MPP Licence Agreement with AbbVie for Glecaprevir/ Pibrentasvir (G/P)

Updated analysis and recommendations, August 2019

In November 2018, the Medicines Patent Pool (MPP) announced a licence agreement with the pharmaceutical company AbbVie for glecaprevir/pibrentasvir (G/P)[1], a fixed-dose combination direct-acting antiviral (DAA) therapy used for the treatment of hepatitis C virus (HCV) infection.[*] The MPP licensing agreement with AbbVie for G/P (AbbVie's licence) can be further sublicensed by MPP for the development, manufacturing and supply of generic versions to a limited number of developing countries and territories.

Background

Glecaprevir (GLE) and pibrentasvir (PIB) are medicinal compounds approved for the treatment and cure of chronic HCV in adults. GLE and PIB were first approved by the US Food and Drug Administration as a fixed-dose combination in 2017. Phase III clinical trials are ongoing in children and adolescents.

Many developed countries faced with the high prices of Gilead's sofosbuvir (SOF)-based regimens – the backbone for pan-genotype HCV treatment – have benefitted from the introduction of the G/P fixed-dose combination in their markets as a competitor product to reduce prices of overall treatment. This trend is reflected in AbbVie's 2018 third quarter earnings report[2] and the company's increasing market share in US and EU markets in 2018[3]. AbbVie is becoming a major competitor for Gilead, who until recently had monopolistic control over pan-genotypic HCV treatment regimens in high-income countries such as the US[4].

As of February 2019, AbbVie has registered G/P mainly in high-income and a few middle-income countries[5], but their plan to register G/P in developing countries or to make it available in the interim until generics are available is not publicly available. For patients who currently cannot be treated satisfactorily with SOF-based regimens, access to G/P to form a salvage regimen is essential; however, AbbVie has not yet accepted requests to procure G/P for MSF projects in developing countries, nor provided any information on how to access G/P on 'compassionate use' grounds.

Key features of the licence

AbbVie's licence constitutes one of the main voluntary licences for HCV treatment. Bristol-Myers Squibb (BMS) and Gilead are the other two pharmaceutical corporations that have granted voluntary licences for their DAAs.

Thus, there are currently three main voluntary licences for DAAs for the treatment of HCV:

- Gilead's 2014, 2015, and 2017 bilateral voluntary licences[6] with Indian generic companies covering the DAAs SOF, ledipasvir (LDV), velpatasvir (VEL), and voxilaprevir (VOX) (hereinafter referred to as Gilead's licences).
- The MPP's 2015 licensing agreement with BMS[7] covering the DAA daclatasvir (DAC) and its combinations (hereinafter referred to as BMS's licence).

[*] Note: Initially published in March 2019, this briefing document was updated in August 2019 to reflect (i) a first amendment to the license agreement concerning changes to the territory of the agreement made on 7 June 2019 (https://medicinespatentpool.org/uploads/2018/11/MPP-AbbVie-Fully-Executed-Amendment-062419.pdf), and (ii) a clarification from MPP in May 2019 that the license covers both adult and paediatric formulations of G/P.

- The MPP's 2018 licensing agreement with AbbVie[8] covering the DAAs G/P (hereinafter referred to as AbbVie's licence).

In March 2015, Médecins Sans Frontières (MSF) published a detailed analysis of Gilead's licences and their potential impact on access to SOF, LDV and VEL[9].

This briefing document examines the key features of AbbVie's voluntary licence to MPP and the extent to which the terms and conditions may contribute to access to generic versions of G/P, together with the other DAA treatment options, in developing countries. This briefing also examines issues and challenges related to realising broader access based on the current terms of the licence.

AbbVie's licence is comprised of a main licence agreement, including terms and conditions, and key exhibits:

- Exhibit A* lists the territories to which the sublicensees can supply the fixed-dose combination of G/P and new G/P formulations containing the licensed compounds.
- Exhibit B lists India as a "manufacturing-only" country.
- Exhibit C lists the patents and patent applications in the territories, of which a significant number are weak secondary patents.
- Exhibit D lists the patent applications in India.
- Exhibit F provides a template for a quarterly progress report to be followed by the sublicensee generic producers.
- The sublicence agreement form[10], which includes the terms and conditions and similar exhibits for sublicensees, including clauses prohibiting diversion of the licensed products in non-territory markets.

