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Managing Pharmaceutical Expenditures: Estimating the Effect of Internal Reference Pricing for Three Pharmacological Categories

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Abstract

Background: Internal reference pricing (IRP) is one of the pharmaceutical pricing approaches, which is widely favored by health policymakers in different countries as a cost-containment tool for managing medicine expenditure. Evidence related to the implementation of this method confirms its usefulness in reducing pharmaceutical costs. Accordingly, the purpose of this study was to calculate potential changes in pharmaceutical expenditure using the IRP method for products belonging to three pharmaceutical categories in the pharmaceutical system of Iran.

Methods: This routine data study assessed the potential effect of IRP in three pharmaceutical categories including statins, non-steroidal anti-inflammatory drugs, and proton pump inhibitors (PPIs). Two scenarios for reference groups (levels 4 and 5 of the ATC code) and four scenarios for the reference price (i.e., the minimum, median, mean, and the mean of three minimum prices in the reference group) were considered in this regard, and the price and sales data source was the report published by the Iranian Food and Drug Administration. Then, cost changes were calculated with each hypothetical scenario. It was assumed that other intervening factors remain unchanged, including consumers and prescribers' behavior.

Results: Based on the results, the two largest potential saving effects belonged to the minimum price scenario and the mean of the scenario of the three minimum prices, respectively. However, the results showed that the consequence of using a price scenario other than the minimum price as the reference price is highly related to the details of the distribution of prices in the related reference group. In addition, appropriate decisions regarding outlier products (e.g., imported products) might have extremely important effects on the result, especially for the mean price scenario. The minimum price scenario concomitant with a premium for superior products can also be considered, but part of it is outside the scope of this study and requires independent research.

Conclusion: Thus if an appropriate scenario is selected for the reference price and group, the IRP method has the potential to reduce the costs of medicines. Therefore, pharmaceutical policymakers must pay enough attention to the details of planning this system and the needed procedure for updating the details of this system.

Keywords: Pricing, Pharmaceutical products, Internal reference pricing (IRP), Statins, Non-steroidal anti-inflammatory drugs, Proton pump inhibitors

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Introduction

Important principles for achieving profitability include providing better products than competitors and using appropriate strategies to achieve the desired market share. In this regard, a firm must be able to properly price its products in order to generate revenue that is proportionate to the value offered to the customer. Pricing is the most important component of a business model and decisions about it have a major impact on the profitability of the firm (1).

Although the same is true for pharmaceutical products (e.g., an increase in health care costs), policymakers are looking for ways to reduce costs. One of the most common approaches is the control of pharmaceutical costs. Until now, different strategies have been used to set prices or control the prices of pharmaceutical products in different countries. The most common strategies include changes in the mark-up of different parts of the supply chain of pharmaceuticals, tax exemption or reduction for pharmaceutical products, promoting the use of generic products, using health technology assessment and value-based pricing, internal reference pricing (IRP), and price-

volume agreements and tenders as tools to control prices, along with cost-plus pricing and external reference pricing (ERP) as pricing strategies (2-4).

Although it is recommended that a combination of different strategies be applied, the IRP method has received considerable attention in recent years given the conditions of the country (5,6). In this method, medicines of equal safety, efficacy, and health outcomes are grouped into the same reference group and a reference price is set for medicines in that reference group. Depending on the details of the IRP implementation system, prices for all products in a reference group will not be necessarily equal to the determined reference price. In some systems, manufacturers can set a price higher than the reference price for their product although they should compete with equivalent cheap drugs (5).

Although little evidence is available on IRP in developing countries, the results of studies in developed countries confirm the usefulness of this method in reducing pharmaceutical costs. IRP is commonly used in the public sector, but large private buyers can use it as well (5).

The pricing of imported drugs is based on ERP in Iran, and the prices of locally produced pharmaceutical products are determined either as a percentage of the original brand price or by the cost-plus method. In this method, which is the most primitive method of pricing, the price is determined by adding a defined margin at the expense (6).

