



Report of the Medicines Patent Pool Expert Advisory Group on the proposed licence agreement between MPP and Novartis on nilotinib

Introduction

The Expert Advisory Group (**EAG**) of the Medicines Patent Pool (**MPP**) submits the following report to the Governance Board of the Medicines Patent Pool (**Board**) on the proposed licence agreement between MPP and Novartis for nilotinib for blood cancer treatment (the **Agreement**).

This report reflects the outcome of consultations with the EAG on 06 October 2022 in Geneva, Switzerland, chaired by Peter Beyer and joined by EAG members Deus Mubangizi, Ellen t' Hoen, Giten Khwairakpam, Gugu Mahlangu, Fatima Suleman, Jan Gheuens, Jennifer Cohn, Jordan Jarvis, Luis Gil Abinader, Martha Gyansa-Lutterodt, Manuel Goncalves, Valérie Paris, and Zeba Aziz. The EAG was joined virtually by three members of the Scientific Advisory Panel André Ilbawi, Gilberto Lopes and Salomé Meyer.

Background, Overview of the Proposed Agreement

The EAG understands that Novartis entered into negotiations with MPP within the context of the Access to Oncology Medicines (ATOM) Initiative. ATOM was launched in May 2022 by the Union for International Cancer Control and joined by a coalition of both non-profit organisations and pharmaceutical companies as well as IFPMA and the MPP as observer. The stated aim of the ATOM Initiative is two-fold: to increase the availability and affordability of cancer medicines, and to increase the capacity to use these medicines appropriately in low- and lower-middle income countries. A core component to the ATOM Initiative is to facilitate the use of voluntary licences for patented cancer medicines of public health importance.

Nilotinib is an approved treatment for chronic myeloid leukaemia (CML) and is on the WHO Essential Medicines List. It is mostly used as second line treatment where CML is resistant to treatment with imatinib that is available as generic form. According to the 2019 Global Burden of Disease Study, globally there are approximately 250,000 prevalent cases of CML out of which 20-25% are resistant to the current generic first-line treatment. Given that CML is a chronic disease, the global patient population eligible for treatment with nilotinib can be estimated at 50,300 - 63,000 patients.

It is also one of the priority drugs for in-licensing identified by MPP in its 2022 Prioritisation List. The compound patent on nilotinib is set to expire in July 2023, but there are a number of secondary patents relating to its salt and crystal forms, as well as its formulation and method of treatment, that continue until 2026-2030 in several low- and middle-income countries (LMICs). Notably, the compound patent was granted in India but the remaining secondary patent applications were withdrawn by Novartis. Thus, nilotinib will be off-patent in India as of July 2023.

The key aspects of the proposed Agreement are as follows:

Scope of Grant of Licence. The proposed Agreement would grant MPP a non-exclusive licence over Novartis's patents with the ability to grant non-exclusive, royalty-bearing sublicences to eligible manufacturers purposes of supplying the product into the defined territories.



Territory. There are two territories defined in the proposed Agreement: the initial Territory of 44 countries, which essentially is in effect until the expiry of the compound patent in India in July 2023, and the Patent Territory, which comprises a list of seven middle-income countries (MICs) – Egypt, Guatemala, Indonesia, Morocco, Pakistan, the Philippines, and Tunisia, in which Novartis has its secondary patents granted or filed.

Patents. There are also two patent exhibits included in the proposed Agreement – one listing the Indian compound patent as the manufacturing patent, and the other listing the secondary patents in the seven countries listed above.

Field of Use. The Field of Use in the proposed Agreement is any use that is consistent with the label approved by relevant regulatory authority in the country of sale for the use of such Product.

Manufacturing. The proposed Agreement allows manufacturing in India till July 2023^{*} and after that date manufacturing under the licence will be possible anywhere in the world where there are no patents on nilotinib, including in India.

Royalties. Royalties are set at 5% of net sales, due only for the sales in Patent Territory, and payable to ATOM for further investment in accordance with the ATOM mission.

