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CURRENT OPINION

The End of the International Reference Pricing System?

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Abstract All 28 EU member states except Sweden and the UK apply international reference pricing (IRP), international price comparison, external reference pricing or cross-reference pricing. The attractiveness of using prices of other countries as a benchmark for decisions within a national price control is obvious. Alternative models for price and reimbursement decision making such as value-based pricing (VBP), i.e. cost-effectiveness analyses, are more complicated. However, IRP provides incentives for stakeholders to take action not in line with optimal (welfare-maximizing) pricing. IRP is costly for two reasons. First, manufacturers are incentivised to limit or delay access to new innovative treatments in countries with small markets and/or a low income, which can be costly in terms of loss of health. Second, all countries also experience a loss of welfare (health) because IRP reduces the opportunities for differential pricing (Ramsey pricing), i.e. using the fact that the ability and willingness to pay differs between countries. Thus, IRP results in less sales revenue to finance research and development of new innovative drugs. We can now observe that payers and manufacturers are engaged in different types of risk-sharing schemes, price–volume negotiations, payback arrangements, confidential discounts, coverage with evidence developments, etc., all with the purpose of returning to the old model of price discrimination and Ramsey pricing. Shortly, real prices for use in IRP systems will cease to exist and, thus, we expect to soon see the end of IRP, a new system for price discrimination and an increasing demand for VBP.

Key Points for Decision Makers

International reference pricing (IRP) creates two types of losers: (1) patients in low-income countries and in those with small markets will experience limited or delayed access to new innovative treatments; and (2) populations in high-income countries that can afford the drugs will not be able to pay as much as they want to finance the research and development of new innovative drugs.

Both payers and manufacturers are engaged in finding payment models in which the real price will differ from the official list price used in the IRP system.

In the future, real prices for use in IRP systems will cease to exist and, thus, we expect to see the end of IRP, a new system for price discrimination, and value-based pricing.

1 Introduction

International reference pricing (IRP), international price comparison, external reference pricing or cross-reference pricing have been a fact of life for multinational pharmaceutical companies for many years. In Sweden, The National Corporation of Swedish Pharmacies used a

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median price model in negotiations with industry to set 'reasonable' prices as early as 1971. However, the opportunities for price comparisons were limited at the time due to the small number of drugs available in many countries at the same time. With the creation of a procedure for mutual recognition for innovative drugs in 1975, the EU internal market in 1992 and the establishment of the European Agency for the Evaluation of Medicinal Products in 1995, most important new drugs become available at the same time in many countries. Thus, IRP developed as an important instrument in pharmaceutical policy in the 1990s, focusing on the management of individual drug prices, rather than the average price level for drugs.

The attractiveness of using prices in other countries as a benchmark for decisions within a national price control system is obvious. First, it appears simple and, second, it provides reassurance for the general public that prices are not higher than in other countries. Alternative models for price referencing based on data on costs, profits and cost effectiveness (value-based pricing) are complicated, open to manipulation and have less face value. There is also the additional attractiveness that the IRP model can be used to drive prices down and, at least in the short run, can produce explicit cost savings. The popularity of the model with policy makers concerned with cost containment is thus understandable.

Its popularity with economists is more guarded due to the potential negative effects on dynamic competition in the longer run. Another concern is the opportunities to manipulate the model through the strategic launch of a new product in different markets. The increasing popularity of IRP has stimulated the development of models and databases in pharmaceutical companies and consultancy firms aimed at managing the sequence of introduction of new drugs in different countries to minimize the negative impact. The success of IRP has been limited due to unpredictable changes in currency rates and government policies. IRP has thus been costly and has mainly created random gains and losses without providing any solution to the issues related to pricing and introduction of innovative pharmaceuticals. Sweden has not adopted IRP; however, discussion is ongoing as to whether Sweden should join the other 27 European countries by applying some version of IRP.

This paper reviews the role of IRP in light of recent developments in the pharmaceutical market place, and it predicts that, despite its popularity, we may soon see the end of IRP as a useful instrument for pricing and cost containment.

