

Analysis of Territorial Access Issues in the MPP/BMS Atazanavir License

Professor Brook K. Baker, Northeastern U. School of Law

December 16, 2013

On December 11, the Medicines Patent Pool announced a new licensing agreement for a 2013 WHO recommended second-line antiretroviral, atazanavir (ATV).¹ At this point, it is important for IP activists, generic companies, and countries to understand both the express territorial coverage of the license (110 countries) and its “effective” territorial coverage as well (144 countries plus the possibility of compulsory license expansion). Because royalty payments are actually limited to situations where granted patents are in effect – and with some exceptions even then, it is also important to identify the limited circumstances where royalties will be imposed. Finally, it is important to analyze some of the licensed or patent-free availability of ritonavir or cobicistat for co-formulated boosting.

No territorial restriction on country of manufacture

First, with respect to territories, an advance in this agreement is that ***ATV can be produced in any country in the world***, including rich countries and the traditional generic producing countries in low- and middle-income countries. This is a significant advance over the MPP’s licensing agreement with Gilead, which unreasonably limited production to India only, presumably because Gilead had a pending patent application in India and because of the known competency of India generic producers. The country of production alone will not affect royalty rights because royalty rights under the agreement, as specified further below, are payable only with respect to sales in a very limited number of countries.

Royalties due only for sales in countries with granted ATV patents with exceptions

BMS has not required any royalty payments except in countries within the territory where an ATV-related patent has been granted or later comes into effect. In other words, in countries where no patent has been filed or where patent application has not been granted, BMS will be entitled to no royalties. This too is an advance over the MPP’s previous license with Gilead where royalties could be paid based on patent applications and/or based on patent applications or granted patents in the country of production.

Even in this clause, the MPP has attempted to create an exception for royalty payments in the case of countries included within the scope of BMS’s prior non-assert agreements with three generic companies covering 49 countries (sub-Saharan Africa and India). Similarly, there are no royalties due on sales of pediatric formulations of ATV. Within the express territory, ATV patents have thus far only

¹ <http://www.medicinespatentpool.org/wp-content/uploads/MPP-License-and-technology-transfer-agreement-Signed.pdf>.

been granted in Georgia, Pakistan, and South Africa (sales South Africa are non-royalty bearing because it was covered by prior agreements). Two other express-territory countries where ATV patents are pending are India (multiple patents) and Ecuador.

110 Countries in the Express Territory

As outlined above, there are 110 countries in the express territory, 61 more than included in BMS' previous licenses. These countries collectively account for approximately 88.4% of people living with HIV in low- and middle-income countries. The list of expressly included countries is attached in Appendix A.

Another 34 Countries in the Effective Territory if BMS's Know-How is Rejected

In addition to the 110 countries expressly included in the license agreement, BMS has listed another 34 countries where it has no patent rights granted or pending. Once again, based on the principle that BMS should not be able to prevent generic competition where it does have any patent right, generic companies will be entitled to produce and export ATV to these 34 countries as well pursuant to paragraph 2.7(C) of the licensing agreement.² (see Appendix B). Note, however, described further below that this right is limited to cases where the licensee does not rely on BMS know-how. The 144 countries in the effective territory cover 90% of people living with HIV in low- and middle-income countries.

People may wonder whether BMS's prior licensees would routinely be able to sell in these and other no-patent countries given the U.S. Federal District Court judgment involving a breach of contract claim filed by BMS against one of its licensees, Mylan, which had sold ATV to PAHO for use in Venezuela. There the court held that Mylan could make direct sales to PAHO without breaching an anti-diversion contractual provision, but that decision is now under appeal. It also appears that BMS has a clear right to terminate the Mylan contract under article 8.1b of its Indemnity from Suit Agreement. Thus, it seems that the MPP license gives far more freedom to act in no-patent countries than was true under the previous BMS voluntary licenses because such licenses could not result in termination of the generic sub-license.