The MPP has invited expressions of interest from potential sublicensees based anywhere in the covered territory and from sublicensees in India to manufacture and sell G/P.

Positive features of the licence

Transparency

Unlike the current negative trend for bilateral licences between Indian generics manufacturers and originator companies, which are often kept confidential and not available in the public domain, the terms and conditions of this licence are available on the MPP website. This transparency allows for a more thorough examination of the licence's potential impact on access to treatment in high-burden and developing countries. The licence contains some information regarding granted and pending patent applications filed in the territory of the licence but does not set forth patents and patent applications in non-territory countries. Patents in low- and middle-income countries that are excluded from the licence have to be cross referenced from other sources such as MedsPaL[11].

Royalty

A number of royalty systems have been adopted in voluntary licensing under the MPP. Gilead's licensing of tenofovir disoproxil fumarate (TDF) to MPP – one of its first voluntary licences – requested a 5 per cent royalty, while a tiered royalty approach was used in the MPP-ViiV Healthcare licence covering dolutegravir (DTG)[12].

Generics manufacturers that supply DTG and DTG-based fixed-dosed combinations to MSF now ask for country of destination information in order to calculate royalties and final prices, which complicates the process of procurement. In addition, one of the critical drawbacks of the tiered royalty approach is that, in order to match the tiered royalty rate with the net sales, the sublicensees fall back to the usual business mode and increase the prices of the end products, thereby shifting the burden of higher costs to procurers, HIV programmes and patients.

* The territory of the agreement as amended in June 2019 is presented in the first amendment to the license: https://medicinespatentpool.org/uploads/2018/11/MPP-AbbVie-Fully-Executed-Amendment-062419.pdf

The AbbVie licence is royalty free, and sublicensees do not have to pay royalties out of their net sales. However, under Section 3.9 of the main license, the sublicensees will have to grant AbbVie an option to and right of first refusal to purchase new G/P formulations from sublicensees for sale in the US and EU, and recommends a 4 per cent royalty on net sales for a 'licence under royalty'. In the event that the MPP embarks on another round of negotiations to include more countries and the rate of royalty is negotiated for the expansion of the geographical coverage of the license, a standard royalty rate for all territories where AbbVie has *granted* patents should not exceed the prescribed 4 per cent under AbbVie's right of first refusal.

No interruption to the use of compulsory licences or patent oppositions

Section 2.3 of the main licence and the sublicence acknowledges the legitimacy for sublicensees to engage in selling the product in countries outside the territory if a compulsory licence is issued.

In effect, countries that face unaffordable prices for HCV treatments and barriers resulting from patents granted on GLE and/or PIB have the very important option to issue compulsory or government use licences and to be lawfully supplied by generics manufacturers of G/P, including from generics manufacturers who are sublicensees of the MPP.

Additionally, the MPP's AbbVie licence overview states that there are no restrictions on sublicensee's filing patent challenges[13]. However, in reality, for new medicines on which a *primary* patent application is pending, Indian generics manufacturers may consider the opportunity of entering a voluntary licence on the concerned products. They consider it as a kind of 'settlement' to mitigate the risk of the pending patent application being granted by the Indian patent office during the process of product development and facing the possibility of expensive and protracted patent infringement proceedings with multinational pharmaceutical corporations if they consider marketing the finished formulation of the new medicine. Thus, potential generics competitors from India who sign the voluntary licence 'settle' oppositions or do not file oppositions[14]. Originator companies on the other hand offer voluntary licences on medicines facing extensive patent challenges from civil society as a tactic to further deter opposition by generics companies or 'settle' oppositions[15]. Therefore, the expectation that companies will freely file patent oppositions is misplaced. This shifts the burden of challenging patent claims to civil society and the impact of such practices on competition in the pharmaceutical sector over the long term are yet to be analysed.

Waiver of data exclusivity

Section 2.4 of the main licence requires that, upon the request of the MPP, AbbVie will provide a waiver on exclusivity of data concerning new chemical entities or other exclusivity in territory countries in order to enable the registration of the generic medicines produced under the licence. Section 3.4 of the sublicence agreement also restricts sublicensees from seeking regulatory exclusivity on products they develop.