In 2002, Sweden introduced a national agency—the Dental and Pharmaceutical Benefits Board, today known as the TLV—with the responsibility of deciding about reimbursement and a national public retail price for prescription drugs. Decisions should be made on explicit criteria of value, including cost effectiveness.

The international financial crisis in late 2008 slowed economic growth. The falling gross domestic product (GDP) in Sweden in 2009 saw pressure on cost containment rather than rational drug prescription. A report from the Ministry of Health and Social Affairs proposed that a new IRP system should be implemented for patented pharmaceuticals 5 years after launch in Sweden [1]. January 2013 saw the Government's Council on Legislation act on pricing and reimbursement of pharmaceuticals introduced [2].

Instead of IRP, a ceiling price model was introduced as a result of agreement between the government and LIF—the research-based pharmaceutical industry in Sweden. According to this agreement, the research-based industry is committed to lowering their prices for selected drugs, corresponding to Swedish kronor (SEK) 400 million (about €45 million) in lower sales revenues for 2014. For the years 2015–2017, new price cuts equivalent to an additional SEK 400 million take effect. If this does not happen, the government intends to once again raise the question of the introduction of IRP. In addition, the report suggests the TLV, in their reassessment of reimbursement decisions for new drugs, will compare the price level in Sweden with prices in other countries, which is also a form of IRP. The government's brief is not detailed; it essentially gives the TLV the responsibility for development of a value-based pricing and reimbursement system.

A recent report by the Swedish Association of Local Authorities and Regions (SALAR) [3] suggested modification of the procedures for pricing and market access in Sweden, whereby the TLV works as a consultant and delivers a report to SALAR, the county council organisation, for SALAR's negotiation of price and reimbursement with the manufacturer. The ongoing discussion and modification of the Swedish system for pricing and market access can partly be seen as a consequence of the IRP system, and we use some examples from Sweden to understand the impact of IRP.

The main purpose of IRP is to reduce the cost of pharmaceuticals. However, healthcare policy has several aims other than simply cost containment: rational prescription of pharmaceuticals (i.e. cost-effective prescription), and a dynamic system encouraging manufacturers to develop new innovative drugs. It is hugely important to understand how an IRP system influences the pharmaceutical market and its impact on all three, at least partly, conflicting aims. The purpose of this paper is to review the impact of IRP in light of recent developments in the pharmaceutical market place and to discuss how IRP complies with the goals of cost-effective and equitable prescription and a sustainable system encouraging the development of new innovative pharmaceuticals.

2 The Basic Mechanism of International Reference Pricing (IRP)

Assume we have three markets (three countries) of the same size for the same product (high-, middle- and low-income markets). Suppose further that a new drug has been developed that is equally effective in all three markets that enables patients to be discharged from hospital 10 days earlier than with usual care treatment. For simplicity, we assume that this effect represents the drug's full value, and we ignore that health improvement itself also commands a value for patients.

In-patient hospital care costs €700 per hospital day in the first country (high-income market), €500 in the second country (middle-income market), and €200 in the third country (low-income market). Cost differences for inpatient care varies, as the general wage and price levels differ between the three countries. One can say that the first is a 'rich' country and the third country is a relatively 'poor' country.

Assume that free pricing applies; the producer wishes to maximize revenue, while buyers of the drug (payers) in each of the countries want to pay as little as possible but still want access to the new therapy in order to satisfy patients' desire to access the best treatment possible.

In the high-income market, the value of the drug is €7000 because it can save 10 treatment days, each of which costs €700. One possible scenario is that the price for treatment with this new drug is set at €6000. This would mean either a surplus to consumers of €1000, which is refundable to the patients, or a profit for the healthcare payer. The €6000 price of the therapy is the revenue to the drug manufacturer to recover research and development costs, marketing, production, distribution, profits, etc. for the new drug.

In the middle-income market, the value of the drug is €5000. Although it can save 10 hospital days, the lower general wages and prices mean that a hospital day only costs €500. The value of the new therapy will therefore be less here than in the first market. One possible scenario is that the price for treatment with this new drug in this middle-income market is set to €4000. This means a surplus for consumers of €1000 per treatment and the drug manufacturer receives €4000 to cover their costs.