In it important to note that the effective territory of the MPP/BMS license could be expanded further if countries were to issue compulsory licenses. As with the

² The key provision of the MPP/BMS license that allows this result is paragraph 2.7(C), which reads as follows: For the avoidance of doubt, it would not be a breach of the Agreement for MPP or its Sublicensees to manufacture or use the Licensed Compounds (in or outside of the Territory) for use, sale, or supply of such Licensed Compounds outside Territory where such use, sale or supply does not (i) infringe Licensed Patent Rights and Non- Territory Patent Rights; and (ii) rely on the Licensed Manufacturing Know-How. For the purposes of this provision, "to infringe" will mean the infringement of a patent in force, or any other activities that are prohibited under applicable laws in relation to Licensed Patent Rights and Non-Territory Patent Rights.

MPP/Gilead license, the MPP has been careful to include a clause³ that allows generic supply whenever a patent right in the country of use is no longer a bar, as when a CL has been issued.

Generic companies are required to take what is essentially an option right to BMS's know-how relating to the production of ATV. However, after examining the know-how, generic licenses will be permitted to reject use of the know-how and reverse-engineer and produce ATV according to their own, non-derivative know-how. Companies would be advised to reject the know-how in writing with notice both to BMS and the MPP. They should also keep careful records of their own, non-derivative manufacturing know-how.

Excluded Territories – 15 countries – where complementary action, including compulsory licensing, is required

It is regrettable that any countries are excluded from the MPP/BMS license. The excluded middle-income countries, at present, include: Argentina, Brazil, Bulgaria, China, Egypt, Indonesia, Lebanon, Malaysia, Mexico, Peru, the Philippines, Romania, Thailand, Turkey and Ukraine.

These countries are not without power to effect their exclusion. Of course, they can complain to BMS and request that they be voluntarily included. However, the countries themselves or even generic licenses could seek the issuances of compulsory or government use licenses. Thailand has previously issued compulsory licenses 2006-2008 on AIDS, cardiovascular, and cancer medicines. Indonesia has issued compulsory licenses much more recently on seven ARVs at the same time. Brazil has previously issued a compulsory license on efavirenz, but it's improvidently negotiated license with BMS for ATV – a license with much worse terms than any license that the MPP has issued – seemingly precludes the issuance of a CL on ATV.

Excluded countries would be much better off if they were to collaborate and coordinate their demands for inclusion and/or their issuance of compulsory licenses. Collective action would not only benefit countries with respect to access to more affordable versions of ATV, it would also put pressure only companies to include such countries in future MPP licenses.

The impact of blockages with respect to AbbVie's ritonavir

Atazanavir has advantages over lopinavir, the other WHO recommended second-line protease inhibitor because it requires a lower dose (300 mg/day instead of 400 mg/twice-a-day) and appears to have fewer adverse side effects. However, like lopinavir, ATV requires boosting with ritonavir, an AbbVie product (the dosage requirement for use with ATV is less though). Unfortunately, AbbVie, an Abbott

³ *Id.*

subsidiary is not yet allowing co-formulation or cross-licensing. Ritonavir is patented, according to the MPP Patent Status Database, in ten countries included in the 110 countries licensed territory. Ritonavir is also licensed in eleven countries not included in the licensed territory (four of them in the effective territory, and six of them in countries where there is also an ATV patent). These countries are listed in Appendix C.

In the future, it is possible that ATV could be co-formulated with cobicistat, a Gilead protease booster, which has already been found non-inferior to ritonavir in one study.⁴ In the event that joint use is registered, the overlap between the MPP/Gilead license and the MPP/BMS license is not perfect as shown in Appendix 4.

Conclusion

There are other issues about the new MPP/BMS license that could and should be analyzed. It is already 15 countries short of covering all low- and middle-income countries and 10% of people living with HIV live in those excluded countries. AIDS activists and countries do not have to take these exclusions lying down. They can take complementary actions either to be included in the BMS license or they can pursue compulsory license alternatives. Despite, this clear 10% shortcoming in coverage, the MPP has made significant advances in this license with respect to the effective area of coverage.

⁴ <http://www.ncbi.nlm.nih.gov/pubmed/23532097>.

