



## Initiatives to challenge patent barriers and their relationship with the price of medicines procured by the Brazilian Unified National Health System

Iniciativas de enfrentamento da barreira patentária e a relação com o preço de medicamentos adquiridos pelo Sistema Único de Saúde

Iniciativas para enfrentarse a la barrera patentaria y su relación con el precio de medicamentos adquiridos por el Sistema Único de Salud

Carolinne Thays Scopel <sup>1</sup>  
Gabriela Costa Chaves <sup>1</sup>

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### Abstract

Since 1996, when antiretroviral (ARV) treatments started being guaranteed to people living with HIV in Brazil, the government has faced the challenge of ensuring sustainability of this policy within a context of incorporating patented medicines. This article sought to analyze the historical series of the price of lopinavir/ritonavir (LPV/r) in Brazil and in the international market also considering the initiatives to challenge patent barriers between 2001 and 2012. The methods used were mapping initiatives to challenge LPV/r patent barriers and the analysis of historical series of its price in Brazil and in the international market. Results show that, between 2001 and 2003, there were efforts to use compulsory licensing as a threat. From 2005 to 2007, initiatives by different stakeholders were identified: declaration of public interest, pre-grant opposition ("support to examination") and civil action. From 2006 to 2008, compulsory licensing initiatives in other countries resulted in a price reduction in Brazil. Between 2009 and 2012, there was a 30% reduction in the Brazilian purchasing price.

*Intellectual Property of Pharmaceutical Products and Process; Drug Price; Anti-Retroviral Agents*

<sup>1</sup> Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.

### Correspondence

C. T. Scopel  
Núcleo de Assistência Farmacêutica, Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz.  
Rua Leopoldo Bulhões 1480, Rio de Janeiro, RJ 21041-210, Brasil.  
carol.thays@gmail.com



## Introduction

The first cases of AIDS in the world were reported in the late 1970s but they were only diagnosed in 1982. In the beginning of the 1980s, the number of AIDS cases in Brazil followed a trend of growth, and from 1998 and 2006 achieved a relative stabilization. In 2012, there were an estimate of 718,000 people living with HIV in Brazil. Of these, 80% had been diagnosed <sup>1</sup>.

Brazil was one the first developing countries to guarantee an integral response to the AIDS epidemic, establishing initiatives for prevention, diagnosis, treatment and care. The Brazilian response was built with the involvement of and the commitment from several stakeholders: users, health care workers, government, private sector and others <sup>2,3</sup>.

Antiretroviral (ARV) treatments started being offered by the government in 1991, but it was only in 1996 that free distribution of the medicines to people living with HIV was established. This allowed that the guarantee of access to treatment could be more structured <sup>2,4</sup>. The implementation of free ARV distribution to people living with HIV was set within the formulation of the National Medicines Policy, established in 1998, which consolidated pharmaceutical services as a political commitment by the Brazilian government <sup>2,5,6</sup>.

Currently, the Brazilian Unified National Health System (SUS) provides 21 ARV, nine of which are produced locally. In the 1990s, with the development of protease inhibitors, among them, the fixed-dose combination lopinavir/ritonavir (LPV/r), there was a considerable improvement in AIDS treatments, including the highly active antiretroviral therapy (HAART) and association of medicines. Since its incorporation into the national treatment guideline, in 2002, LPV/r has an increased role in therapeutic schemes in Brazil <sup>3,7</sup>. It is currently being indicated as a part of a second line scheme <sup>8</sup>.

The first efforts to respond to the AIDS epidemic aimed at ensuring access to treatment. The next challenge was to ensure the sustainability of this response, progressively increasing the number of people in treatment and dealing with the incorporation of new medicines into the therapeutic arsenal.

Internationally, the Agreement on Trade-Related Aspects of Intellectual Property Rights (Trips) came into effect in 1995. All members of the World Trade Organization had to adapt their industrial property to become compliant with the new legal framework, which meant granting patents in the pharmaceutical sector.

The monopoly situation created by the grant of patents or the expectation that a patent ap-

plication will be granted enables companies to set high prices by restricting production, commercialization of generics and competition. This monopoly is deepened because, in the pharmaceutical sector, there is a overlap of patent applications for medicines, that can indefinitely extend the monopoly of those medicines – a practice known as evergreening <sup>9</sup>.

