GRUPO DE TRABALHO SOBRE
PROPRIEDADE INTELECTUAL

Associação Brasileira
Interdisciplinar de AIDS

Civil society demands a response from the government in relation to the contract of ARV drug atazanavir
International agreement brings to light deficiencies of contract established in Brazil

12/17/2013 - The recently announced license agreement for the patent of the anti-aids drug atazanavir, signed between the U.S. company Bristol Myers Squibb (BMS) and the Medicines Patent Pool (MPP), is a warning for Brazil. In November 2011, it was signed between the BMS and the Brazilian public laboratory Farmanguinhos, an agreement for the same purpose (patent license), but with very different terms. Besides being marked by unfavorable access to medicine clauses, the agreement signed in Brazil is severely delayed. The signing of the international agreement between BMS and MPP can serve as an opportunity to bring about a transparent discussion about the direction of the agreement signed in Brazil and its revision.

"A red signal should now be lit at the Health Ministry, so that the race to reach increasingly larger amounts of PDPs (Partnerships for Productive Development) does not run over the quality of the negotiation of these contracts," said Marcela Vieira, coordinator of the Working Group for Intellectual Property (GTPI/Rebrip). When analyzing the contract signed in Brazil for atazanavir, GTPI identified flaws in the negotiation and implementation of the agreement and points at damages for SUS (NHS). "The way it is going, the contract is generating freezing of prices and the obligation to purchase the product from BMS even after the end of its patent monopoly. This goes against the sustainability of universal access policy to AIDS drugs, "says Marcela.

The agreement between BMS and Farmanguinhos provides for acquisition of drugs, technology transfer and licensing of the patent. In short, Brazil has agreed to buy the drug from BMS for pre-determined terms and prices while internalizing technology and learning to produce on its own. When domestic production begins, Brazil will pay royalties and continue supplying half the national demand with imported product from BMS.

Regarding the acquisition of the drug, prices are frozen at R$ 3.40 (about US$ 1.67) per unit (version of 200mg) since signing of the contract in 2011. That is to say, no price reduction has been observed yet as promised when the contract was announced. The cheaper generic version available in the international market costs US$ 0.48, **a price that is about 4 times less than the price currently paid in Brazil**. Furthermore, that which defines the duration of the obligation to purchase the product from BMS is the date on which Farmanguinhos will obtain the generic version registry, which will be produced in Brazil. According to the contract schedule, this registry should have been ready in 2012, but up to the present this has not happened. This delay may mean that Brazil will have the obligation to purchase the product from BMS until 2018, even after the patent in Brazil expires in 2017.

Regarding technology, the contract signed in Brazil may not be aligned with global treatment trends. Atazanavir needs to be taken along with another drug, which enhances its effect, ritonavir. The fixed-dose combination of atazanavir with ritonavir facilitates treatment compliance. However, the contract signed in Brazil expressly prohibits manufacture of this fixed-dose combination. Now, in the contract between BMS and MPP, which is intended for any producer in any country, no such prohibition exists. "This comparison can be seen as an indication that Brazil negotiated its agreement in a poor way and did not make prevail the need of the patient," says Jorge Beloqui, from the GIV - *Grupo de Incentivo à Vida* [Incentive to Life Group]. In addition, in the MPP contract technology transfer has no additional cost, while in Brazil the high price of the drug is justified by the cost of technology transfer.

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"Embedding the cost of technology transfer in the price paid to acquire the product is a questionable strategy because it loses sight of how much is actually being paid for the technology, besides putting the health resources at the service of the development agenda", remarks Beloqui. This choice is made in a context of underfunding of the SUS and where price reduction of medicines is increasingly required to support new treatment goals, such as to treat 100,000 people more for HIV/AIDS in 2014, as recently announced by the MoH. "The Brazilian population is more aware about how public resources are used, but the government is not aware of its obligation towards transparency," says Beloqui.

The contract for the production of atazanavir in Brazil is one of the 88 PDPs (Partnerships for Productive Development) announced by the Ministry of Health. According to the legal framework of PDPs (ORDINANCE No. 837, OF APRIL 18, 2012): "Each PDP will be assessed at the end of the first period of twelve (12) months, for the purpose of verifying the expected in the production process progress and/or technology transfer". The PDP for atazanavir has just turned two years old, so GTPI has requested, through the access to information act, these monitoring reports, where delays could be confirmed. The Ministry of Health's response, however, is that these and any other document relating to PDPs is confidential and its disclosure would be a threat to national security.

