Minutes of the Meeting of the Eurasian Community for Access to Treatment with Gilead

November 03, 2020, ZOOM conference

Gilead representatives:

- Alexey Brevnov, Director, Government and Public Affairs Director, Russia
- Mark Snyder, Executive Director, Public Affairs
- Rhiannon Bid, Associate Director, Public Affairs
- Larkin Callaghan, Senior Director, Public Affairs
- Ryan McKeel, Executive Director, Public Affairs
- Omoro Omoighe, Director, Public Affairs

EACT representatives:

	Name	Organization, Country
1	Denis Godlevskiy	ITPCru, Russia
2	Grigoriy Vergus	ITPCru, Russia
3	Maria Shibaeva	ITPCru, Russia
4	Sergey Golovin	ITPCru, Russia
5	Tatyana Khan	ITPCru, Russia
6	Aleksey Mikhaylov	ITPCru, Russia
7	Irina Statkevich	PO Positive Movement, Belarus
8	Nurali Amanzholov	Central Asian Association of PLWH, Kazakhstan
9	Mykyta Trofymenko	100%Life, Ukraine
10	Sergey Uchaev	ISHONCH VA HAYET, Uzbekistan
11	Tamar Zurashvili	Georgian Harm Reduction Network, Georgia
12	Pavel Savin	PF "Answer", Kazakhstan
13	Alex Schneider	Life4me+, Switzerland
14	Evgeniy Pisemskiy	NGO Phoenix PLUS, Russia
15	Anahit Harutyunyan	NNG Positive People Armenian Network, Armenia
16	Sergey Biryukov	NGO "AGEP'C", Kazakhstan

Beginning of the meeting. Presentation of the participants.

Question: The first question relates to TAF as a monocomponent for treatment of hepatitis B, as well as TAF as part of a combination for treatment of HIV infection.

Answer: TAF based options for the treatment of HIV infection is represented by drugs “Biktarvy” and “Genvoya”. In Russia, these drugs were registered about a year ago, in Kazakhstan, they are available via the RADIAN and Fast-Track Cities programs. There are currently no plans to register TAF based regimens in other EECA countries. However, all countries of the region are covered by a voluntary license between generic manufacturers and the Medicines Patent Pool, and there are also bilateral agreements.

TAF based options for treatment of hepatitis B (Vemlidy) is registered in Kyrgyzstan and Uzbekistan through our partner Delta Medical, and the drug was also registered and available in Russia.

Question: Quite a long time ago, your company operated in Russia through the Delta Medical company, during the cooperation with which various delays, protractions, etc. were observed. Are there any similar problems in cooperation with this company in other EECA countries? This question is based on the experience of Russia.

Answer: We are not aware of such difficulties, perhaps, if you have information about any difficulties, we ask you to report it.

Question: First there was TDF, then TAF appeared as a drug that does not wash out calcium from the body. Gilead encourages switching to TAF, but it is much more expensive than TDF. Also, based on the numerous studies, it became known that the drug taking results in a significant weight gain. In case of taking TAF with dolutegravir, the weight gain is even more significant, about 10-15 kg. So, there is a dual situation - when taking TDF, the patient has bone problems, and when taking TAF, obesity progresses. There is a trend in European countries where doctors switch patients from TAF to TDF. Does the company have a further strategy to promote these drugs with these side effects in mind?

Answer: Yes, indeed, we are aware of the trend of switching patients from TDF to TAF. Generally, patients prefer to take a drug with a more favorable treatment profile for kidney and bone problems. In terms of weight gain, tenofovir has a weight loss effect, and when switching from TDF to TAF, weight gain will be more evident in these patients.

Comment of the representative from Switzerland: There are also patients who switch from TAF to nevirapine/lamivudine and are experiencing a 5 kg weight loss, suggesting that there was a previous weight gain associated with the use of TAF.

Answer: When more information on the effects of TAF on the weight gain is accumulated, we can return to this subject.

Question: Do you have any information about a possible entry of generic bictegravir into the market?

Answer: We do not have such information at the moment, we can give you an answer later.