The AIDS epidemic made explicit the conflict between access and intellectual property. Several ARV are or have been under patent protection, leading to high prices offered to governments. The analysis of LPV/r case allows to draw an outline of the economic barriers created for the access to patented medicines in the context of the implementation of the international system of intellectual property <sup>7</sup>.

Thus, by mapping the initiatives that aim at to overcoming LPV/r's patent barrier, it might be possible to highlight explanatory elements of the evolution of its price in Brazil. A patent barrier is the monopoly that arises from, at least, one pending patent application or, at least, one granted patent. Initiatives to challenge this barrier are those which seek to reduce this monopoly. We assume that even if these initiatives do not lead to the patent's rejection, revocation or licensing, they may have effects on the dynamics of medicines price.

The outline of this path seeks to analyze the historical series of LPV/r prices in Brazil and in the international market in light of the initiatives to challenge patent barriers. In order to do so, we assume that there is a relationship between these initiatives and the medicines price, suggesting a possible effect of the former on the latter.

## Methods

This is a longitudinal case study covering the period from 2001 to 2012. It investigates initiatives to challenge patent barriers as explanatory elements of the evolution of LPV/r's treatment cost.

The study comprised the following methodological steps: non-exhaustive literature review, identification of Brazilian initiatives to challenge patent barriers for LPV/r, comparison between the historical series of LPV/r's price in Brazil and in the international market.

The initiatives to challenge patent barriers for LPV/r in Brazil were mapped out and systematized chronologically, as well as classified according to their proponents: the government, national public and private manufactures and civil society organizations.

We obtained unit prices in US dollars (US\$) for LPV/r in Brazil from the STI, AIDS and Viral

Hepatitis Department of the Ministry of Health through the Access to Information Law. The cost of one treatment per year was calculated by multiplying the number of daily pills by 365 days. In order to compare Brazilian and international prices, prices for the brand (Abbott) and international generic alternatives were obtained from the documents *Accessing ARVs: Untangling the Web of Price Reductions for Developing Countries* from 2001 to 2012<sup>10,11,12,13,14,15,16,17,18,19,20,21</sup>.

The information was systematized in electronic spreadsheets. We constructed a graph with the estimates of cost per treatment per year. Between 2001 and 2006, the adopted dosage form was 133/33mg of LPV/r capsules six times a day. From 2007 on, the adopted dosage form became 200/50mg LPV/r tablets four times a day. Therefore, in order to estimate and compare costs over different years, we calculated treatment costs per individual based on the recommended dosage form adopted by the Brazilian government in each year.

## Results and discussion

In Brazil, the Industrial Property Law (LPI; *Law 9,279/96*) was approved to become compliant to Trips Agreement and also included provisions that went beyond the minimum requirements of the agreement, having negative consequences such as high prices for the ARV adopted by SUS<sup>22,23,24,25</sup>. The first medicines that inaugurated the adoption of patented products were efavirenz, nelfinavir and LPV/r<sup>26</sup>.

These products were protected through pipeline patents or revalidation patents, considered a Trips-plus provision. This allowed the retroactive patent protection of pharmaceutical products and processes whose patent applications were filed in other countries, as long as there were no local efforts to explore the invention. Additionally, there was no technical examination in Brazil and applications could be filed even after the priority period. Thus, even though the invention was already in the public domain, a patent monopoly was granted in Brazil<sup>27,28</sup>.

When the LPI came into effect in Brazil, it had an immediate effect on medicine costs and on the sustainability of the programs due to its direct impact on the public budget<sup>26</sup>. Studies comparing prices of some medicines in Brazil with generic versions in the international market show a large discrepancy in the price offered by the patent holder<sup>29</sup>.

Another Trips-plus provision that was included in the LPI was the sole paragraph of article 40, which ensures a minimum patent term of ten

years from the time it is granted. If the examination is delayed by more than ten years, the term of the patent will be greater than twenty years. In some countries, high prices of ARV have been a limiting factor for access to treatment, while in Brazil it threatens the sustainability of the medicines' supply by SUS<sup>26</sup>. In Brazil, users do not directly pay for the treatments. Medicines are provided through the SUS, according to the treatment guideline.

Some safeguards were included in the Trips agreement, from a public health perspective, in order to minimize the negative impacts of patent protection on health policies. It was up to each country to incorporate them into their legislations<sup>22,23</sup>. These safeguards seek to enable the entry of generic versions into the market and to promote competition as a means for reducing prices and enabling access in the context of a monopoly.