Ordinance 837 also provides that PDPs may be terminated if "the schedule established in the PDP is not complied with" (Article 11), as seems to be the case of the contract for the production of atazanavir. "A large amount of public money is involved in this PDP; scarier than the possible deficiencies of the contract is the way the government has rejected any possibility of dialogue, there are SUS principles and obligations of public laboratories that cannot be ignored," concludes Marcela.

Summary of Bristol-Farmanguinhos agreement:

Object:
•Supply of the product (Farmanguinhos commits to buy atazanavir from BMS)
•Technology transfer (BMS undertakes to train Farmanguinhos in the production of a domestic version of atazanavir – generic version)
•Sublicensing of patent exploration PI 9701877-5, which expires on 07/01/2017. (BMS, patent holder, permits Farmanguinhos to use the information contained therein in exchange for the payment of royalties)

Schedule:
•11/11/2011 – Agreement signed between BMS and Farmanguinhos
•11/31/2012 – Agreement made official by the Ministry of Health
•Time for Execution: 5 years (that only begin to be counted from the date of the registration of the national version of atazanavir)

Public Spending Involved:
•Around R$ 475 million (about US$ 233 mi) for product acquisition and BMS technology (spending in the course of 5 years).
•The cost of the domestic generic version produced by Farmanguinhos, which is still unknown.
•4.5% of royalties to be paid to BMS calculated over the net sales of the domestic version produced by Farmanguinhos.

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Some Troublesome Points of Bristol-Farmanguinhos Agreement

Clause	Contents	Analysis
1.1	PRODUCT: "All other presentations, dosages, formulations, compositions, including but not limited to, fixed-dose combinations, such as atazanavir sulfate and ritonavir (...) are expressly excluded from this Agreement "	Farmanguinhos will acquire the technology, but will only be able to produce atazanavir in capsule form and in doses of 200mg and 300mg. It is a limiting factor insofar as new formulations containing atazanavir possibly will be recommended and used as new treatment options. Brazil is at risk of having to pay too much to make a product that is to be replaced.
1.1 and 2.2.1	TERRITORY: "It means Brazil". "One or any of its affiliates cannot during the term of this agreement promote, distribute, market, sell (...) any product containing the API or PRODUCT outside the TERRITORY"	Brazil is prohibited from using its production of atazanavir to collaborate with other countries to combat AIDS. Even to make donations of medicines for humanitarian purposes (clause 14.1.1), Brazil must request permission from BMS. In other licenses negotiated in other countries, the geographical scope is a central point of negotiation. Given its key role in the global fight against AIDS, it was expected that Brazil had not been concerned only with its domestic market.
9.1 / 9.5	"The buyer must pay royalties to the supplier quarterly, by sublicense of the patent related to atazanavir sulfate, a value corresponding to 4.5% to be calculated on the net value of sales by product manufactured and sold by the buyer to the Ministry of Health of Brazil, as of the date of the first sale of the product manufactured by the acquirer and until expiration of the patent". "The payment of Royalties by the pharmochemical Brazilian company relates to the production of the NATIONAL API in the TERRITORY, shall not relieve the purchaser of its obligation to pay royalties on the finished product manufactured by the purchaser as provided in this clause".	In addition to paying a high royalty (4.5%), the agreement provides for a "double" royalty situation. Farmanguinhos pays and the private Brazilian company that will produce the active pharmaceutical ingredient of atazanavir also pays. Bristol also made technology transfer agreements with laboratories in South Africa and India. These agreements also involve training, transfer of knowledge for the production and handling of the active ingredient and support for regulatory requirements. These agreements are royalty free.
8.5 / 8.5.2	"The Purchaser agrees to purchase from the Supplier the entire demand of the Ministry of Health of Brazil for the product during the first 3 years after the grant of the drug registration." "During the fourth and fifth years after obtaining the drug registration, the supplier should provide the equivalent of 50% of the total demand of the Ministry of Health of Brazil for the product".	The deadlines for this transfer seem very long. In total five years. On a similar agreement between Bristol and Indian company Emcure, the transfer was announced in 2006 and in 2008, Emcure obtained the market approval. Besides seeming too extended, if some delay occurs Brazil can be compromised to buy the product from Bristol even after the end of the company's patent (expiring in 2017). It is not clear if the agreement lasts until the patent expires, or until the period of 5 years is finished (counted from the drug registration).
1.1	PATENT: "It means the molecule and pharmaceutical composition patent of atazanavir sulfate (PI9701877-5), which the supplier is duly authorized to sublicense to the purchaser."	There is a patent application filed by BMS pending (PI 0509595-6) and relates to atazanavir bisulfate. This patent is not mentioned in the agreement. If granted, may this patent impose any barrier to domestic production of atazanavir?

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