In the low-income market, the drug is only valued at €2000 because the 10 hospital days saved are only worth €200 each. Healthcare payers (or patients) cannot be expected to pay more than €2000 for the new therapy. The price is set to €1800; thus, the consumer surplus is €200 and revenue to the drug manufacturer is €1800.

How much then will total revenues be for the drug manufacturer? We sum the revenues in the three markets to €11,800 (6000 + 4000 + 1800). Note that this pricing strategy can only work if the seller has some market power, for example, due to a patent. The seller must also have some knowledge about the purchasers' willingness to pay; in this case, information about the cost offset from fewer days of hospitalization. The seller must also be able to prevent resale from one country to another, i.e. prevent parallel trade.

In an alternative scenario with price transparency and an IRP regulation policy, only one price will be seen in the three markets, as the drug manufacturer can no longer price discriminate between the markets. The manufacturer could set the price at such a low level that the drug can be sold in all three markets, e.g. €1800 per treatment. Total revenues would then be €5400 from all three markets, i.e. considerably less than the €11,800 gained via price discrimination.

The manufacturer could also choose to set the price to €4000 per treatment and sell the drug only in the high- and middle-income markets and exclude the low-income market. This would give a total income of €8000 (€2600 more than €5400).

However, this is not a particularly attractive pricing strategy from a social welfare perspective for two reasons. First, this pricing strategy means patients in the low-income market would not have access to the new medication. Second, the high-income market must be prepared to pay slightly more for the new drug treatment than they actually need to. This means the drug manufacturer will receive less revenue from sales and thus a smaller margin to use for research and development of new effective drugs in the future. We can therefore identify two losers: the patients in the poor country, and those in the wealthier countries who lose access to new and effective medicines the manufacturer has lost the incentive to produce. This simple analysis could explain the basic mechanism behind IRP and can be used to understand the incentives for strategic product launches and for launch delays and how these can affect the effectiveness of regulation. Figure 1 demonstrates price discrimination, and Fig. 2 shows a situation without price discrimination.

3 Use of IRP in Different Countries

The European regulated pricing model, or the EU pricing model, is associated with the introduction of IRP and parallel trade in Europe and a price corridor with small differences in price.

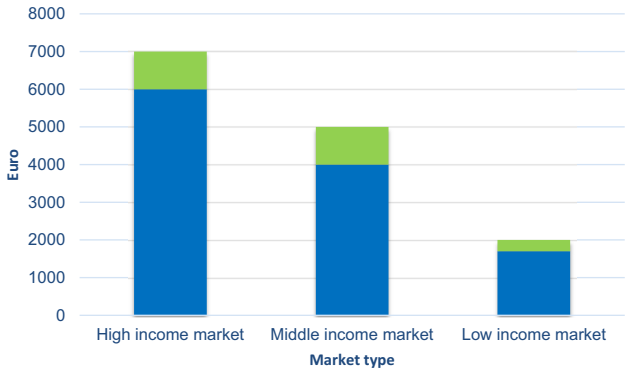

Fig. 1 Price of a hypothetical drug in a high-, middle- and low-income country with price discrimination. *Blue* is revenue to drug manufacturer, *green* is consumer surplus, i.e. value minus contribution to drug manufacturer

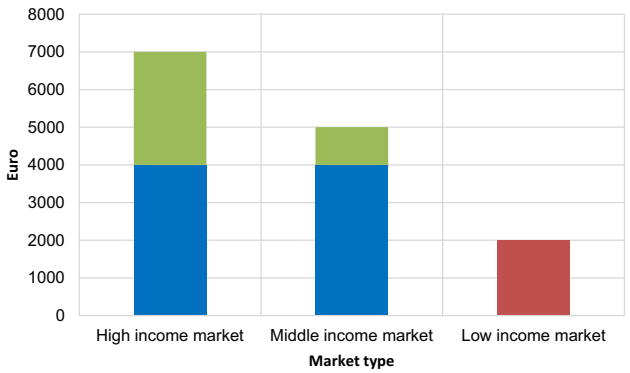

Fig. 2 Price of a hypothetical drug in a high-, middle- and low-income country without price discrimination. In high- and middle-income markets, the *green area* illustrates the consumer surplus and the lower funding for research and development in these countries. *Blue* is revenue to the drug manufacturer. In the low-income market, the *red area* illustrates value to consumers not achieved due to lower access to drug treatment for patients in the low-income country

In 2013, a total of 29 European countries (26 of the 28 EU member states plus Iceland, Norway and Switzerland) used some kind of IRP [4]. Only Sweden and the UK did not apply IRP.