According to the World Health Organization (WHO) guideline on pricing policies, the cost-plus method is generally not a viable method of pricing medicines, and it is e recommended that countries should not use this method as a general drug pricing policy (2). The WHO has recommended that the drug pricing system gets changed from the cost-plus method to the reference pricing method. One of the major disadvantages of the cost-plus method is the elimination of the motivation for cost-cutting competitions among the firms. Around 2017, the pricing regime in the country was revised so that the prices of domestically produced drugs were calculated either based on a percentage of the original brand price or the use of a modified cost-plus bundle, where research and development and marketing costs are considered for companies that have received a good manufacturing practice certification (7), which can be an incentive for quality improvement.

Overall, the pharmaceutical policymakers of Iran have been paying more attention to the pricing debate in recent years and are looking into the possible effects of using other pricing methods. Therefore, to provide the necessary information to decision-makers in the country, this study aimed to review and summarize the experienced practices in other countries in terms of determining the details of the IRP implementation and predicting the effect of this method on the country through selecting three drug categories and calculating expected changes in their expenditure, assuming no changes in other influencing factors.

Materials and Methods

Generally, three basic steps are needed for implementing the IRP method (8):

1. Determining the reference level (group): It can be based on the active ingredient, pharmacological group, or treatment group.
2. Identifying the reference price: Different scenarios exist in this regard. It could be the lowest (minimum) price, the mean of the three minimum prices, the mean of the three minimum prices plus 10%, the mean price of medicines or the mean price of generic medicines in the reference group, and the median price.
3. Deciding whether only the off-patent generic products of the relevant group are covered by this policy or patent products are included as well.

To achieve the aim of the study, the relevant literature was searched for the experiences and recommendations of other countries on IRP details, including criteria for selecting drug categories appropriate for IRP, and common approaches for defining reference prices and groups. As a result, three pharmaceutical categories were investigated, including statins, non-steroidal anti-inflammatory drugs (NSAIDs), and proton pump inhibitors (PPIs). Moreover, levels 4 and 5 of the anatomical therapeutic chemical (ATC) classification system were considered as two scenarios for the reference group. Levels 4 and 5 show pharmacological subgroups and the chemical substance, respectively.

Next, the distribution of the prices of each selected drug was investigated, and the outlier prices were identified and their cause was investigated as well. Then, the reference price in different scenarios was calculated for two situations, namely, with and without taking into account the outlier prices in calculations. The needed sales and price data for each selected drug were individually extracted for each company from the Iranian Food and Drug Administration website and the report provided by the Iran pharmaceutical market sales database (21 March 2017 to 20 March 2018).

Considering different doses of medicine in the market, the WHO defined daily dose (DDD) approach was used to estimate prices per DDD for each drug. Then, the costs were calculated for different price scenarios (i.e., minimum, median, mean, and mean of three minimum prices) and two reference groups (i.e., levels 4 and 5 of the ATC classification system). Finally, changes in expenditure with each scenario compared to the observed expenditure were calculated, and cost changes were measured in percentages and the currency in Iranian rial. The Microsoft Excel software was used to perform calculations.

Results

First, the data were examined to exclude incorrect data from calculations. The related results are shown in Table 1.

Table 1. Reference Prices for Each Scenario With and Without Outlier Prices

Pharmacological Category	Generic Name	DDD (mg)	Minimum Price*	Median Price		Mean Price		Mean of Three Minimum Prices
				Without Outlier	With Outlier	Without Outlier	With Outlier	
NSAIDs	Tolmetin	700	14,469	15,854	15,854	15,854	15,854	15,854
	Celecoxib	200	1,175	2,105	2,019	5,235	2,036	1,238
	Diclofenac	100	900	1,796	1,752	3,135	1,862	1,147
	Ibuprofen	1200	970	3,344	2,402	16,029	3,826	1,506
	Indomethacin	100	840	2,914	2,914	2,629	2,629	1,746
	Naproxen	500	2,163	2,875	2,864	4,957	3,453	2,179
	Piroxicam	20	1,800	1,848	1,834	5,362	1,878	1,823
	Level 4	-	840	2,348	2,103	7,642	2,909	869
PPIs	Omeprazole	20	1,201	1,846	1,816	2,162	1,851	1,397
	Esomeprazole	30	787	5,250	5,250	5,048	5,045	2,127
	Lansoprazole	30	4,332	5,300	5,300	5,361	5,332	4,393
	Pantoprazole	40	2,896	4,516	4,492	5,666	4,593	3,206
	Level 4	-	787	4,785	4,657	5,060	4,405	1,156
Statins	Atorvastatin	20	873	1,378	1,371	2,411	2,126	874
	Lovastatin	45	1,262	1,461	1,461	1,478	1,478	1,300
	Rosuvastatin	10	750	4,000	4,000	4,249	3,932	1,605
	Simvastatin	30	2,484	2,535	2,535	2,531	2,531	2,508
	Level 4	-	750	2,421	2,307	3,246	2,980	833