These safeguards may act at different moments: if the product is already patented, there are instruments that make it possible to obtain generic alternatives during the term of patent (compulsory licensing and parallel importation); if a patent application has been filed, but not yet granted, it may be possible to technically challenge (oppositions); and to adopt guidelines to ensure a restrictive examination of the patentability requirements. Lastly, there is also the possibility of developing research with patented product and process, including carrying out necessary tests for obtaining market approval by country's drug regulatory authorities (experimental use and Bolar exception).

### **Government and civil society strategies: from price negotiations to demands for compulsory licensing**

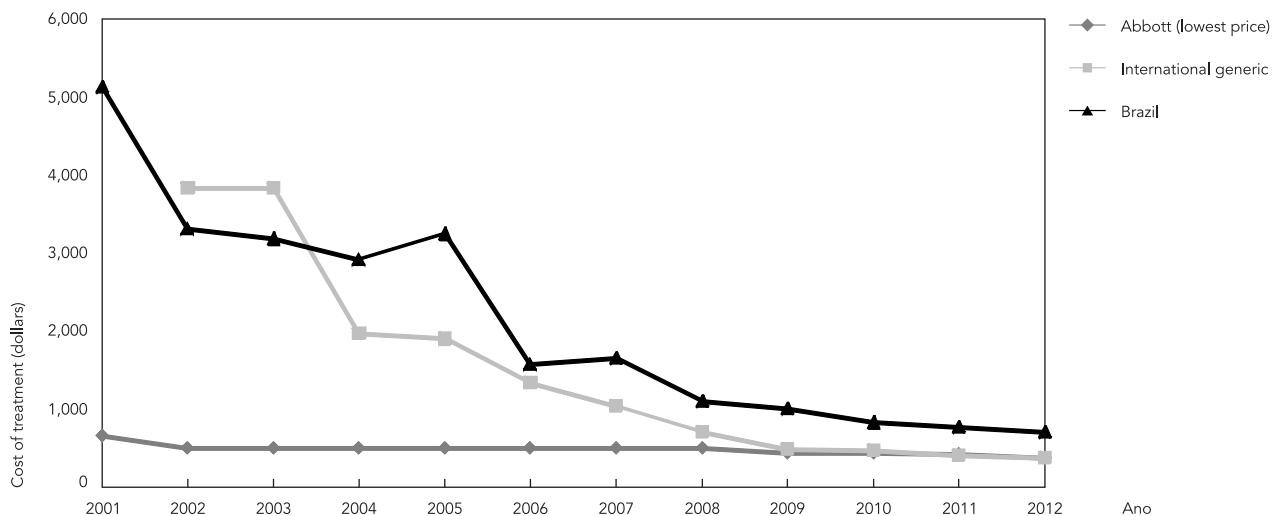
Between 2001 and 2003, initiatives were mostly governmental, such as the use of threats to issue compulsory license in order to achieve price reduction during negotiations with patent holders and in changes in the Brazilian legislation.

The possibility of issuing a compulsory license was used as an important instrument for price negotiation in Brazil. Between 2001 and 2003, the Brazilian government negotiated a discount for several patented medicines<sup>30</sup>. About launched LPV/r in 2000 and, in 2001, there were no generic versions available in the market. That year, the cost per treatment paid by Brazil was more than five times higher than the cost per treatment with prices offered to least developed countries (Figure 1).

In 2001, as a result of the negotiation, there was a considerable reduction in the price for

Figure 1

Cost per treatment per year of lopinavir/ritonavir (LPV/r) in US dollars, between 2001 and 2012, for the lowest price offered by Abbott, for the generic with lowest price internationally, and for the purchasing price in Brazil.



some medicines, among them LPV/r, which had a 46% price reduction, according to the literature (Figure 2). In addition the reduction in LPV/r's price, other measures were identified in that period: changes in the Brazilian legislation in order to include the Bolar exception and the prior consent of the Brazilian Health Regulatory Agency (Anvisa) for examining pharmaceutical patents application<sup>30</sup>. According to the analysis of the historical series of cost per treatment (Figure 1), there was a 35% reduction between 2001 and 2002.

In 2002, a generic version of LPV/r was launched. However, the price charged by the company that year was higher than what was sold by Abbott in Brazil.