Overall, the impact of IRP on prices elsewhere is not well understood. This is partly because the different countries in Europe include different drugs in their pharmaceutical reference 'baskets' and employ different algorithms to determine the reference price for a given product [5]. The number of countries in the baskets varies from one in Luxembourg (who use the price in the country from where it is imported) to 31 in Hungary and Poland [4]. For example, both France and the Netherlands include four countries in their reference basket. However, the French basket includes Germany, Italy, Spain and the UK. The Netherlands basket includes Belgium, France, Germany and the UK [4]. In France, the reference price is based on the principle that the initial listing price should not be lower than the lowest price observed in the comparator countries. In Netherlands, the reference price is determined by calculating the average price in the comparator countries [5].

Italy and Slovakia can be said to have 27 countries in their basket, as they use the prices of all EU countries. Spain uses the lowest available price, which means that country selection varies according to availability of the drug in different countries.

Countries typically use ex-factory prices to derive external reference prices. However, the Netherlands uses pharmacy retail prices.

Outside Europe, IRP was adopted in emerging markets such as Columbia and Egypt; China and India have expressed interest in IRP [6]. Emerging markets adopting IRP tend to have chosen to include similar countries in their reference basket, while several countries in Europe rely on EU-5 prices [7]. In a recent study of 28 EU member states plus Iceland, Norway and Switzerland, France was most frequently referenced, followed by Germany, the UK, Austria and Spain [5].

The market share of pharmaceuticals that are subject to IRP also varies considerably. For example, in France, IRP was applied to 8 % of drugs introduced between 2007 and 2011, whereas in Spain IRP applies to about 80 % of pharmaceuticals [6].

4 The Impact of IRP on Prices

The impact of IRP on prices in a given country depends on the methodology used for IRP. A reimbursement price set in one country can have both a direct and an indirect impact on reimbursement prices and policies in other countries. A direct impact is a result of country 'A' including the reference country 'B' in the algorithm used in the regulation system. An indirect impact may be that the price in another country, 'C', is included in country B's basket; therefore, the drug price in country A will be influenced by a new drug price in country C even if country C is not actually in country A's basket.

An analysis of interrelations between different price-setting schemes is therefore needed to explain and understand the behaviour of pharmaceutical companies. Stargardt and Schreyögg [7] tried to quantify the theoretical cross-border spill-over effect of IRP schemes on pharmaceutical prices in the former EU-15 countries. They found that the relationship between direct and indirect impacts of a price change depends on the method applied to set reimbursement prices. For example, a price reduction of €1.00 in Germany resulted in a reduced maximum reimbursement price in former EU-15 countries from €0.15 in

Austria to €0.36 in Italy. As a result, it is likely that the manufacturer would try to set a single international price for a product or at least try to keep international prices in a certain 'price corridor'.

5 The Impact of IRP on Volumes—Delayed Launch in Some Countries

IRP has an impact on the pharmaceutical industry and its decision making in several ways. First, IRP means that a price regulator's demand and acceptance of only a low price for a new product in one national market can lead manufacturers to refrain from launching their product in this market. This is because the low price can jeopardise their pricing strategy in other markets because of IRP. In fact, IRP provides an incentive to completely withhold a new drug from a market in which prices are significantly below the average EU price [8]. This is particularly important for smaller countries when large countries reference them. A manufacturer is incentivised to prevent price reductions in the larger market by withholding or delaying launch until the impact on other countries' prices is reduced, for example, until patent expiry or other regulatory measures may apply, e.g. procurements and price volume agreements.

