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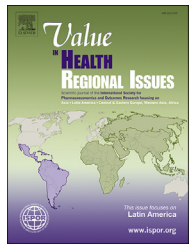

Health Policy Analysis

The Impact of Price Negotiations on Public Procurement Prices and Access to 8 Innovative Cancer Medicines in a Middle-Income Country: The Case of Mexico

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ABSTRACT

Background: To mitigate the effect of high prices, in 2008 Mexico established a commission that negotiates single procurement prices for patented medicines in the public sector. **Objectives:** We assessed the possible effect of price negotiations on the prices of new essential cancer medicines in Mexico between 2010 and 2016 and on access to these new cancer medicines. **Methods:** We retrieved the public procurement prices and volume of 8 selected innovative cancer medicines in Mexico in addition to their maximum retail prices in the private sector. We calculated the median, interquartile (25%-75%) range, and maximum and minimum public procurement prices to analyze price changes and trends. We assessed changes between the maximum retail prices and the public procurement prices and changes in the volume procured from 2010 to 2016. **Results:** Between 2010 and 2016, the prices of selected patented cancer medicines in the public sector decreased by 40% to 85%, expressed in US dollars. When expressed in Mexican pesos, public prices for 5 medicines reduced and others remained stable, whereas prices increased in the private sector over the same period. Procurement prices were not uniform between and within public institutions. The volumes of selected cancer medicines supplied in the public sector increased over the years, suggesting better access. **Conclusion:** Although direct causality is difficult to prove, the establishment of the negotiating commission seems to have led to reduced prices and possibly better access in the public sector. Medicine procurement by public hospitals should be monitored to ensure that negotiated prices benefit all institutions.

Keywords: access, cancer medicines, high prices, Mexico, patented medicines, price negotiation.

Introduction

Many innovative medicines are entering the market targeting complex diseases, such as HIV, hepatitis C, orphan diseases, and cancer. Many of these medicines show better health outcomes[1] and have been classified as essential.[2] Yet most new essential medicines are available at high prices, posing a threat to the financial sustainability of health systems and therefore limiting their accessibility.[3–5] Low- and middle-income countries (LMIC) sometimes face even higher prices than high-income countries.[6]

A major example of new high-cost essential medicines is cancer medicines.[3,5] Providing access to this type of medicine represents a challenge to improving cancer care because a large proportion of cancer care costs is attributable to pharmacologic treatment.[4,7] The high prices of these medicines make them unaffordable and inaccessible in most countries.[8] Because LMICs bear an increasing cancer burden, it is important to consider policies and strategies to address the costs of these medicines.[7,9,10] Some high-income countries have mitigated the effect of high prices through various measures, such as managed entry agreements, health-technology assessments, reimbursement policies, and price negotiations.[11–13]

In middle-income countries, medicines can account for a large proportion of health expenditure. Comprehensive pharmaceutical policies are needed to contain pharmaceutical expenditures while ensuring access to innovative (often patented) medicines.[14,15] To mitigate the effect of high prices and increase public procurement efficiency and access to innovative medicines, in 2008 Mexico created the Coordinating Commission for the Negotiation of Prices of Medicines (CCNPMIS) to negotiate with the pharmaceutical

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industry. The CCNPMIS negotiates single public procurement prices of single sourced (mostly patented) medicines listed in the national formulary, that is, essential innovative medicines.

In Mexico, access to medicines is divided between the private and public sectors. The private sector consists of for-profit facilities and pharmacies, where patients can procure medicines by paying mainly out of pocket.[16,17] The public health sector consists of 5 different social health insurance (SHI) institutions, which provide healthcare to more than 50% of the population. These organizations provide health coverage, care, and medicines to the private sector and government employees free of charge at the point of service. Each organization has its own health facilities, management, and list of medicines based on the national formulary, which is based on clinical evidence, safety, and cost-effectiveness criteria.[18–20] The Ministry of Health (MoH) provides healthcare and medicines to people ineligible for SHI and affiliated with the government's People's Health Insurance (Seguro Popular de Salud [SPS]) (approximately 40% of the population) through state and federal health facilities with their own pharmacies. The MoH facilities can have a list of selected medicines based on the national formulary or according to SPS coverage, which is also based on the national formulary.[18,19,21]