As shown in Figure 2, in 2003, another negotiation process between the Brazilian Ministry of Health and patent holders was necessary due to the high cost of the medicines. The threat to issue compulsory licensing was once again used as a strategy and a reduction in price was agreed upon that led to a 37% reduction in total spending for ARV<sup>30</sup>.

Additionally, another normative change was proposed in 2003 with the decree that detailed the used of compulsory licensing for public interest and national emergency cases<sup>31</sup>. That change established the possibility of importing products from producers other than the patent holder, if a compulsory license were issued.

Between 2003 and 2004, the price of the Indian generic version had a near 50% reduction, ending up well below the purchasing cost in Brazil, which had been slowly decreasing since 2002, as can be seen in Figure 1. In that same period, the protease inhibitor atazanavir was introduced in Brazil and quickly became LPV/r's main competitor as a therapeutic substitute<sup>5</sup>. However, these two events seem not to have had an immediate impact on the price of LPV/r in Brazil. There was a increase in the cost of LPV/r purchased by Brazil between 2004 and 2005 (Figure 1).

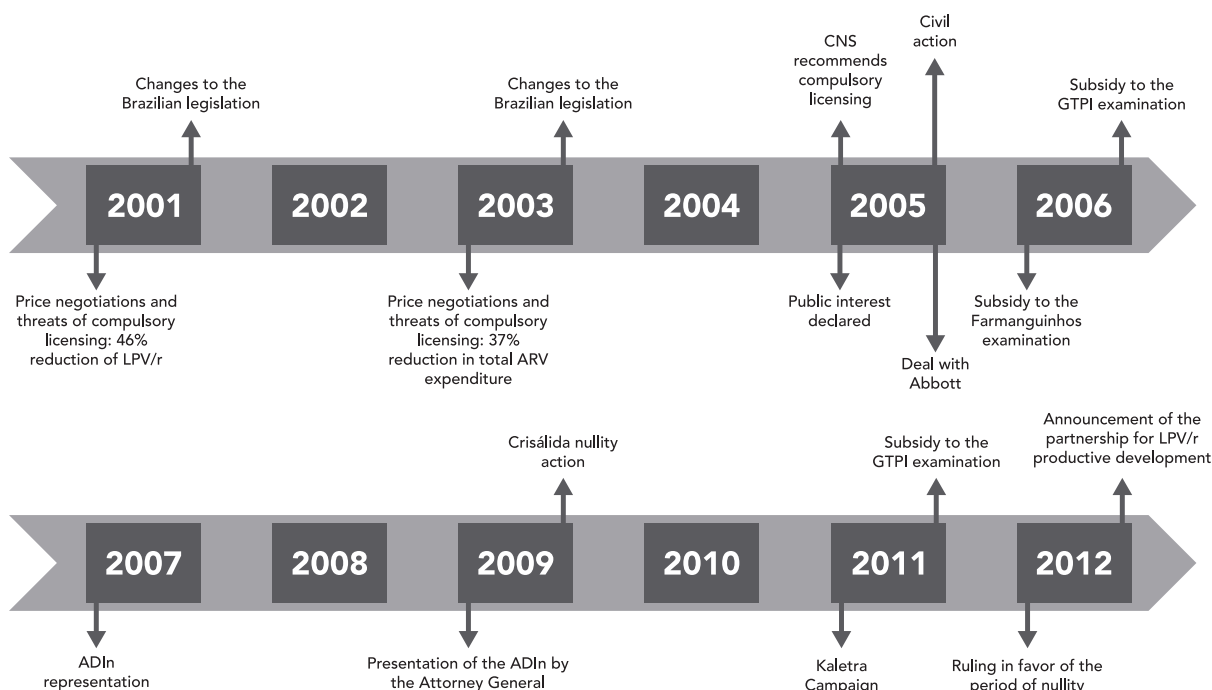
In the period between 2005 and 2007, there were also a series of initiatives led mainly by civil society. There were also government initiatives and one initiative by a national public manufacturer.

As we have already discussed (Figure 2), until 2005, Brazil used the threat of compulsory licensing in order to successfully negotiate price reductions for several patented drugs. Giving into Brazilian threats of compulsory licensing, the pharmaceutical industry preferred to reduce prices than have their patents compulsorily licensed. But, over time, that negotiation tactic began to lose credibility and became inefficient, so that the prices reached were unsatisfactory<sup>26,27,29</sup>.