In addition, Section 2.4 of the main licence requires that AbbVie provide, upon MPP's request, a copy of clinical data to facilitate product registration in the listed territories.

This provision to support the registration sought by generics manufacturers who are sublicensees in territories of the licence is an important one. Some national drug regulatory authorities may insist on data from the originator before proceeding with registration of a generic version in cases where the originator has not already registered the drug.

Challenging aspects of the licence

Issues with the development and marketing of the new formulations of G/P

The definition of licensed compounds (contained in Section 1.7 of the main licence with MPP and Section 1.10 of the sublicence agreement) explicitly refers to G/P in a fixed-dose combination form. Article 1.12 defines new G/P formulations as new formulations that contain the licensed compounds. Based on an analysis of these clauses and as confirmed by the MPP, AbbVie's license is applicable to both adult and paediatric formulations of G/P, including potential long-acting injectable formulations.

Paediatric and long-acting injectable formulations

AbbVie's paediatric clinical trials for G/P are ongoing. While the license applies to paediatric formulations of the drug, the exclusion of a majority of high-burden countries undermines the potential benefits for paediatric patients (see first amendment to the license agreement for territory where G/P can be supplied[16]). As highlighted below, two countries that account for almost one quarter of all people living with HCV globally – China and India – are not in the territory of the licence. As such, neither adults nor children with HCV in these countries will benefit from the license. The license can be used for potential long-acting injectable formulations, an innovation that could dramatically improve patient adherence, possibly reduce treatment to one dose and reduce costs. As AbbVie does not seem to have any long-acting injectable formulations in the pipeline, generics manufacturers could become potential developers and suppliers of this important formulation to meet the needs of people in low- and middle-income countries.

However, the 'grant-back' terms in the license agreement may raise questions about possible restrictions on marketing of new formulations developed by sublicensees. Article 3.9 of the main license agreement contains a grant-back clause for sublicensees covering new formulations developed after taking the current license agreement. Accordingly, if any new G/P formulation is developed by sublicensees, the MPP will require sublicensees to provide AbbVie the option to (and the right of first refusal to) obtain the sole right to purchase the new G/P formulation for sale in the US and EU, or a sole license to any patents and know-how necessary to use the new G/P formulations in the US and EU (Article 3.9(a)). The grant-back clause also requires sublicensees to offer AbbVie an option to a non-exclusive and royalty-free license to commercialise the new G/P formulation outside of the US and EU and outside of the Territory defined by the current license (Article 3.9(b)).

The grant-back obligations mean AbbVie will benefit from new G/P formulations developed by sublicensees to supply non-Territory countries under the non-exclusive grant-back license. However, there is no reciprocal benefit that would allow a generic producer to supply non-territory markets should they develop a new formulation. For example, while the grant-back clause would potentially allow AbbVie to commercialise a new long-acting formulation developed by a generics company in India (which is currently outside the territory of supply under the current license), this would not trigger an equivalent exchange allowing the generics company to supply the new long-acting formulation in India and other non-territory countries.

Further scrutiny and analysis of the grant-back clause is required to understand its potential impact on competition among manufacturers who wish to develop new formulations of G/P in the future. On a practical level, such clauses may create disincentives for generics producers to come forward to develop long-acting formulations as their market access in high-burden countries is heavily restricted by the license.

Single formulation of GLE or PIB

The main licence and sublicence agreement do not enable sublicensees to work on the single formulations of GLE or PIB, or to develop fixed-dose combinations containing GLE or PIB and other approved DAA compounds. This may potentially trigger a problem if there is a medical need for the single formulation of GLE or PIB to be provided together with other DAAs.

Based on experiences with HIV treatment, it is possible that patients for whom treatment fails due to resistance may benefit from different combinations of second-line drugs. In the context of HCV treatment, if treatment failure occurs with first-line DAAs, resistance testing may indicate other combinations of DAAs with PIB that could be used for re-treatment. While this would require further studies, it may provide a viable option for salvage treatment. However, the current licence terms do not allow flexibility to develop alternative formulations other than fixed-dose combinations containing G/P. In contrast, BMS's licence on DAC does not restrict sublicensees from combining DAC with other drugs to develop new fixed-dose combinations.