Note. DDD: The World Health Organization defined daily dose. *All prices have been mentioned in rials/DDD for 2017.

In this study, all outlier prices were higher than the prices of similar products. Therefore, reference prices calculated with or without outliers were the same for the scenarios of the minimum price and the mean of the three minimum prices. For this reason, in the case of these two scenarios, only one value has been mentioned in Table 1. There were no outlier prices for some drugs such as tolmetin, indomethacin, lovastatin, and simvastatin. Thus, reference prices with and without outlier data were equal for each scenario of every drug. The largest difference between the reference price with and without outlier prices belonged to the mean price scenario (Table 1).

Table 2 provides another part of the information used to perform calculations, including the value and volume of the observed sale for individual drugs, along with drug categories. Based on the obtained data, the highest and lowest sales in the NSAID category were related to ibuprofen and tolmetin, respectively. In the case of PPIs, the highest sale was obtained for pantoprazole while the lowest one belonged to lansoprazole. Finally, among statins, atorvastatin and simvastatin had the highest and lowest sales, respectively.

Table 3 presents the cost values in four scenarios for the reference price (i.e., minimum, median, mean, and the mean of three minimum prices) and two scenarios for the reference group (levels 4 and 5 of the ATC code). As shown, if the lowest price was chosen as the reference price, the IRP at both levels of 4 and 5 of the ATC code led to maximum cost saving. After this price scenario, the highest cost reduction was related to the mean of the three minimum prices.

As regards the reference price equal to the mean price, the result was almost the opposite. In the NSAID group, this scenario increased the costs in all drugs and levels except for tolmetin. In PPIs, this reference price increased the costs for levels 4 and 5 of all drugs and pantoprazole. Regarding statins, a reduction in costs was observed only for simvastatin whereas elevated costs were calculated for other members of the statins group in both reference groups of levels 4 and 5 of the ATC code.

Turning to the median price as the reference price, cost reductions were obtained at all levels and drugs of the NSAID group except for naproxen and indomethacin. In PPIs, the cost increase was obtained only in the case of IRP at level 4 of the ATC code. In terms of the statin group, costs reduced only for rosuvastatin and simvastatin.

A part of the findings of this study was related to calculations with and without outlier prices. The comparison of the obtained values from calculating the reference price in these two situations showed that the value of the reference price was not different with and without outlier prices in the scenarios of the minimum price and the mean of the three minimum prices. This is not surprising because outlier prices were higher than the price of the other members of the group. In the case of lovastatin, tolmetin, and indomethacin, the results did not change with or without outlier prices. Although the removal of outlier data reduced the mean price and costs

Table 2. Value and Volume of Sales Observed for Each Pharmacological Category and Individual Drug in 2017

Pharmacological Category	Generic Name	Sales Volume (DDD)	Sales Value (Rial)
NSAIDs	Tolmetin	2,715,114	45,606,970,000
	Celeoxib	170,963,470	540,058,253,089
	Diclofenac	210,862,339	684,639,578,591
	Ibuprofen	222,680,839	1,018,931,310,300
	Indomethacin	39,865,097	100,952,514,763
	Naproxen	140,582,221	369,335,040,852
	Piroxicam	18,954,025	36,330,217,409
	Total	**806,623,111**	**2,795,853,885,004**
PPIs	Omeprazole	390,905,600	896,339,402,369
	Esomeprazole	59,373,479	384,854,192,607
	Lansoprazole	54,485,218	312,113,126,011
	Pantoprazole	404,995,510	2,114,753,801,995
	Total	**909,759,807**	**3,708,060,522,982**
Statins	Atorvastatin	1,073,999,159	1,463,023,301,947
	Lovastatin	16,829,536	23,250,430,613
	Rosuvastatin	174,161,811	713,209,902,269
	Simvastatin	8,622,160	21,918,258,344
	Total	**1,273,612,666.89**	**2,221,401,893,172**

Note. DDD: The World Health Organization defined daily dose.