Before the creation of the CCNPMIS, each public health institution negotiated prices of essential innovative medicines directly with pharmaceutical companies, resulting in high variability in procurement prices across the public sector and inefficiencies in pharmaceutical spending and procurement.[22,23] The CCNPMIS provides uniform and single procurement prices applicable to the whole public sector in Mexico and promotes better procurement conditions.[24] The CCNPMIS is formed by members of the 2 main SHI institutions (called Instituto Mexicano del Seguro Social and Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado), and members of the MoH, Ministry of Economics, and Ministry of Finance.[22,23] The CCNPMIS determines which medicines will be considered for negotiation (medicines with a valid patent or single-sourced medicines, included in the national formulary, without therapeutic substitutes), prepares technical and economic grounds for negotiation (eg, estimated demand and procurement volume, economic evidence, public procurement prices, prices and procurement conditions in international markets), and carries out the actual negotiations with the pharmaceutical companies.[22,23] The negotiations result in a framework contract applicable to all public institutions only,[22,23] with single and uniform prices, procurement conditions, and a list of authorized providers and distributors.[22] In addition, the CCNPMIS is expected to promote compliance with these price and procurement conditions.[24]

Since its creation, the number of medicines negotiated and the participation of companies in the negotiations with the commission has increased.[22,25] Some previous research has documented the challenges the CCNPMIS faces and its effect on antiretroviral (ARV) prices, but not on other medicines.[23,26,27] It is unclear whether the negotiated prices have been respected during procurement procedures[28] and whether the negotiations ultimately have improved access. Therefore, using patented cancer medicines as example, this study assessed the effect of the CCNPMIS negotiations from 2010 to 2016 on 4 aspects: uniformity of procurement prices in the public sector, the level of negotiated prices in the public sector, a comparison of these prices with those in the private sector, and whether access to negotiated medicines increased in the public sector.

Methods

We collected data on public procurement prices and quantities used for selected innovative essential cancer medicines to assess public procurement prices from 2010 to 2016. The CCNPMIS only negotiates prices for the public sector for patented medicines included in the national formulary.

Medicines of Study

Through the national transparency platform (Plataforma Nacional de Transparencia[29]), we requested the list of medicines negotiated by the CCNPMIS from 2009 to 2015; the negotiated prices of each year apply for the procurement prices of the following year.[24] Cancer medicines account for approximately 15% of the total of medicines listed in the national formulary.[30] Likewise, cancer medicines are the second largest group of medicines negotiated by the commission (after infectious diseases, including ARVs), accounting for approximately 15% of the total of negotiated medicines each year.[31] We selected cancer medicines with the following characteristics: (1) medicines negotiated in each negotiation round from 2009 to 2015; (2) medicines included in SHI institutional lists and covered by SPS, and included in the World Health Organization's Model List of Essential Medicines 2015 and 2017; and (3) with patent validity until after 2017. We excluded medicines that were negotiated only for some years and that had lost patent protection during the period of study or for which patent information was not available, and medicines not covered by SHI or the SPS. This led to the selection of the following medicines, representing approximately 40% of the total of negotiated cancer medicines each year: bevacizumab, dasatinib, imatinib, nilotinib, sorafenib, and sunitinib. Despite that their prices were only negotiated since 2014 and 2011, respectively, we also added rituximab and trastuzumab because of their inclusion into the World Health Organization's Model List of Essential Medicines, their coverage by SPS and SHI, and their wide use across the country[2,32] (Table 1) (see Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.04.006 for additional information on cancer medicines negotiated from 2009 to 2015).

Data Source

From the Plataforma Nacional de Transparencia,[29] we only obtained yearly procurement data from all public institutions (49 health institutions, see Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.04.006) providing cancer care in Mexico, for 2010 to 2016. These data included the quantity procured, expenditure, and price actually paid for each medicine. We also requested information on the actual negotiated prices, but the CCNPMIS refused to provide such information owing to its confidentiality. To make comparisons with the private sector, we used the maximum retail prices (MRPs) as reported by the Ministry of Economics[33] as a proxy of prices in the private sector. The MRP is the maximum price that the pharmaceutical industry voluntarily sets and reports to the Ministry of Economics.[33,34] Prices of medicines in the private sector cannot be higher than the MRP and may actually be lower. Although not ideal, the MRP was our only reliable source of private-sector prices. Unfortunately, MRPs were not available for rituximab and trastuzumab.