Questions regarding patent territory and patent landscape

Patent landscape in territory and non-territory countries

Exhibits C and D of the main licence and the sublicence agreement provide detail on patents granted and patent applications filed in territory countries and one non-territory country, India, which is a manufacturing-only country.

Based on the information provided in the two Exhibits, a considerable number of patent applications are filed for derivatives and changes of the base compounds of GLE and PIB, confirming an 'evergreening' strategy being used by the pharmaceutical corporation.

In addition, Exhibit C shows that AbbVie holds patents or has pending patent applications in only eight territories* out of the 96 territories listed in Exhibit A of the first amendment to the license agreement.[16] A number of the applications listed in these eight countries are not yet granted.

In addition, all five patent applications filed in India remain pending, including applications on the base compounds of GLE and PIB. As patent applicants cannot institute a suit for infringement until the patent is granted, Indian generics companies should be able to develop and sell generic versions of G/P domestically without necessarily resorting to the voluntary licence, particularly as it does not cover the domestic market in the territory (Exhibit A) of the licence. However, generics manufacturers might also need to wait for Indian Patent Office decisions on the pending patent applications of the base compounds of PIB and GLE before marketing generic versions in the domestic market. If these patents are granted, there is a risk that the patent holder can initiate suits against generics manufacturers right after the grant of the patent.

Besides India, primary patent applications have been filed and remain pending in territory countries Egypt and Pakistan, and also in some non-territory countries, such as Brazil[17].

Territory where generic G/P can be supplied

The current territorial coverage of AbbVie's licence includes 96 countries and territories, and overlaps with the territorial coverage of BMS's licence[18] and Gilead's licences[19] – the other two main voluntary licences on DAAs. There are however a number of issues with the current coverage.

The MPP Expert Advisory Group (EAG) report on the licence agreement expresses the EAG's criticism that the licence covers "significantly fewer people living with HCV (47.5%) than other HCV licenses"[20]. In particular, the EAG notes that the exclusion of India from the territory is a "disappointment" – as the country is home to over 6 million people living with HCV[20]. Some high-prevalence countries are covered by AbbVie's licence, such as Nigeria, Uganda, Tanzania, Ethiopia, Morocco, Cameroon, Zimbabwe, Sierra Leone, Egypt, Myanmar, Cambodia, Nepal, South Africa, Pakistan, Indonesia, Vietnam, Philippines and Georgia. However, a number of other high-prevalence countries are noticeably excluded.

* Bolivia, Egypt, Indonesia, Philippines, Pakistan, Turkmenistan, Vietnam, South Africa.

Table 1: Included and excluded countries accounting for 80% of global HCV infections

Countries accounting for 80% of global viraemic HCV infections (listed in descending order according to the size of their epidemics[21])	**Covered by AbbVie's Licence**
China	**N**
Pakistan	**Y**
India	**N**
Egypt	**Y**
Russian Federation	**N**
United States of America	**N**
Nigeria	**Y**
Brazil	**N**
Democratic Republic of the Congo	**Y**
Ukraine	**N**
Bangladesh	**Y**
Uzbekistan	**N**
Indonesia	**Y**
Vietnam	**Y**
Japan	**N**
Italy	**N**
Ethiopia	**Y**
Philippines	**Y**
Syrian Arab Republic	**N**
Romania	**N**
Mexico	**N**
Angola	**Y**
Kazakhstan	**N**
Turkey	**N**
Thailand	**N**
Colombia	**N**
Ghana	**Y**
Algeria	**N**
Spain	**N**

Complete Exclusion from Territory of the Licence

Of the four countries that account for almost 40% of all people living with HCV globally – China, Pakistan, India and Egypt – China (with almost 10 million people living with HCV) and India (with over 6 million people living with HCV)[21] are not in the territory of the licence.

Notably, the EAG's criticism described above was made based on the comparison of this licence with the other DAA licences, but the EAG concluded with a view that "it is better to sign the licence now, so as to allow generics manufacturers to begin development as soon as possible"[22]. However, it is worth noting that there are disappointing features that are common to all of the three main DAA licences. None of the three includes upper-middle income countries with a high burden of HCV, such as Brazil, China, Colombia, Kazakhstan, Mexico, Russia and Turkey[23], which together are home to about 14 million people living with HCV infection, or about 38% of people living with HCV globally[24].