Table 3. Expected Value and its Change in Each Scenario in Comparison With the Observed Expenditure in 2017 With and Without Outlier Prices

Pharmacological Category	Level	Minimum Price*	Median Price		Mean Price		Mean of Three Minimum Prices
			Without Outlier	With Outlier	Without Outlier	With Outlier	
NSAIDs	Level 5	812,883 (-71%)	2,081,792 (-25.5%)	2,081,792 (-25.5%)	2,937,417 (+5.5%)	2,937,417 (+5.5%)	1,106,208 (-60.5 %)
	Level 4	677,364 (-76%)	1,696,650 (-39.3 %)	1,894,338 (-32.24%)	2,347,056 (-16.05 %)	6,156,944 (+120.50%)	701,663 (-75 %)
PPIs	Level 5	1,925,650 (-48%)	3,151,579 (-15%)	3,151,579 (-15%)	3,777,850 (+1.8%)	3,777,850 (+1.8%)	2,210,261 (-40.4 %)
	Level 4	716,436 (-80.7%)	4,236,881 (+14%)	4,353,384 (+17.4%)	4,008,320 (+8 %)	4,604,256 (+24%)	1,051,859 (-71.6 %)
Statins	Level 5	1,111,534 (-50%)	2,224,137 (+0.12%)	2,224,137 (+0.12 %)	5,915,307 (+166%)	5,915,307 (+166 %)	1,262,341 (-43.17 %)
	Level 4	955,213 (-57%)	3,010,312 (+36 %)	3,083,103 (+39 %)	3,814,837 (+71 %)	4,133,610 (+86 %)	1,060,748 (-52 %)

Note. All amounts are in million rials. The numbers in parentheses are the percentage of change in costs.

in the mean price scenario compared to those for the situation including outlier prices, the use of mean prices in NSAIDs led to the elevation of the costs of indomethacin and naproxen and the total cost at level 5. However, the use of the median price scenario decreased the costs at all levels and drugs except for naproxen and indomethacin. In PPIs, an increase was observed only in the total cost at levels 4 and 5 in the mean price scenario. In the median price scenario for PPIs, an increase in costs was observed only for IRP at level 4. Regarding statins, only the cost of simvastatin and rosuvastatin reduced by eliminating outlier prices from calculations regarding mean and median price scenarios.

In general, the highest cost reduction was observed when the IRP was calculated with the reference price equal to the minimum price and the mean of the three minimum prices on a larger scale (in this example, level 4). In the case of the studied drug categories in this study, the worst-case scenario (the highest cost) was related to the mean reference price when it was selected at the broader level (level 4), especially by entering outlier prices.

Discussion

Over the past few decades, several studies have focused on the pricing of pharmaceutical products, confirming the effect of IRP on reducing these prices (9,10). Some experiences show that changing the reference pricing system from the ERP to the IRP could lead to significant

differences in the cost of medicines simultaneously by increasing people's satisfaction (11).

Considering the importance of this issue, the present study sought to estimate changes in the cost of the drugs of three selected pharmacological categories in the case of using IRP, assuming that other variables remain unchanged. This section discusses the research findings.

The findings of the present study demonstrated that, considering the above-mentioned assumption, the consequence of IRP for three pharmaceutical categories with different price scenarios and reference groups entirely depends on the selected scenario and the distribution of prices.

A study conducted in Denmark reported that the highest drop in the price and economic impact was related to drugs that had to be taken for a long time. There was no significant effect on drugs used in acute and short-term situations. The mentioned study examined 228 cholesterol-lowering compounds, 251 anti-ulcer compounds, and 152 antibiotics. The findings revealed that the effect of IRP was more noticeable when the competition was more in a group of drugs that could be substituted with each other (12). Bearing in mind this issue and the high consumption of the three groups of drugs including NSAIDs, PPIs, and statins in Iran, the three mentioned drug groups were selected for evaluation in the current study.