Analysis and Reporting

We first carried out a descriptive statistical analysis to describe the variability of prices because prices were not uniform and did not follow a normal distribution. We assessed the median, interquartile (25%-75%) range, and minimum and maximum public procurement prices of each medicine per year as prices per defined daily dose in Mexican pesos (Mex$/DDD) and in US dollars (USD$/DDD)[35] considering inflation rates.[36] Although the framework contract resulting from the negotiations is likely to report prices in local currency, we present prices in both USD and local currency. Presenting prices in USD provides an international

Table 1 – Medicines included in the study.

- Bevacizumab 400 mg per vial, box with 1 vial
- Dasatinib 50 mg, box with 60 tablets
- Imatinib 100 mg, box with 60 tablets
- Nilotinib 200 mg, box with 112 tablets
- Sorafenib 200 mg, box with 112 tablets
- Sunitinib 12.5 mg, box with 28 tablets
- Trastuzumab 440 mg per vial, box with 1 vial
- Rituximab 500 mg per vial, box with 1 vial

perspective of Mexican prices, and because the exchange rate has fluctuated from Mex$12/USD in 2012 to Mex$18/USD in 2016, shows the price variations between currencies. We computed DDDs from the amount of milligrams contained in each package based on the values reported by the German national Anatomic-Therapeutic-Chemical classification[37] because the World Health Organization has not defined DDDs for most cancer medicines.

We considered the public procurement volume of medicines as a proxy measure of access in the public sector. We used standard drug utilization research methods[38] to report total expenditures and total numbers of DDDs procured for all selected medicines from 2010 to 2016.

Results

Public Procurement Prices of Negotiated Medicines

Figure 1 shows the median public procurement prices of each selected medicine in the public sector in USD corrected for inflation. All medicines showed price decreases. The price decreases for most medicines in comparison to the previous year ranged approximately from 2% to 40%, with imatinib and rituximab showing price decreases up to 70%. Nevertheless, in Mex$ (see Appendix 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.04.006), bevacizumab and nilotinib had 1 price drop from 2010 to 2011, and prices did not decrease any further. Dasatinib had constant prices from 2010 to 2016; and trastuzumab had constant prices, without significant price decreases throughout the period of study. For all other medicines, the median prices in Mex$ decreased by approximately 2% to 30% from the previous year. The price differences between 2010 and 2016 for most medicines were above 40%, except for imatinib and rituximab (85% for both).

For all medicines, the procurement prices showed price variations between and within hospitals (see Appendices 4 and 5 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.04.006). Imatinib and rituximab showed the highest price variation (both ranging from -70% to more than 500% difference from the median); price differences persisted until 2016. The other medicines (bevacizumab, dasatinib, nilotinib, sorafenib, sunitinib, and trastuzumab) also showed price differences ranging from -50% to more than 300% difference from the median. Dasatinib and sorafenib showed the least variations in prices throughout the years.

Price Difference Between the Private and the Public Sector

Figure 2 shows the ratio between the MRP and the calculated median public procurement price in the public sector for 6 medicines of study. In general, prices in the public sector were approximately 30% to 60% lower than the MRP. This difference increased over the years for all medicines, in particular in 2016 for imatinib, as private prices continued to rise while public prices largely remained stable. Results are unavailable for rituximab and trastuzumab because companies do not report an MRP for these 2 medicines.[33]

Use and Access to Cancer Medicines

Figure 3 shows the total expenditures and the total amounts of DDDs procured for the 8 selected cancer medicines per year by all public institutions in Mexico. The figure shows that the amounts of DDDs procured of these medicines increased since 2010, thus indicating a likely increase in the use of these medicines. Nevertheless, expenditure decreased since 2014. During the period of study, the volume of medicines procured increased from 200 000 DDD to nearly 600 000 DDD for almost the same amount in USD (USD$203 million in 2016 vs USD$220 million in 2010) (see Aippendx 6 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.04.006 for disaggregated graphs for each medicine of study).

Discussion

We measured pricing trends of 8 innovative essential cancer medicines in the public sector in Mexico in an effort to assess the role of the CCNPMIS. Our results show potentially positive outcomes from the CCNPMIS negotiations that include a decrease in prices of all medicines when expressed in USD; prices in the public sector that have remained lower than in the private sector and have not increased throughout the years (when expressed in Mex$); and quantities of medicines procured in the public sector, while the expenditure has decreased, indicating increased use and suggesting better access for patients. Nevertheless, our results also show that the procurement prices of these medicines varied considerably between and within institutions, proving the lack of compliance with negotiated prices.