According to Grangeiro et al.<sup>26</sup>, during that time, it was announced that the sustainability of the ARV supply in Brazil would be at risk if costs continued to rise in the same proportion. In 2005,

Figure 2

Time line of initiatives seeking to challenge patent barrier of the lopinavir/ritonavir (LPV/r).



ADIn: Direct Action of Unconstitutionality; ARV: antiretrovirals; CNS: Brazilian National Health Council; Farmanguinhos: Institute of Drug Technology, Oswaldo Cruz Foundation; GTPI: Working Group on Intellectual Property.

Note: changes to the Brazilian legislation in 2001 – Bolar exception and previous consent. Changes to the Brazilian legislation in 2003 – detailing of compulsory licensing use.

LPV/r accounted for around 30% of governmental ARV expenditures of R\$ 1 billion<sup>32</sup>. That year, there was a 66% increase in ARV expenditures, according to the literature, breaking the reduction tendency observed between 2000 and 2004. Some factors associated with the increase were: the weakened national pharmaceutical industry and negotiations with unsatisfactory results<sup>26</sup>.

In 2005, there were four initiatives to challenge patent barrier (Figure 2). In March of that year, Brazil announced its intention to issue a compulsory license for three medicines if producers did not provide a voluntary license. In June of that year, during negotiations with Abbott to reduce LPV/r's price, the Brazilian government declared it to be of public interest – the first step for issuing a compulsory license – and gave Abbott a deadline to offer a reasonable price<sup>7,27,29,33,34</sup>.

The issue of high medication prices threatening the sustainability of the ARV supply was also discussed in a meeting of the Brazilian National

Health Council (CNS) in August 2005. Based on considerations made by council members, CNS unanimously approved a resolution in favor of issuing a compulsory license and local production of LPV/r and other patented medicines, given the lack of satisfactory negotiations for reducing prices<sup>32,35</sup>.

However, after four months of negotiations, in October 2005, a deal was signed between the Ministry of Health and Abbott ensuring a 46% price reduction. Even with this discount, the price of the medicine was still much higher than the lowest price offered internationally by Abbott and than the estimated production cost. There were other restrictions in the agreement<sup>7,27</sup>. Despite the CNS initiative, the Ministry of Health did not issue a compulsory license for LPV/r and opted instead for an agreement with the pharmaceutical company<sup>36</sup>.

In December 2005, due to the lack of a compulsory license, the Working Group on Intellectual Property of the Brazilian Network for

the Integration of Peoples (GTPI/Rebrip), along with the Federal Prosecutor, filed a civil action against the Brazilian government and Abbott, demanding that a compulsory license be issued for LPV/r. However, the initial judicial response was negative, due to fear of retaliation from developed countries, possible medicine shortages and doubts regarding local production capacity. The authors of the civil action appealed against the decision. The appeal is still pending<sup>27,29</sup>. In this case, there is a clear reproduction of pharmaceutical companies and developed countries' discourse by the Brazilian judiciary, with no critical analysis of the topic<sup>36</sup>.

Between 2005 and 2006, with LPV/r having been declared of public interest, CNS's recommendation that a compulsory license be issued and the collective action, even after an agreement was reached with Abbott, LPV/r's cost dropped once again, by more than 51% (Figure 1). Dhamija et al.<sup>37</sup> state that, after 2006, there was a stabilization in the prices of several medicines, which is reflected in the price of LPV/r.

#### **New stakeholders and new strategies to challenge patent barriers**

Starting in 2006, in addition to government and civil society initiatives, there were efforts to confront the LPV/r patent barrier by other stakeholders: public and private national manufacturers and the Attorney General.

In 2006, the Institute of Drug Technology (Farmanguinhos), a unit of Oswaldo Cruz Foundation (Fiocruz), presented a pre-grant opposition (support to examination) for one of the patent applications for LPV/r. That same year, on World AIDS Day, GTPI/Rebrip presented another pre-grant opposition contesting the same patent application (Figure 2). As a result of these initiatives, that application was rejected by the Brazilian National Institute of Industrial Property (INPI) in 2010 (INPI. Base de dados do INPI. <https://gru.inpi.gov.br/pPI/jsp/patentes/PatenteSearchBasico.jsp>, accessed on 01/May/2014)<sup>38</sup>. However, the large number of patent applications field in Brazil generates uncertainties regarding whether the rejection of this application does put the medicine in the public domain.