Question: When do you plan to submit the dossier for the inclusion of BIC/TAF/FTC in the list of VEDs in Russia? Do you have any control over the registration policy of generics licensed by you through the Patent Pool?

Answer: Our company is generally committed to expanding access to drugs around the world, including Russia. The EDL currently includes drugs for treatment of HIV infection and hepatitis C. We received the marketing authorization for Biktarvy in January 2020, and in the near future we plan to apply for inclusion of the drug in the EDL so that the commission considers its inclusion at the first meeting in April 2021.

In our opinion it would be inappropriate to assume that we can control the registration policies of generic manufacturing companies. Issuance of marketing authorizations falls within the competence of national government authorities and is independently regulated by each state. The agreements that the company has concluded with the Medicines Patent Pool have a certain validity area in which Russia is not included.

Question: Does the company have plans to expand its licenses for bictegravir to companies other than Hetero, perhaps, in order to increase competition?

Answer: At the moment we cannot answer this question, we will be able to provide an answer later.

Question from the representative of Kazakhstan: The fact is that bictegravir has not yet been registered in the Republic of Kazakhstan, despite the fact that a lot of work has been done to introduce the drug into the new protocol for treatment of HIV infection in adults where it was included in the first-line regimens. During the year, Hetero changed plans for registration of bictegravir, and, unfortunately, the registration documents have not been submitted as of today. This makes it much more difficult for us to provide HIV patients with new and effective drugs. We would also like to note that there is a risk of setting a non-competitive price due to a single supplier on the market. We would also like to know whether there will be the license extension to other generic suppliers of bictegravir?

Answer: Thank you, we will pass this questions on and clarify this information.

Question: Do you have any news on the inclusion of bictegravir in the WHO protocols, since access to dolutegravir cannot be considered complete?

Answer: We need to clarify this information, and later we will be able to provide an answer. To note, it will be a combination with bictegravir, since Gilead does not produce bictegravir as a separate monocomponent.

Question: Does Gilead have an intention to apply for inclusion of Truvada in the EDL?

Answer: In Russia, Truvada is represented on the commercial market. We have no plans to apply for its inclusion in the EDL. We made several such attempts, setting fairly low prices, but these applications did not receive appropriate approval from the Ministry of Health Commission. Currently, the company's strategy is to promote innovative schemes that include TAF.

Comment of the representative from Switzerland: In this case, the issue of TAF price arises, since it is easier to purchase TDF with lamivudine at a price of less than 1000 rubles. In this case, the company runs the risk of losing the market as happened in Europe where a large number of generics appeared, since Gilead did not reduce the price.

Comment of the Company's representative: Thank you for your comment, we will pass on your opinion to our colleagues in the commercial department.

Question: What are your plans to further reduce prices for SOF-based drugs in Russia?

Answer: In March 2020, our company reduced the prices for two drugs containing sofosbuvir - Sovaldi and Epclusa by more than 20%. We strive to strike a balance between making drugs available to patients and healthcare facilities while supporting investment in research and development. Considering these long-term interests, we also do not exclude the possible reduction of prices for sofosbuvir.

Question: Up to what price?

Answer: Currently we do not have such information, but we can clarify it.

Question: Can you provide information on the price at which the company supplied sofosbuvir to Armenia on the order of the Ministry?

Answer: We do not have such information, we can provide it later.

Question: When do you plan to complete clinical trials of remdesivir? In some countries of our region, it will be difficult to register the drug without successfully completed Phase III trials.

Answer: Veklury is the trade name for remdesivir. Ithas been evaluated in several studies, in particular, in the completed Phase III clinical trials including the ACCT-1 trial. This study was conducted in 10 countries and showed that hospitalization time was significantly reduced for the patients taking remdesivir. Based on these data, Veklury has been approved or authorized

for temporary use as a treatment of COVID-19 in more than 50 countries of the world; we are ready to provide the results of these studies to the regulatory authorities of the countries, upon request.

Question: How do you assess the risks of the generics development and their introduction into circulation due to the mechanism of compulsory licensing in the EECA and EAEU countries?