Prices of Medicines in the Public Sector

We found that between 2010 and 2016 the prices of all medicines decreased (when expressed in USD), particularly for imatinib and rituximab. Three medicines (bevacizumab, dasatinib, nilotinib) did not show much price changes in Mex$, which might be explained by the extent of their use by public institutions and available therapeutic equivalents[23] (eg, nilotinib is a therapeutic equivalent for imatinib).[30] Previous research on prices of ARV medicines in the public sector in Mexico reported that price reductions were minimal and prices were often similar to the prices in the previous year,[26,27] raising concerns about the CCNPMIS ability to obtain further discounts in prices of medicines.[26] Nevertheless, our results show that, when converted to USD, the prices of all medicines decreased throughout the years of study. These findings indicate the ability of the CCNPMIS to reduce USD prices and thereby to prevent price increases in Mexican pesos despite inflation and devaluations.

The prices of rituximab and imatinib showed the most considerable decreases during the period of study. Between 2010 and 2016, the price in USD of imatinib dropped by 85%. A possible reason is that imatinib will go off patent in 2018, which may reduce the bargaining power of the patent owner,[22] or the patent owner might be preparing for generic competition in the public sector. This raises the question of whether the bargaining power of the Commission is restricted to the period immediately before patent expiration. Rituximab was not included in the price negotiations until 2014 but also showed a price drop over the years. This price decrease may have also been a result of market competition with a biosimilar medicine available in the market and for public procurement from 2010 until 2014. This biosimilar lost its market license in 2014,[39] leaving the originator product as the only product available for public procurement. Once the lower

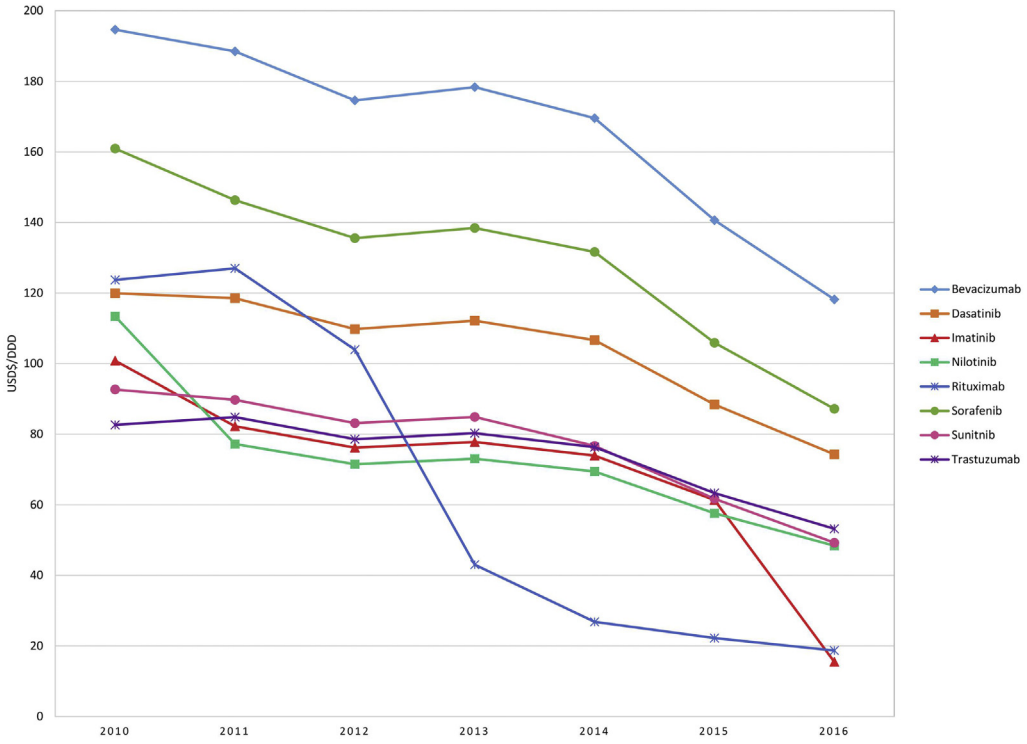

Fig. 1 – Median public procurement prices of innovative cancer medicines in the public sector in Mexico (2010–2016). DDD indicates defined daily dose; USD$, US dollar corrected for inflation.