The LPI establishes the possibility of presenting pre-grant opposition (support to examination), before they are granted, or nullity, after they are granted (post-grant opposition). This strategy is internationally known as patent opposition. Up to the end of the period of patent examination, interested parties could submit technical informations to the INPI. This procedure seeks to prevent that monopolies be granted if the re-

quirements for patentability are not met – novelty, inventiveness and industrial application<sup>7,27</sup>, preventing the emergency strategy.

At least twelve patent requests related to LPV/r were deposited in Brazil. With the last request being granted, the monopoly will be extended by nine more years beyond the expiration of the first patent request in Brazil – until 2025 (INPI. Base de dados do INPI. <https://gru.inpi.gov.br/pPI/jsp/patentes/PatenteSearchBasico.jsp>, accessed on 01/May/2014)<sup>39</sup>.

In 2007, GTPI/Rebrip, through the National Pharmacist Federation (Fenafar) filed a representation requesting that the Attorney General file a Direct Action of Unconstitutionality (ADIn, in Portuguese) against the pipeline mechanism at the Federal Supreme Court. The ADIn is a mechanism that enables stakeholders to contest the constitutionality of a given law<sup>29</sup>.

The representation sought to show that pipeline patents are unconstitutional. It is worth noting that the inventions that were meant to be protected by this mechanism were already in the public domain and therefore did not meet the novelty requirement<sup>36</sup>. It is estimated that 340 medicines have been protected through pipeline patents, including ritonavir and lopinavir<sup>27,28,40</sup>.

This initiative did not address LPV/r specifically, but sought to annul the article of the LPI that made this form of patenting possible. This way, other patent applications could also be annulled. Other medicines for which a patent was granted through pipeline are: atorvastatin, imatinib and olanzapine. Between 2009 and 2010, it is estimated that Brazil paid between 704% and 5,622% more for these medicines than it would have spent on equivalent generic medicines<sup>41</sup>.

There is another study on the effect of pipeline patents on the prices of five ARV: abacavir, nelfinavir, efavirenz, amprenavir and LPV/r. The prices of generic versions available internationally were compared with the value paid by the Ministry of Health between 2001 and 2007. It was estimated that, in that period, Brazil paid between US\$ 420 and US\$ 519 million more, when compared with the reference prices from World Health Organization or Doctors without Borders, respectively<sup>28</sup>.

In May 2009, in response to Fenafar's representation on behalf of GTPI/Rebrip, the Attorney General presented the ADIn 4,234 to the Supreme Court, questioning the validity of pipeline patents. Several *amici curiae* were presented both in favor and against the ADIn<sup>28</sup>.

The Court's decision is still pending. This delay may weaken the effect of the initiative, as most of the patents of the products produced through pipeline have expired. Meanwhile, other judicial

actions are addressing the topic on a case by case basis. The Supreme Court's decision has extensive implications for access to medicines, since it sets a precedent for addressing old issues regarding the patenting in Brazil <sup>10,11,12,13,14,15,16,17,18,19,20,21</sup>.

### **International initiatives and local effects**

Though the methods we have used in this study prioritized initiatives for overcoming patent barriers in Brazil, we also found international initiatives in the literature which deserve to be discussed in light of the price evolution.

Between 2006 and 2008, the Thai government issued compulsory licenses for seven medicines, including LPV/r <sup>42,43</sup>. In response to the Thai compulsory license, Abbott made changes to their price discrimination policy and to the offer of differentiated prices in middle-income countries. The reduction of LPV/r prices in 40 countries, including Brazil, shows the influence of the international context in other countries <sup>27</sup>. As shown in Figure 1, from 2008 on, treatment costs for LPV/r was around US\$ 1,000 per year, the value Abbott offered middle-income countries. In May 2007, Brazil issued a compulsory license for efavirenz. In the post-compulsory licenses context, LPV/r's price fell continuously.

The practice of differential prices (or tiered pricing) is the sale of essential medicines to low and middle-income countries at lower prices than in developed countries and has been proposed as an alternative to high prices of medicines. However, market segmentation according to consumers' alleged capacity to pay is also a profit maximization strategy and is not necessarily more effective than competition <sup>44</sup>.

In special situations, especially when markets are small and uncertain, production capacity is limited or there are delays in overcoming barriers to competition, the practice of differential prices may contribute to increasing access, as in the case of drug-resistant tuberculosis. However, when markets are considerably large and several forms of production are available, price differentiation has a low performance when compared with competition in reducing sustainable prices – which has been shown for ARV, drug combinations for malaria, visceral leishmaniasis and vaccines against pneumococcus <sup>44</sup>.