A manufacturer is incentivised to strategically launch products. This is the reason for the development of a consulting market, where consultant firms support the manufacturer and explore different strategies for launches by exploiting differences in price-setting algorithms and IRP baskets throughout the European market. From a manufacturer's point of view, it is most profitable to first launch a product in relatively unregulated markets, traditionally Germany and the UK, that do not directly control prices of individual drugs. If these markets are also included in other countries' IRP baskets, these countries are even more attractive because IRP leads to high prices in the referencing countries. Consequently, the manufacturers' launch strategy will target these countries in a second wave as the high prices in the most attractive countries could also be used to negotiate a relatively high price in the reference pricing counties. The third wave would be to launch the product in countries with low price levels in package sizes not marketed in those countries targeted in the first waves [7]. Manufacturers are once again incentivised to view Germany and the UK as candidates for the early launch of new innovative products. These countries also have roughly the largest markets in Europe and are often referenced by IRP countries.

6 Response of Various Stakeholders to IRP

In our example, a single international price for a product will not generate as much revenue as a strategy with price discrimination, which is only possible if markets can be kept separate. Large incentives exist for the manufacturer to discriminate prices between purchasers who can afford high prices and those who cannot. Therefore, a reasonable strategy would be to try to reduce price transparency in order to reduce the likelihood of spill-over effects due to IRP. Manufacturers can attempt this in several ways. It would be attractive to a manufacturer to aim for high list prices in countries that have high prices and that are frequently used in IRP baskets; at the same time, they can offer confidential discounts or rebates, or at least discounted prices, that are difficult to include in the IRP index.

Payers and manufacturers create several types of risk-sharing agreements. 'Payback' is a mechanism whereby manufacturers agree to return some revenues over a predetermined level to healthcare providers or payers as a lump sum in order to distort the impact of IRP in other markets. The French price volume agreements, with paybacks by companies if volumes are exceeded, are another way of achieving differential pricing.

Several other options may be available. For example, Spain operates a general discount system wherein manufacturers must return a certain percent of their annual sales to the Minister of Health. In the UK, the manufacturer sets the prices freely but, at the same time, the profit margins are regulated and are not allowed to exceed a predefined level. If so, the manufacturers must pay back or reduce the price the subsequent year. Other options are risk-sharing agreements wherein the payer only pays for the treatment if it is effective or provides a certain predefined outcome. Bortezomib (Velcade®) for the treatment of multiple myeloma is one example; Carlson et al. [9] found 34 examples of coverage with evidence development in their review. Such options include a high list price and a simultaneous discount offered to the payer in a magnitude that might not be known for any part ex ante but only ex post when treatment performance can be evaluated.

7 A Case Study—Abiraterone (Zytiga®)

IRP also impacts drug prices and pharmaceutical uptake in countries not using IRP. We use an example of a recently launched drug for the treatment of prostate cancer, Zytiga®, to illustrate the impact of IRP on the uptake of new innovative pharmaceuticals [10]. The TLV denied

reimbursement for Zytiga® in 2012. It was considered an effective and safe drug treatment for advanced prostate cancer, postponing progression and prolonging mean overall survival by about 5 months and providing a quality-adjusted life-year (QALY) gain of 0.38. However, at the price the manufacturer claimed, the incremental cost per QALY gain, i.e. the incremental cost-effectiveness ratio (ICER), was estimated at SEK1.1 million (about €130,000). This was higher than any earlier ICER accepted by the TLV and thus exceeded its unofficial threshold. Therefore, TLV could not include Zytiga® in the national reimbursement scheme [10].

For drugs not granted reimbursement by the TLV, there is a second way into the Swedish market, and that is to enter into agreements with county councils. The manufacturer's next step was to attempt to 'negotiate' a new price with the NLT, an organisation within the association for county councils. The NLT can negotiate an agreement with the manufacturer; however, because the county councils purchase the pharmaceuticals and pay the bill, the NLT's agreement must be confirmed by the county councils before it can be effective. The NLT's responsibility is simply to negotiate with the manufacturer in order to avoid different prices within Sweden that could result in regional variations in access to the drug ('postcode prescriptions'). The final agreement must be signed by all 21 county councils before it can be applied throughout the entire country.