Of the five BRICS countries, only South Africa is covered under the territories of all three main DAA licences (see Table 2, below). Brazil, Russia and China are excluded from all of them. India is excluded from the AbbVie licence on G/P but covered under the territory of the Gilead and BMS licences. India's exclusion is a disturbing development (see analysis under "Countries that can produce", below).

Table 2: BRICS countries under the main DAA voluntary licences

BRICS countries	Gilead's licences	BMS's licence	AbbVie's licence
China	N	N	N
India	Y	Y	N*
Russia	N	N	N
Brazil	N	N	N
South Africa	Y	Y	Y

* India is listed as a manufacturing-only country

According to Article 2.3 of the sublicence agreement and the MPP's AbbVie licence overview[13], sales outside the territory are permitted if no granted patent is being infringed. However, an analysis of the patent landscape of low- and middle-income countries that are excluded from this licence based on information obtained from MedsPaL highlights the limitation of this provision: there are only a limited number of countries outside the territory of the licence where sublicensees might not be at risk of infringement for the time being.

The first column in Table 3, below, shows that in at least 21 low- and middle-income countries excluded from the licence, patents on PIB and/or GLE have already been granted. Column 2 lists an additional nine low- and middle-income countries with pending patent applications. However, stringent IP enforcement provisions in many of these countries – for example Brazil, Costa Rica, India and Thailand – allow pharmaceutical corporations to claim damages retrospectively to the time when the patent application was published, if the patent was eventually granted to them. For a situation like this, the AbbVie licence does not clarify the freedom to operate for sublicensees when patent applications remain pending in countries outside of the territory when the licence was signed.

Neither the licence nor other key documents provide information on how such risk could be mitigated, for instance through a possible non-assertion commitment from AbbVie to ensure that it would not pursue retrospective damages against sublicensees who bid for and supply government programmes in countries where patent applications were pending but then subsequently granted. It is unlikely that sublicensees will launch-at-risk in these markets unless the pending applications are rejected. These decisions may not come for several years, thus delaying the possibility of achieving earlier access to more affordable alternatives.

The fourth column of Table 3 lists the only two countries – Nicaragua and El Salvador – where patent applications have not been filed. This means sublicensees should be able to supply in these two countries as non-territory markets. However, a potential risk may remain due to the time lag between the current legal status and the time when sublicensees have actually developed the products. If AbbVie chose to pursue secondary patents during this period of time, the window of freedom to operate would close.

The licence also provides no information on how this risk could be mitigated, for instance through a possible non-assertion commitment by AbbVie to ensure that it would not pursue any patent rights in countries where patent applications were not filed as of the time when the licence was signed.

Table 3: GLE and PIB patent landscape in low- and middle-income countries excluded from AbbVie's licence

Granted patents on PIB and/or GLE		Pending patent applications on PIB and/or GLE	Patent status unknown	No relevant patent applications filed
Albania	Malaysia	Brazil	Algeria	El Salvador
Armenia	Mexico	Costa Rica	Cuba	Nicaragua
Azerbaijan	Moldova	Dominican Republic	Iran	
Belarus	Mongolia	Ecuador	Jamaica	
Bosnia &	Montenegro	Guatemala	Korea DPR	
Herzegovina	Peru	India	Syria	
China	Russia	Paraguay		
Colombia	Serbia	Thailand		
Kazakhstan	Tajikistan	Venezuela		
Kyrgyz Republic	Turkey			
Macedonia	Ukraine			

Countries listed in Table 3 can use TRIPS flexibilities to overcome barriers posed by local patents on DAAs and exclusion from voluntary licences. For example, to scale-up HCV treatment and make it available in the public health system throughout the country, the government of Malaysia issued a "government use" licence on the patented drug sofosbuvir in 2017. This enables the Ministry of Health to provide pan-genotypic treatment using sofosbuvir in combination with the off-patent drug daclatasvir at the lowest possible price[25]. This decision affirmed its commitment to help the more than 500,000 people living with HCV in Malaysia access lifesaving treatment. Malaysia's policy decision to utilise TRIPS flexibilities also put pressure on Gilead to expand its DAA licences with generics companies and to add Malaysia, Thailand, Ukraine and Belarus to the territory of its licence.