Other elements must be taken into account: price differentiation does not necessarily result in the lowest sustainable prices, nor does it ensure reductions over time; there are no clear international rules for establishing differential prices; and this practice gives little deciding power to governments, leaving this important issue in the hands of private companies <sup>44</sup>.

Between 2009 and 2012, we can define a period with actions focused on pre- and post-grant oppositions. The use of Trips safeguard may be an important alternative in the change in the pattern of initiatives for challenge patent barriers, as generic versions available in the international market tend to decrease as a consequence of countries with production capacity are becoming Trips compliant.

In 2009, within the context of the Brazilian industry policy of incentivizing local production, there was one initiative by a national private company. In September, the pharmaceutical company Cristália presented a post-grant opposition in the Court regarding the LPV/r patent, granted in 1997 through the pipeline mechanism. With the same motivation as the ADIn, the allegation is that the patent was granted without an analysis of the patentability requirements and without an examination by Anvisa. In February 2012, the Federal Court of Rio de Janeiro ruled in favor of the post-grant opposition request, annulling LPV/r's original patent <sup>10,11,12,13,14,15,16,17,18,19,20,21,45</sup>.

From 2009 on, the price of the international generic became comparable with the lowest price offered by Abbott to other countries. These prices dropped until 2012, reaching a value around US\$ 400, probably close to production costs. A previous study showed the importance of raw materials cost in determining ARV prices; other factors, such as workforce, scale, transportation, among others, had a smaller impact. Since raw materials for certain second line medicines, such as LPV/r, are patented in many countries, this leads to an increase in the price of these ingredients and of an overall production costs <sup>46</sup>.

In November 2011, groups defending public health in twelve countries launched a global campaign, challenging Abbott for the monopoly of the LPV/r fixed-dose combination. The "Global Kaletra Campaign" (Figure 2), as it was known, sought to give visibility to the globalization of problems that seemed to be local. The campaign aimed at stimulating competition with generic drugs in order to reduce price and to make new fixed-dose combinations possible through the presentation of patent oppositions (support to examinations) or requests for compulsory licensing <sup>10,11,12,13,14,15,16,17,18,19,20,21,47</sup>.

Brazil participated in this campaign and one of its actions was the pre-grant opposition, presented by GTPI/Rebrip, against the patent application that covers the heat-stable dosage form, filed in 2004, by Abbott. This initiative sought to avoid the inappropriate extension of the monopoly. INPI granted a priority examination of this patent application in order to speed up the analysis. The

patent application is still pending, but INPI's technical report states that the application does not meet patentability requirements, because it is obvious to someone with technical expertise in the subject <sup>10,11,12,13,14,15,16,17,18,19,20,21,48</sup>.

Some medium term effects of the initiatives are: decisions due to judicial dispute and the Partnership for Productive Development (PDP) for the local production of LPV/r.

Within the current industrial policy, in 2012, a PDP was announced for the combination LPV/r, as shown in Figure 2. The proposal involves three public manufacturers (Farmanguinhos, Furp and Iquego) and one private manufacturer (Cristália) <sup>10,11,12,13,14,15,16,17,18,19,20,21,49</sup>, without involving the patent holder as a responsible for the technology transfer. Among its goals, this policy seeks to reduce prices <sup>50</sup>, but further studies are required to establish its benefits for this reduction.

It is interpreted that this approach, with the goal of establishing a local production, considered the possibilities established in the Brazilian legislation for experimental use and the Bolar exception, since these efforts are taking place during the patent term. National producer's bet to develop this medicine must have taken into account the fact that the last patent granted to LPV/r is about to expire – in 2017.

The period between 2009 and 2012, shown in Figure 1, shows that there was a 30% reduction in purchasing price in Brazil, without reaching the values of the two other curves, showing that price reduction possibly reached its limit.

Finally, analyzing the evolution of LPV/r's treatment costs in light of initiatives to challenge patent barriers enabled us to point out explanatory elements of the dynamics of the prices the Brazilian government obtained over time.

The variations between the different sources of data on treatment costs in Brazil and on international prices are limitations of this study. It is also not possible to guarantee the correlation of cause and effect between the initiatives and the prices, but we are able to suggest a relationship between these two variables.