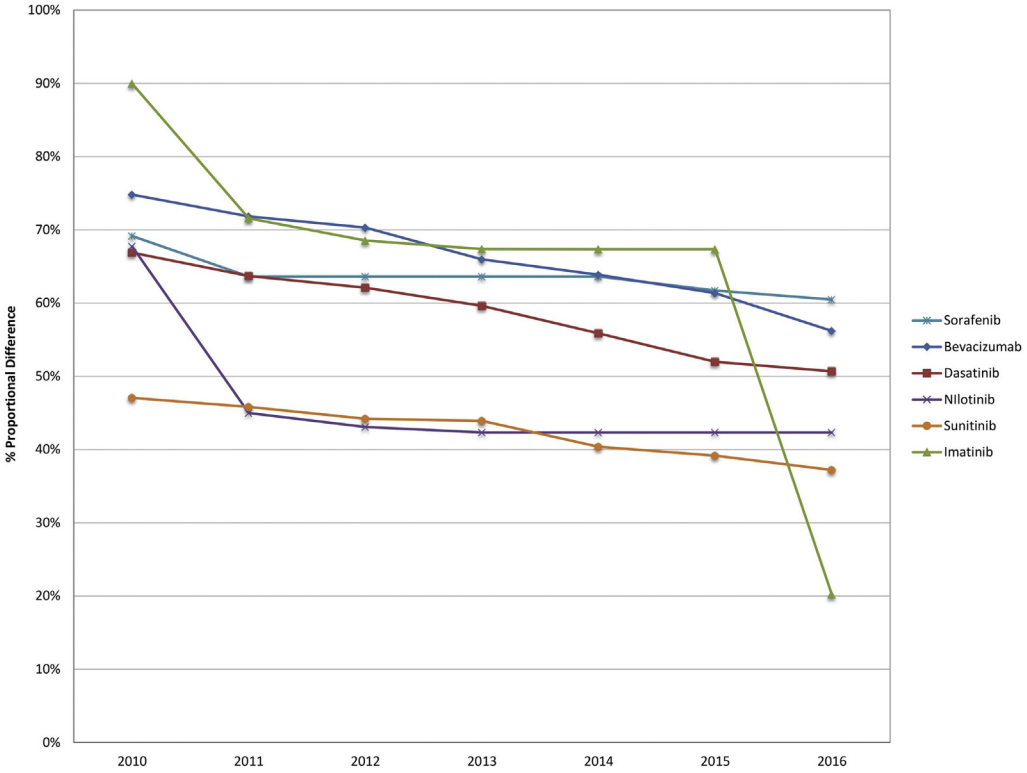

Fig. 2 – Public procurement price as a proportion of private maximum retail prices (2010-2016).

Fig. 3 – Annual total expenditure and DDDs procured of eight selected innovative cancer medicines by the public sector in Mexico (2010-2016). DDD indicates defined daily dose; USD$, US dollars corrected for inflation.

price had been negotiated, the price of rituximab then remained at that level. Both imatinib and rituximab also have been subject to patient access programs in other countries,[11,40–42] which may have an effect on the companies' willingness to provide better prices.

The price negotiations result in a framework contract applicable to all public institutions[22] that provides homogenous pricing and procurement conditions. Yet, we found large variations in the public procurement prices of these medicines between and within public institutions. Possible explanations are the lack of awareness of the negotiated prices within institutions and some institutions making direct purchases with non-authorized distributors.[22] Procuring medicines at lower and higher prices than the negotiated price can undermine the CCNPMIS's impact when suppliers underbid or overbid the negotiated price, and thus should be discouraged. The CCNPMIS and the government seem to have failed to monitor the compliance with price and procurement conditions[24] in the public sector in Mexico.

The CCNPMIS could be strengthened by joining forces with other countries and negotiating agencies by consolidating demand and increasing the influence of the region in negotiations with the pharmaceutical industry.[4,43] For example, Andean countries have conducted ARV price negotiations with some contractual and regulation limitations.[43–45] In 2003 and 2005, Latin American countries formed the "ARV Negotiation Monitoring Group" to negotiate and obtain ARVs at lower prices.[46] In 2015, Union of South American Nations and Southern Common Market countries created a committee for joint negotiations and pooled procurement for high-cost medicines.[4]

Price Differences Between the Private and Public Sectors

The difference between the MRP and the median public procurement price increased over the years for all medicines, with prices in the public sector up to 60% lower than the MRP. This finding is consistent with other medicines in Mexico where the prices of medicines in the public sector tend to be more than 30% lower than in the private sector.[16] Thus, the CCNPMIS has been able to prevent increases in public procurement prices despite price increases in the private sector.[22]

Other countries have also created entities that negotiate public procurement prices of medicines directly with the pharmaceutical industry to achieve and maintain lower public procurement prices. Uruguay established the Centralized Procurement Unit for Medicines and Related Supplies to optimize the centralized procurement of medicines through consolidation of demand.[46] Thailand has used economic analysis and benefits assessment to negotiate prices of medicines before listing them in their reimbursement lists,[42,47,48] leading to better prices and access to high-cost medicines. Acting as a single negotiating entity increases the government's negotiation power.