Other countries facing challenges in procuring generic DAAs due to local patents and voluntary licence terms that exclude them from the territories of the licences are also looking at the option of using a compulsory licence. In Chile, for instance, members of Congress have requested that the Ministry of Health declare public health reasons for the compulsory licence of patents associated with sofosbuvir[26]. However, pharmaceutical lobbies and their political allies continue to pressure countries to refrain from exercising their legitimate rights under TRIPS and the Doha Declaration. This is an ongoing challenge that stakeholders and institutions working to increase access to HCV treatment must address together with concerned governments.

Countries partially excluded from the territories of the three main DAA licences

Even if there is overlap in the territories of the three main licences (about 40 countries are covered by all three), there are several countries that are inadequately covered, as shown in Table 4.

Countries excluded from AbbVie's licence that are covered only by BMS's licence on DAC (such as Azerbaijan, Ecuador, Costa Rica, Jamaica, Iraq and Syria) may need to seek alternative solutions to access generic versions of pan-genotypic regimens, such as through compulsory licences or alternative suppliers if there are no local patents.

For Jordan, which is not covered by the BMS or Gilead licences, AbbVie's licence offers an alternative pan-genotypic option to the country as it has been included in the territory.

For countries covered by both Gilead's and BMS's licences – where affordable generic versions SOF, DAC, and the SOF/LED and SOF/VEL combinations are already available – G/P could be essential in retreatment of patients who have not been cured with first-line DAA therapies and for those with kidney disease who cannot use SOF-based regimens. If generic G/P can compete in terms of price with the pan-genotypic SOF/DAC combination, it may also find a role in first-line treatment in these countries.

Table 4: Countries and territories partially excluded from the three main DAA voluntary licences

Country	In AbbVie/MPP licence	In BMS/MPP licence	In Gilead licence
Antigua and Barbuda	Y	N	Y
Algeria	N	Y	Y
Azerbaijan	N	Y	N
Belize	Y	Y	N
Belarus	N	N	Y
Costa Rica	N	Y	N
Cuba	N	N	Y
Ecuador	N	Y	N
Egypt	Y	N	N†
El Salvador	N	Y	Y
Georgia	Y	Y	N
Grenada	Y	Y	N
Honduras	N	Y	Y
India	N*	Y	Y
Iraq	N	Y	N
Jamaica	N	Y	N
Jordan	Y	N	N

Continued

Country	In AbbVie/MPP licence	In BMS/MPP licence	In Gilead licence
Korea, DPR	N	Y	Y
Kyrgyzstan	N	N	Y
Malaysia	N	N	Y
Mongolia	N	Y	Y
Nevis	Y	N	N
Niue	Y	Y	N
Nicaragua	N	Y	Y
Paraguay	N	Y	Y
Saint Lucia	Y	Y	N
Syria	N	Y	N
Tanzania	Y	N	Y
Tonga	N	Y	Y
Ukraine	N	N	Y
Uzbekistan	N	Y	Y
West Bank of Gaza	Y	Y	N
Yemen	Y	Y	N

* The AbbVie-MPP license lists India as a non-territory and manufacturing-only country

† Egypt is excluded from the main Gilead license, but as the primary patents on SOF are not granted in Egypt, a generic version of the product is available in Egypt.

Countries that can produce

The development and manufacture of the fixed-dose combination of G/P by sublicensees may take place anywhere in the territory of the licence, according to Section 2.1 (b) and (c) of the licence. India is mentioned as a manufacturing-only country in the licence agreement. This means that a generic producer in any country of the territory of the licence and India can possibly enter into a sublicence agreement if they fulfil the qualification set forth under Section 3.3 of the main licence agreement concerning their manufacturing capacity and quality assurance status[27]. However, because India is a manufacture-only country and not covered by the territory of the license, generics producers in India can supply solely in the territory of the licence, but not domestically. This approach is highly problematic for major producing countries with large HCV epidemics such as India because it leaves patients and public health programmes without access to generic G/P manufactured by local sublicensees.