## Final considerations

Brazil is politically and legally committed to pharmaceutical services and treatment provision. However, the Trips Agreement represented a challenge to health policy makers, as the possibility of patenting pharmaceuticals made high prices for essential medicines possible.

The Trips Agreement establishes a minimum standard for the protection of intellectual property, and countries are free to establish their national standards and legislation, including the incorporation of safeguards for protecting public health. Though initiatives show that the safeguards established in Trips and incorporated into the LPI have not been used to their fullest potential, price reductions for medicines under monopolies also do not occur spontaneously and without direct or indirect efforts to put pressure on these monopolies.

Nationally, negotiating prices through threats of compulsory licensing was an important and widely used initiative. Different stakeholders also contested patent applications at different times. Though it was not this study's goal to compare the strategy which most contributed to price reductions, we suggest that a combination of strategies may establish a favorable environment for price reduction.

Internationally, identifying generic versions and mapping out initiatives for overcoming patent barriers in other countries may contribute to a price reduction environment, as evidenced by compulsory licensing in Thailand and changes to the company's price offer to other countries, including Brazil.

We were able to map out and characterize different stakeholders' actions and goals to challenge patent barriers, which include direct efforts to reduce price, a search for local production alternatives and greater visibility for the effects of patent protection on access.

More detailed studies are needed, with tools that are capable of overcoming this study's limitations and that may add other explanatory elements regarding price reductions of patented medicines in Brazil. However, we believe this study contributes to identifying some of these elements about the dynamics of medicines price.



## Contributors

C. T. Scopel designed the study and was responsible for data collection and analysis, writing and revising the final text. G. C. Chaves contributed to organizing the study, discussing the data, writing and revising the final text.

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## Resumo

Desde 1996, com a consolidação da oferta do tratamento antirretroviral (ARV) às pessoas vivendo com HIV no Brasil, o governo tem como desafio assegurar a sustentabilidade desta oferta num contexto de incorporação de medicamentos patenteados. O artigo teve como objetivo analisar a série histórica do preço do lopinavir/ritonavir (LPV/r) no Brasil e no mercado internacional à luz de iniciativas de enfrentamento da barreira patentária no período de 2001 a 2012. A metodologia consistiu em mapeamento de iniciativas de enfrentamento da barreira patentária para o LPV/r e análise da série histórica do preço no Brasil e no mercado internacional. Os resultados encontrados apontam que, entre 2001 e 2003, identificaram-se esforços de ameaça de licença compulsória. De 2005 a 2007, identificaram-se iniciativas por diferentes atores: declaração de interesse público, subsídios ao exame e ação civil pública. De 2006 e 2008, iniciativas internacionais de licença compulsória resultaram na redução do preço no Brasil. Entre 2009 e 2012, observa-se uma redução do preço de aquisição pelo Brasil de 30%.

Propriedade Intelectual de Produtos e Processos Farmacêuticos; Preço de Medicamento; Antirretrovirais

## Resumen

Desde 1996, con la consolidación de la oferta de tratamiento antirretroviral (ARV) para las personas viviendo con VIH, el Gobierno de Brasil tiene el desafío de asegurar la sostenibilidad de dicha oferta en un contexto de incorporación de medicamentos patentados. El objetivo de este artículo es analizar la serie histórica del precio del lopinavir/ritonavir (LPV/r) en Brasil y en el mercado internacional, a la luz de iniciativas para enfrentar la barrera patentaria durante el período de 2001 a 2012. La metodología consistió en un mapeo de iniciativas para hacer frente a la barrera patentaria del LPV/r y el análisis de la serie histórica de sus precios de adquisición por el SUS y en el mercado internacional. Entre 2001 y 2003 se identificaron esfuerzos por obtener reducciones de precio de LPV/r, mediante la amenaza de expedición de licencia obligatoria. De 2005 a 2007, se identificaron varias iniciativas de diferentes actores, tales como, la expedición de declaración de interés público, presentación de subsidios para el examen de solicitudes de patente de este medicamento y la interposición de acción civil pública. Entre 2006 y 2008, la expedición de licencias obligatorias en el marco de iniciativas internacionales, propiciaron reducciones de precio de LPV/r en Brasil. La reducción promedio del precio de adquisición por parte SUS fue de 30% entre 2009 y 2012.

Propiedad Intelectual de Productos y Procesos Farmacéuticos; Precio de Medicamento; Antirretrovirales

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