Appendix A – Included Territories

Afghanistan	Madagascar*
Angola*	Malawi*
Antigua and Barbuda	Maldives
Armenia*	Mali*
Azerbaijan	Marshall Island
Bangladesh	Mauritania*
Belarus*	Mauritius*
Belize	Micronesia, Federated States
Benin*	Moldova
Bhutan	Mongolia
Bolivia	Mozambique*
Botswana*	Myanmar
Burkina Faso*	Namibia*
Burundi*	Nauru
Cambodia	Nepal
Cameroon*	Nicaragua*
Cape Verde*	Niger*
Central African Republic*	Nigeria*
Chad*	Pakistan
Comoros*	Palau
Congo, Dem. Rep. *	Panama
Congo, Rep. *	Papua New Guinea
Costa Rica	Rwanda*
Côte d'Ivoire*	Samoa
Cuba São	Tomé and Príncipe*
Djibouti*	Senegal*
Dominica	Seychelles*
Dominican Republic*	Sierra Leone*
Ecuador	Solomon Islands
El Salvador	Somalia*
Eritrea*	South Africa*
Ethiopia*	South Sudan
Fiji	Sri Lanka
Gabon*	St. Kitts and Nevis
Gambia, The*	St. Lucia
Georgia St.	Vincent and the Grenadines
Ghana*	Sudan*
Grenada	Suriname
Guatemala	Swaziland*
Guinea*	Syrian Arab Republic
Guinea-Bissau*	Tajikistan
Guyana	Tanzania*
Haiti	Timor-Leste
Honduras	Togo*
India*	Tonga
Iraq	Turkmenistan
Jamaica	Tuvalu
Kazakhstan	Uganda*
Kenya*	Uzbekistan

Kiribati
Korea, Dem. Rep.
Kyrgyz Republic
Lao PDR
Lesotho*
Liberia*
Libya

Vanuatu
West Bank and Gaza
Yemen, Rep.
Zambia*
Zimbabwe*

*Country previously included in one or more BMS agreements in relation to Licensed Patent Rights

Appendix B

Countries with no current ATV Patent

Country
Albania
Algeria
Andorra
Anguilla
Aruba
Bahamas
Barbados
Bosnia and Herzegovina
British Virgin Islands
Brunei
Colombia
Equatorial Guinea
Iran
Jordan
Kosovo
Kuwait
Macedonia
Mayotte
Montenegro
Montserrat
Morocco
Oman
Paraguay
Qatar
San Marino
Saudi Arabia
Serbia
Trinidad and Tobago
Tunisia
Turks & Caicos Islands
United Arab Emirates
Uruguay
Venezuela
Vietnam

Appendix C

Countries within the Territory where ritonavir is patented

	Country	RTV patent
	Armenia	Granted
	Azerbaijan	Granted
	Belarus	Granted
	Kazakhstan	Granted
	Kyrgyzstan	Granted
	Republic of Moldova	Granted
	South Africa	Granted
	Sri Lanka	Granted
	Tajikistan	Granted
	Turkmenistan	Granted

Countries outside the Territory where ritonavir is patented

	Country	RTV patent
	Albania	Granted
	Bosnia and Herzegovina	Granted
	Brazil*	Filed
	China*	Filed
	Mexico*	Granted
	Montenegro	Granted
	Philippines*	Granted
	Turkey*	Granted
	Ukraine*	Granted
	Vietnam	Granted

* ATV patent also granted

Appendix 4

Countries included in ATV and not in COB license (17 countries)

Country
Azerbaijan
Belarus
Botswana
Costa Rica
Ecuador
El Salvador
Federated States of Micronesia
Iraq
Kazakhstan
Korea DPR
Libya
Marshall Islands
Namibia
Panama
Sri Lanka
Turkmenistan
West Bank and Gaza

Countries included in COB and not in ATV License (10 countries)

Country
Anguilla
Aruba
Bahamas
Barbados
British Virgin Islands
Equatorial Guinea
Montserrat
Trinidad and Tobago
Turks & Caicos Islands
Vietnam