Although it is the first time a voluntary licence between MPP and a pharmaceutical company has singled out India as a manufacturing-only country, this approach has already been used in other licences. For instance, similar exclusions have been adopted in the licences on Gilead's tenofovir alafenamide (TAF), ViiV's DTG, AbbVie's lopinavir/ritonavir (LPV/r), and BMS's atazanavir (ATV)[28], in which countries like China are not included in licence territories but Chinese generics producers can and have joined the sublicences as producers for export to other countries in the territory only.

This practice, now endorsed and expanded by the MPP's voluntary licence agreements, raises ethical questions about harnessing the capacity of developing countries to develop, produce and supply quality medicines while at the same time prohibiting generics companies from responding to considerable unmet medical needs domestically. As noted above, the EAG of the MPP expressed concern with respect to the exclusion of India in this licence. However, the EAG did not lay it down as a red line in this license or as a problem the MPP must tackle in future licensing negotiations.

Questions on the transparency of the registration progress in countries

According to Section 3.5 of the sublicence agreement, the sublicensee should report to the MPP on a quarterly basis about the progress of the product development and registration processes. In addition, the clause reads that "Licensor [MPP] agrees that information contained in quarterly and other such reports shall be treated as Confidential Information; provided, however, that such information may be shared with AbbVie (with AbbVie treating such reports as Confidential Information); and that aggregated data may be publicly disclosed by Licensor [MPP]"[29]. Exhibit F of the sublicence further provides the template for the quarterly reporting which contains information on the timelines for product development and timelines for regulatory approval dossier

filings to the US Food and Drug Administration (FDA) and World Health Organization (WHO, under its pre-qualification programme), and filings on the country level[30].

The implementation of the licence in territory countries is critical to ensure that the promises made by all parties are realised, including concrete access to medicines produced under the licence for patients in need. It is therefore important that public health agencies and civil society organisations, including patient groups, have up-to-date information about which generic medicines are available in their countries. This can be ensured if regulatory progress is made as transparent as possible under the licence. In this regard, the current terms and practices for the reporting of progress under the licence raises concerns on two levels.

Firstly, it is unclear whether it is justifiable to treat all information contained in quarterly reports as confidential. This is a particular concern for information regarding the time of dossier filing to the relevant regulatory bodies in territory countries, which is critical to allowing public health agencies, procurement entities and patients to estimate when products could be made available in a given country. Such information is rendered to regulatory authorities at the national level responsible for drug registration and should by nature be made publicly available.

Secondly, while the current terms state that aggregated data on the overall registration progress may be published by the MPP, it is unclear why disaggregated data, especially concerning the time of regulatory dossier filings, could not be considered for publication and regular quarterly updates. While the recently added section on the MPP website – "Update on Progress of Sublicensees"[31] – is a positive step, more detailed information would be useful for a host of stakeholders working to improve people's access to HCV treatment.

Conclusions and recommendations

While the AbbVie/MPP licence has some positive characteristics, there are multiple shortcomings that can be improved, concerning both the practical implications of the licence terms and the licence's influence on access to affordable generic DAAs for patients in developing countries.

We recommend that AbbVie and the MPP revisit the licence and amend relevant clauses to:

- Provide greater clarification on sublicensees' freedom to operate when patent applications remain pending in countries excluded from the licence territory.
- Expand the licence territory to include – at a minimum – "manufacturing-only" countries like India and additional middle-income countries with high HCV prevalence, including China.
- Extend the territory of the license agreement to cover all low- and middle-income countries so that adult and paediatric patients in these countries can benefit from G/P formulations.
- Make publicly available disaggregated information of the progress of registration of generic medicines produced under the licence, enabling easier public monitoring and procurement forecasting.
- Ensure that sublicensees who develop long-acting injectables can market the formulation in all low- and middle-income countries.

We recommend that governments excluded from voluntary licences (1) review the voluntary licence together with patent status of G/P to assess their negative impact on competition and (2) apply TRIPS flexibilities such as a compulsory licence if necessary to reduce prices of HCV treatment in their country.

We recommend that procurers and funders provide sustainable, long-term funding for civil society to challenge patents to improve access to generic HCV treatment in countries with high HCV prevalence who are excluded from the territory of the license.

References

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