Access to Innovative Medicines

We found that the number of medicines procured increased over the years for all medicines of study. Because in Mexico most cancer care is provided in the public sector,[49] increased quantities procured suggests an increase in their use between 2010 and 2016. For most cancer medicines, expenditure decreased while the amount procured increased (see Appendix 6 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2019.04.006).

Lowering the price of cancer medicines can improve access to medicines.[50] Nevertheless, negotiations alone do not guarantee better access and optimal prices.[51] In addition to price negotiations, Mexico also implemented pooled procurement, mainly for generic medicines,[25] but recently also for patented (negotiated) medicines.[52] Yet, Mexico could also consider additional measures to reduce the price of patented medicines, such as compulsory

licensing and other pricing mechanisms.[53,54] For example, in Thailand's E2 list program for high-cost medicines, pooled procurement, compulsory licenses, and other patient access programs have been used to improve access to medicines such as imatinib, trastuzumab, and letrozole.[15,42] Brazil used price negotiations and compulsory licensing, leading to improved access to patented medicines.[51]

Strengths and Limitations

The main strength of this study is that we were able to get the actual prices paid by all relevant facilities in the public sector, allowing an assessment of price trends and use of innovative cancer medicines in the public sector and therefore of the CCNPMIS. We used the MRP as a proxy to compare prices between the private and public sectors. Although we were unable to retrieve actual private-sector prices and other information on markups and aspects influencing prices in the private sector, the MRP was a reliable tool because it is the maximum price that a medicine can have in the national market and allowed us to see price increases in the private sector. Nevertheless, we were unable to compare the actual paid procurement prices against the negotiated prices because the actual negotiated prices are confidential. We then assumed that the median prices paid by the institutions were the negotiated procurement price because these were the most commonly paid prices. We could not use the minimum prices as a proxy for the negotiated price because these were prices paid only once or by 1 institution. As well, we were unable to retrieve data from before 2010, limiting the possibility to assess the CCNPMIS from its inception. According to the law,[55] public institutions are only required to keep procurement records for 5 years. Most institutions reported that they did not have procurement records before 2010 anymore. Also, data lacked or were incomplete for some states (2 states did not provide data). This may have led to an under- or overestimation of the prices, the amount of medicines procured, and the real expenditure of these medicines. In addition, we used the most common product presentations that represented approximately 80% of the procured pharmaceutical volume, which may have led to some underestimation of the impact on medicine prices. Furthermore, all medicines of study are registered in the national formulary[30] for use as cancer medicines; therefore, we did not take into consideration the use for non-cancer indications for some of these medicines (eg, rituximab, bevacizumab).

Conclusion and Recommendations

Lowering the price of medicines by nationally aligned negotiations can help to increase access to cancer medicines in LMICs.[7,50] Price negotiations by the governments as an active economic player in price setting based on market dominance is a key strategy to improve access to high-cost medicines.[27,56] Since its creation, the CCNPMIS seems to have prevented price increases in the public sector, has contributed to savings in pharmaceutical expenditure, and has promoted institutional collaboration and information sharing.[22,25] The CCNPMIS in Mexico could, therefore, serve as an example for other countries to control prices and pharmaceutical expenditure.[22]

Based on our findings, we recommend that Mexico should further strengthen its negotiating power by making the inclusion of a medicine into the national formulary subject to the outcome of the price negotiations. Second, because many institutions continue to procure from unauthorized providers at prices different than those negotiated, the CCNPMIS should develop performance indicators[22,23] based on medicine needs, actual access to this type of medicine, procurement processes, budget, and purchasing power. Based on such monitoring and evaluating mechanisms, it can better ensure contract compliance by health institutions and distributors.[23,57] Finally, we recommend that more research is to be done to identify the exact reasons why health institutions procure medicines at different prices from those negotiated by the commission.

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Supplemental Material

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