In the present study, it was predicted that the use of IRP with the appropriate scenario would lead to a reduction in the cost of drugs. Based on the results, the highest cost reduction was related to the mean of the three minimum prices after the price scenario based on the minimum price. Although this study was observational and estimated the costs with the assumption that other real-world variables (e.g., consumer behavior) will remain constant, studies performed in different countries confirmed cost reductions following this pricing strategy, and effective solutions are available in cases that changes in other variables hamper the cost reduction. For example, previous research reviewed 16 studies describing 9 reference-pricing policies from 6 countries including Britain, Canada, Spain, Colombia, Germany, and Norway. It was reported that reference pricing plans lead to a decrease in drug prices while increments in the utilization of targeted medications while reducing payer and patient expenditures. In addition, these policies did not increase the use of medical services such as physician office visits and hospitalization (13).

Another remarkable point found in the present study was the necessity of paying attention to outlier prices in calculating the reference price. As explained earlier, the outlier price in this study means the price of products that are significantly different, for some reasons such as being imported, from the price of similar products of the reference group. One of the substantial points mentioned in the literature related to IRP is making decisions regarding including imported products in the IRP system. For example, a previous study found that a reduction in the prices of originator products was significantly higher compared to generic drugs. Further, further reductions in prices were observed in markets that took advantage of well-developed competitions between generic products before implementing the reference pricing system (9).

In this regard, the results of the present study clearly showed that if products with high prices (e.g., imported brands which usually have prices extremely higher compared to similar products) are included in reference groups, decisions about including or excluding their prices in calculating the reference price can be highly important depending on the selected scenarios. When the minimum price scenario or the mean of the three minimum prices was chosen, the outlier price did not affect the reference price. It is worth reminding that this conclusion can be violated if the number of group members is so small that at least one of these three prices belongs to an outlier product in the scenario of the mean of three minimum prices. Turning to the reference price scenario equal to the mean of all prices, the inclusion of outlier prices resulted in a reference price higher than the current price of many members of the group, which, in turn, increased the costs. Regarding the median price scenario, the outcome heavily relies on the details of the price distribution in the relevant reference group.

It should also be noted that if imported products are supposed to be priced based on a pricing method different from locally produced counterparts (i.e., a method other than the IRP), the result would change to some extent because it was assumed that these products would also be priced under the IRP system. Moreover, the only difference in the two cases with or without outlier prices was whether the prices of these products are supposed to be included in the reference price calculations.

Finally, it is noteworthy that although many studies have addressed the role of IRP in diminishing prices (5,9,10), there are a number of other issues that need to be considered when it comes to implementation, including the need for the periodical review of the outcomes of the pricing system and the impacts of the time interval through studying the short-, medium- and long-term consequences of applying IRP (9).

Conclusion

Having in mind the need to control pharmaceutical costs and successful experiences of the IRP method, the present study estimated the potential reduction in costs related to three pharmacological categories by assuming the fixity of other intervening variables. The results showed the high potential of this pricing system in reducing drug costs. Among various price scenarios, the scenario of the mean of three minimum prices seems desirable because while resulting in cost reductions, can provide the needed flexibility and competitive environment, and thus reducing the likelihood of damage to the quality or disruption

of drug supply. In this regard, applying the minimum price scenario concomitant with a premium for superior products can also be considered although part of that is outside the scope of this study and requires independent research. Another important point drawn from the present study was that when a price scenario other than the minimum price is to be used, paying attention to the details of the price distribution and appropriate decisions regarding outliers (e.g., imported products) are of non-negligible importance. Therefore, the details of pricing with the IRP method needs to be updated in the alignment of changes in the market and the production costs and prices of the included products.

Ethical Issues

The present study was approved by the Ethics Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1397.1045). The results of the study will be made available to the relevant organization. Given that all applied information in this study was formerly publicly available, there were no other ethical considerations.

Conflict of Interests

The authors declare that there is no conflict of interests.

Authors' Contributions

MR participated in analyzing data, performing calculations, and writing the article draft and its revision. In addition, ZB extracted the data and collaborated in calculations and article drafting. Finally, NM participated in designing the methodology and scientific revision of the article.

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