces the demands and requests of a global demand of users and payers from a set of coordinated and organized countries. In the second place, a substantial change in the patents system is required as well as the creation of other mechanisms to promote and reward innovation,^(30,31) in line with the non-monopolistic incentives systems which establish, with respect to the R&D, the adequate level and guidance as well as a fair and international financing that guarantees a fair access to innovation for the population from all the countries.^(5,12,32-34)

END NOTES

a. The first case is known as drug product manufactured by a single company (single source drug) and the second as drug product manufactured by more than one company (multiple source drug).

b. This analysis is based on the standard or conventional microeconomic theory. There are several articles and free introductory courses available online, which can be used by a reader without previous information on economic analysis to delve into or verify the studies included in this article. Among the several intermediate handbooks that are used in courses of microeconomics the following authors can be mentioned: Varian⁽⁵⁾ and Stiglitz and Walsh.⁽⁶⁾

c. It is possible that all the suppliers of a certain drug agree upon advertising their drug collectively. However, if one or several companies refuse to pay for the collective advertising, it would be difficult to exclude them from receiving the benefits.

d. It is important to bear in mind that a new drug is not necessarily an innovative drug (which entails a therapeutic contribution in respect to the existing options in terms of better effectiveness, fewer secondary effects, among others).

e. The USA is, in that sense, one of the few, but relevant exceptions, due to the market volume – almost half of the global pharmaceutical market – to the importance of the R&D pharmaceutical industry, and to the unshakable support that the

United States government provides to the interests and demands of that industry, at the expense of the needs and priorities of society in its own country and abroad.

f. It was, for instance, the case of Ecuador up to 2014. The main issue of this price regulation strategy is that it does not encourage companies to increase efficiency by reducing the cost of production.

g. Following the reasoning explained above, the efforts made by the great pharmaceutical industry in an attempt to justify high and increasing prices of new drugs by stating the allegedly high and increasing costs arising when introducing a new product in the market do not seem reasonable. The reduction in the number of new drugs and in their therapeutic contribution, despite the sustained and even increasing level of investment in

R&D, probably occurs as a consequence of several factors. According to certain authors, one of the most important factors is that the current scheme to incentivize innovation is inadequate and bankrupt. It consists in granting patents and other monopolistic rights to the new products, which frequently entail a minimum or none contribution in terms of therapeutic effects and, on the contrary, they foster activities as the development of Me-too drugs or defensive patents. In this sense, the allegedly high and increasing cost of launching a new drug to the market can be an argument both to justify the high prices of drugs and to question the efficiency of the industry and of the current incentives to innovation scheme.

h. It would be more appropriate to name this value as "reference financing," as indeed it does not determine directly the price but the value that would be funded by the health system.

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