Early in 2013, the NLT entered into an agreement with the manufacturer for a price that was lower than that requested in the TLV application [11]. However, this lower price is confidential. The price decided by the TLV is a public list price and is not able to be negotiated with healthcare providers. Manufacturers are not allowed to give discounts to healthcare providers in Sweden when the TLV has decided a national list price. The TLV list price appears in the price baskets of many other countries and, because of IRP, a low official list price will influence and reduce the accepted price for Zytiga® in many European countries. Hence, the manufacturer struggles hard for a high official list price, but at the same time can accept a lower non-disclosed negotiated real selling price. As at April 2015, Zytiga® has still not been granted reimbursement by the TLV because the it considers the official list price to be too high. However, Zytiga® is on the market in Sweden, and the real price paid is the discounted confidential price agreed between the NLT and the manufacturer.

The price agreement between the manufacturer and the NLT for Zytiga® in the treatment of prostate cancer includes two components. The first is a general discount and the second a risk-sharing component, whereby the manufacturer pays back to the county council if Zytiga® treatment does not reach the expected outcome within 3 months [11].

8 Discussion

A major change in the pharmaceutical market place is the increasing importance of third-party payment for new drugs, mainly through public health insurance. Drugs have been included in public financing systems for healthcare recently, and the patient co-payment for drugs is generally still higher than for other healthcare services. The introduction of reimbursement of pharmaceuticals changed the market, and in the early 1990s, cost-effectiveness analysis was introduced to guide pricing and reimbursement decisions. Lately, new drugs have been introduced at prices that put treatment costs at €40,000 per year or more (mainly cancer and orphan drugs). This has rendered co-payments redundant as an instrument to control use and expenditure [12]. Access to the market is thus determined by payers' decisions, which must balance available budgets against expected outcomes for different uses of resources.

We have explained how, in this new situation, both payers and manufacturers of new drugs are incentivised to enter into agreements that give more patients access to the drug, and at the same time increase the revenue for the manufacturer. We are thus returning to the old model of price discrimination that existed before the establishment of the common market in Europe. At that time, prices were lower in low-income countries, which was made possible by restrictions on parallel importing. A new feature of the price discrimination model is that discussions are opened to allow different prices for different indications for a drug. This is possible in a situation where both parties in the market can control what is used for which group of patients.

In a situation where price discrimination with non-disclosed rebates or market access agreements is the norm, which makes it difficult to identify the price, the basis for IRP is eroded. An example of this is the suggested IRP for Sweden, which only includes a handful of countries that still have official prices. In a few years, some of these countries may also have to change their pricing and reimbursing system, making it necessary to exclude them from the comparison. We predict the death of IRP, simply because there would be no countries to reference, either because the prices are not disclosed, or because several different prices are paid for different indications and payers. This will not eliminate the interest in comparing prices, but it will eliminate the use of publicly recorded prices as an instrument for a simple cost-containment policy.

The Zytiga® case in Sweden illustrates the new trend whereby manufacturers and public payers have started to negotiate risk-sharing agreements and special pricing agreements. When indications were initially not recommended for reimbursement, they were often subsequently approved with risk-sharing agreements or special pricing agreements [13]. Price–volume agreements, free drugs or discounts, volume and price caps, and schemes involving performance- or outcome-based payments are all examples of risk-sharing agreements. It is likely that pressure from patients and physicians to fund costly new treatments has contributed to the development of new innovative risk-sharing agreements between manufacturers and public and private payers.

Price is important for the uptake of effective drug treatments. The introduction of new cancer drugs provides many examples. For countries with lower incomes, the relative price of the drug is higher, both in terms of affordability and in relative terms in relation to other resources used in the healthcare system. We can observe that a significant number of EU countries have very low rates of use of new innovative cancer drugs [14, 15]. An opportunity to adjust the price to the ability to pay in different markets, and for different groups of patients, would create greater value from the treatment. Parallel trade also restricts opportunities for price discrimination, and our arguments therefore also apply to restriction in parallel trade; for example, payment per patient treated rather than number of packages used.