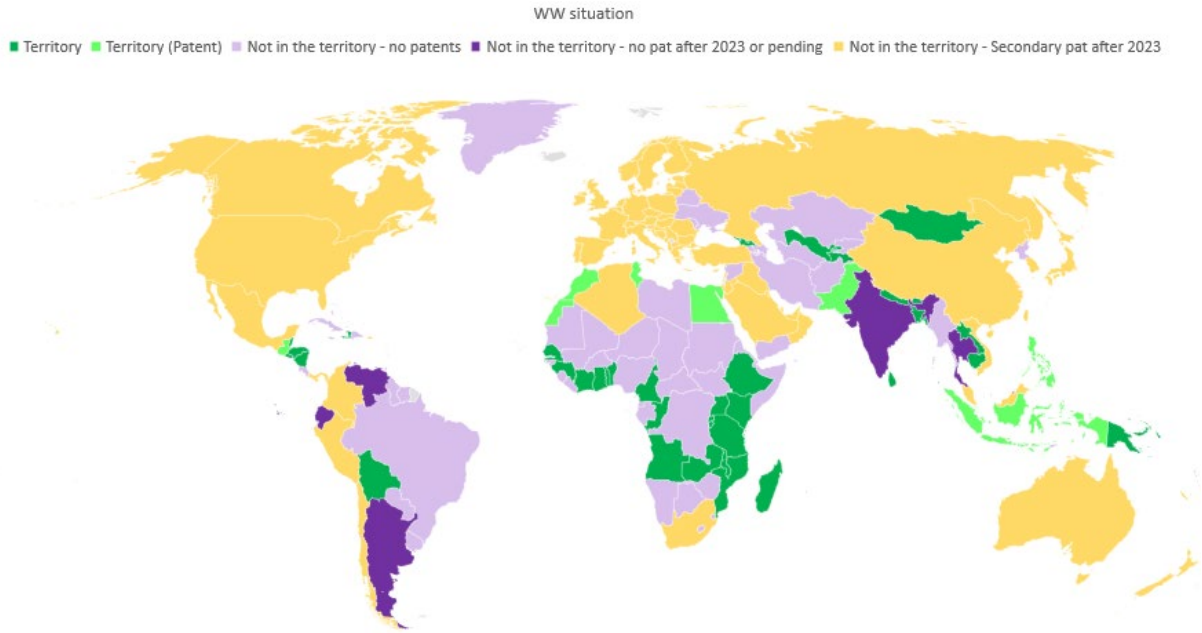
Compatibility with TRIPS flexibilities. The proposed Agreement contains language that provides that nothing in the Agreement shall be interpreted as preventing activities by the sublicensees that would not infringe upon Novartis's Patents granted and in force in a particular country.

The EAG understands that the nominal territory of 44 countries was selected by Novartis to align with the ATOM Target Country list. However, the EAG's analysis concludes that this number is essentially irrelevant – it is highly unlikely that a generic version of nilotinib will launch prior to the expiry of the compound patent in India in July 2023, and after that, the "true" territory will be the Patent Territory – the seven countries in which Novartis has secondary patents granted or pending. Thus, according to the data available in MedsPaL, after July 2023, a generic company will be able to sell generic nilotinib in 108 LMICs and 22 high-income countries (see Map below). This is independent of the license agreement as Novartis has no valid relevant patents in these countries. The proposed Agreement reiterates this fact through non-infringement language, which states that nothing in the Agreement would prevent a licensee from engaging in activities that would not infringe a patent granted and in force in that country.

The added value of the license agreement as of July 2023 will be that it allows generic entry in Egypt, Guatemala, Indonesia, Morocco, Pakistan, the Philippines, and Tunisia. The EAG noted that in Pakistan a local generic version is already in development independently from the proposed agreement and in Egypt secondary patents are pending, but are not granted which may also allow for generic entry independent of the license agreement. The estimated

^{*} Note from MPP Management: subsequent to the EAG review, the Agreement was further refined to make clear that manufacture could also take place in the seven countries of the Patent Territory.

patient population in these seven countries in need of nilotinib is 900-1100 patients (4600 prevalent patients of whom 20-25% are imatinib intolerant/resistant).



Assessment of the Proposed Agreement in light of MPP's Statutes

In line with the Terms of Reference for the EAG the "EAG will provide the Governance Board and the Executive Director with advice regarding Patent Pool licence negotiations and assessing whether the terms and conditions of the proposed licence agreements meet the key requirements as set out by the Medicines Patent Pool Statutes." The ToRs. define two requirements against which the EAG has to assess the results of the final negotiations: (i) do the results sufficiently meet the requirements set out in the Statutes, and (ii) do the negotiation results offer sufficient added value over the status quo?

Relevant Considerations in the Statutes of the Medicines Patent Pool

The EAG finds that the proposed Agreement meets the requirements in the Statutes, as summarised in the table below.