A further question is how IRP for medicines in Europe affects general welfare in the long run, and whether the short-term distributional implications in the form of higher prices in previously low price countries can be defended. From a global perspective, one can argue that, by taking on a greater burden for financing the fixed development costs (by paying a higher price), rich countries—more than the relatively poorer countries (with lower prices)—could contribute to the development of new effective drugs and to those drugs being spread to the poorer countries. Dissemination of new drugs would probably not occur to the same extent as today if price differentiation via different risk-sharing schemes, payback systems and confidential discounts was not possible. IRP (and parallel trade) counteracts this opportunity to price differentiate, and therefore effectively reduces the availability of new drugs in relatively poorer countries.

However, there are also potential gains for both payers and the industry to introduce more flexibility in pricing within a country [16]. The value of the use varies with the number of patients treated, with different indications, and more flexible pricing can increase both value and revenue. We thus see new market access strategies in which payers and producers cooperate to find different solutions to the problem of limited or delayed access to new innovative medicines. Discounts, paybacks and risk-sharing agreements are in fact different strategies to discriminate prices and to increase and accelerate access to novel innovative treatments.

The research and development behind a product is used by all consumers and is a common cost. The cost is the same regardless of the number of people consuming the product. Significant common costs indicates optimal (welfare-maximizing) pricing to set different prices for different users: Ramsey pricing [17]. Significant joint costs can never be covered with pricing based on marginal costs [18].

Ramsey pricing takes advantage of the fact that different consumers have different price sensitivities: those who are relatively insensitive to the price pay more. This principle is used in many fields, such as when airlines charge more for travellers in rush hour than at other times. Those who pay the higher price would have to pay even more if part of the common expenses had not been covered by discounted tickets.

The cost structure of the drug, with a large shared cost for research and development, is a typical case of Ramsey pricing [17]. Ramsey pricing can be said to fulfil the same function as patent, trademark and copyright, which provides opportunities to cover the common development costs and thus provide incentives for producers to develop new products. Even those countries that pay lower drug prices help to cover some of the common costs, leading to lower prices in high-price countries than if those countries were servicing all the common costs.

IRP, as well as parallel trade and price controls, tend to reduce the scope for price discrimination and the use of different markets' price sensitivity [19]. Producers must then choose other pricing strategies, such as a uniform price for all users or countries.

Persson et al. [20] suggest a modification to the current reimbursement system in Sweden, whereby payment for pharmaceuticals is split between regional and national levels. The idea is that the contribution from the national government is a fixed amount based on expected sales, and a lower price is used at the regional level where the county and councils buy the drug from the pharmaceutical companies. The system is expected to make new innovative pharmaceuticals accessible to a larger number of patients and to provide more consumer surplus without reducing the producer surplus (profit to the manufacturer). In short, the county councils pay the marginal cost of production while the state pays for the innovation. Persson et al. [20] suggest that the higher national price should be the list price included in the IRP, with no impact on the healthcare provider's lower local price. All this has the purpose of not restricting the uptake of new drugs and at the same time avoiding cross-reference pricing via the IRP system.

The examples of Zytiga® in Sweden could be considered as illustrations of how to reach an agreement between the payer and the manufacturer about the payment without disclosing the real price. Time to approval by regulatory authority is no longer of primary importance for the manufacturer's revenue and to encourage investment in the development of new pharmaceuticals. Approval for reimbursement by national reimbursement authorities and/or national treatment guidelines is of increasing importance for the manufacturer's revenues and for the spread and availability of new innovative and effective drug treatments.

We now see payers and manufacturers enter into several types of risk-sharing schemes, price volume negotiations, payback arrangements, confidential discounts, coverage with evidence developments, etc., all with the purpose of returning to the old model of price discrimination. In short, real prices for use in IRP systems will no longer exist and, thus, we expect to soon see the end of IRP and a new system for price discrimination and an increasing demand for value-based pricing.

Compliance with Ethical Standards

The study received an unrestricted grant from Janssen-Cilag AB. The funding assured the authors' independence in design, interpretation, writing and publishing of the study. The authors, Bengt Jönsson and Ulf Persson, have no conflicts of interest to declare.

Authors' contribution Both authors contributed jointly to design, content, analysis and interpretation, and were actively involved in all stages of the work. Ulf Persson is the guarantor for the overall content.

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