Statutes	Terms in Proposed Licence
Negotiating terms and conditions of licence agreements with the aim to maximise public health benefits, taking into account the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property of the WHO (GSPOA); WTO Doha Declaration	<ul style="list-style-type: none"> Provisions ensuring that sales inside or outside the territory are not a breach of the Agreement if the sales do not infringe Novartis's patents granted and in force. No limitations to use TRIPS flexibilities
Entering into licence agreements with patent holding entities, and sublicense agreements with generic manufacturers and other appropriate sublicensees on a non-exclusive and no-discriminatory basis	<ul style="list-style-type: none"> MPP to enter into non-exclusive sublicences chosen through MPP's Expression of Interest Portal

As and when necessary, enforcing terms and conditions of licence agreements, with appropriate dispute resolution mechanisms	<ul style="list-style-type: none"> • MPP takes on significant obligations to monitor and enforce terms of agreements; specifies stepwise escalation of disputes, including resolution with executives and arbitration (WIPO rules)
Requiring stringent quality criteria for licensed products	<ul style="list-style-type: none"> • Requires all licensed products to be made in accordance with WHO PQ or SRA standards
Including anti-diversion and traceability mechanisms	<ul style="list-style-type: none"> • Sublicensees required to implement a system of batch control and tracing as a means of identifying and tracing licensed products to monitor potential diversions

Assessment of the Proposed Agreement in light of the *Status Quo*

The ToRs require the EAG “to make best efforts to decide its recommendations by consensus. To the extent that consensus cannot be reached, the differing viewpoints expressed shall be detailed in the report to the attention of the Board.”

The EAG did not reach consensus on whether the proposed licence agreement added sufficient value over the status quo. In accordance with the MPP By-laws (Art. 16.4), where consensus cannot be reached, the differing viewpoints expressed are detailed in this report to the Board.

The EAG understood and agreed on the unique challenges in facilitating access to medicines for non-communicable diseases (NCDs) in general, and cancer medicines in particular, in LMICs. Among many other challenges, there is a lack of international funding for procurement of NCD drugs, the substantial investment in diagnostics and other medical infrastructure is often lacking. As such, the EAG agreed on the critical importance of demonstrating that MPP can successfully make an intervention in this area despite these challenges. The EAG very much appreciated the presentation of the Management on the challenges to convince originator companies to license NCD drugs to the MPP and the underlying reasons.

The EAG agreed in its assessment that the improvement over the status quo would be that the Agreement would allow early generic entry in seven countries as of July 2023 when nilotinib will go generic in India with or without a licence. Given that nilotinib is generally used as a second-line treatment for a relatively rare cancer – CML – the benefits in these countries are likely to be small. This could be considered an improvement over the status quo. The fact that the number of countries and patients is small is not without precedent as the MPP had engaged in targeted/limited interventions in the past (e.g., a licence with AbbVie for one South African patent on lopinavir/ritonavir in 2015). The seven countries are also middle-income countries.

There were however different views among the EAG whether this improvement over the status quo would be enough to enter into a new disease area, and sufficient to justify what was seen as the negative aspects of the agreement. Globally there were two opposite point of views:

One point of view was that entering the area of NCDs with such a limited agreement would set the bar for future agreements very low and thus set a very low benchmark. This would create the risk that for NCDs the scope of future license agreements may remain very limited in the

future. The very limited territory as well as the link to ATOM which is closely linked to the pharmaceutical industry would bear a reputational risk for the MPP. In addition, the EAG noted that if the “success” of this licence was viewed as important for future licences with Novartis, it was unclear precisely what the success factors were given the limited territory and low demand.

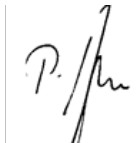
The other point of view was that the proposed agreement would be an important sign and would allow to open the MPP for NCDs demonstrating that this is possible. The expectation would be that other companies as well as Novartis with other cancer treatments would follow suit and territory would improve over time when companies get more used to using the MPP for NCD treatments.

The EAG agreed that in any case, the MPP should not tie its targeted territory to ATOM’s more limited territory, noting the strong links of ATOM with the pharmaceutical industry. MPP’s mandate is much broader than ATOM, and the inclusion of certain MICs with better healthcare infrastructure would be important to achieve greater impact on access to cancer medicines.

The EAG recommended to the Management that for future agreements in the area of NCDs, the Management consults the EAG earlier in the negotiation process to enable a critical review that may help in the process as well as prepare the EAG’s final assessment.

Conclusion

The EAG concludes that the proposed Agreement with Novartis is consistent with MPP’s mandate as defined in its Statutes. However, the EAG members were unable to reach consensus on whether the proposed Agreement represents a sufficient improvement over the *status quo* given that it covers a new disease area. If the Board decides to approve the proposed agreement, the EAG would recommend the Board to publicly communicate clearly that the potential benefits will be limited to the seven countries, and that the Agreement should be viewed as an exploratory test case and not as a benchmark for future agreements in the area of NCDs.



Peter Beyer
Chair, Expert Advisory Group
Date: 14 October 2022