Answer: We can say about the Russian market. We would like to emphasize that the EAEU countries are included in the voluntary license for remdesivir, consequently, in this case the compulsory licensing mechanism is not relevant for them. It is known from Russian open sources that the potential issuance of a compulsory license for remdesivir is being considered by the Government of the Russian Federation, but it is difficult for us to assess the possibility of such issuance. For our part, we are committed to providing remdesivir to all patients who need it and ready to meet the demand.

Question: What will be the price for remdesivir in Russia?

Answer: In Russia, remdesivir was included in the EDL, and now we have submitted documents for the price registration. The price for Veklury will be registered in accordance with the rules and methods for calculating maximum sale prices accepted in the country.

Question: Recently, WHO has stopped recommending the use of remdesivir, based on studies related to very severe patients. However, there are studies that show that remdesivir can help keep patients away from intensive care when taken early, especially in conjunction with blood thinners and vitamin D. Do you have a promotional strategy for the drug? Will the company conduct additional clinical trials since, in our opinion, the fact that WHO does not recommend remdesivir discourage the widespread use of the drug.

Answer: Currently there are several studies on remdesivir where the drug is used in combinations. Work is also in progress to create an inhalation form of the drug for its possible use on an outpatient basis for non-hospitalized patients. The full results of the National Institute of Allergy and Infectious Diseases' Solidarity study were recently published, and you can find this information on our website. Some time ago, there were articles in The New England Journal of Medicine, which pointed out that more trials are needed to understand when is the best time to start remdesivir treatment. There is also a study in progress in France where remdesivir is used for different categories of patients.

Question: Russia already has a COVID-19 vaccine that can be obtained, vaccination is about to begin in the UK, and this process will be launched in Europe before the end of the year. But the vaccine does not guarantee against coronavirus infection. Are you planning to study the interaction between vaccination and subsequent use of remdesivir? For example, in Switzerland, the research has been stopped due to an impending vaccination program.

Answer: This is an important question. We will clarify the information and come back to you with an response.

Question: Have you experienced any problems with exporting ARV drugs to EECA countries due to COVID restrictions? If so, what is the scale of the problem? How did you overcome the obstacles?

Answer: Currently, the only restrictions at the moment for the countries of the region associated with the COVID-19 is the reduced airline capacity and the number of flights going to the region, but this has not impacted the supply of our products and there were no disruptions to supply. For example, before the pandemic, the number of flights to Ukraine was about 5-6 per month, now it has decreased to two flights per month. In Russia, COVID-19

restrictions have also not led to interruptions as all products that have received market authorization are produced locally.

Question: From 2021, new uniform rules for the registration of medicines will come into force in the Eurasian Economic Union. Is the company preparing for registration/re-registration of its medicines in the EAEU? What difficulties are expected? What are the solutions in your opinion?

Answer: Our company is fully prepared to bring registration dossiers in line with the uniform rules of the EAEU, and we plan to do this in full by 2025. We see some differences in country registration procedures that need to be dealt with. Firstly, we are talking about the differences in the format of the dossiers in Russia and other EAEU countries. Secondly, there are no publicly available criteria for validating dossiers submitted electronically. Thirdly, virtual GMP inspections are impossible due to the COVID-19 pandemic. In our opinion, the only long-term solution to these differences related problems is the harmonization of the EAEU requirements.

Question: Many pharmaceutical companies seek advice on clinical trial protocols from patient organizations, and such cooperation takes place in Janssen and ViiV in Europe. When conducting trials in Russia, do you plan to include patient organizations in the process of protocols discussing at an early stage?

Answer: At the global level, we practice inclusion of representatives of patient organizations in the process of protocols evaluation. As regards Russia, we will clarify the information and answer later.

Comment of the representative from Switzerland: It is important to include representatives from different countries in this process in order to convey the information correctly in the appropriate language. We are ready to cooperate with you in this direction. EECA is a large and important region.

Comment of the Company's representative: Yes, that's the case. Over the past 1.5-2 years, our clinical trials department has advanced and we are ready to continue the work.

Question: In Russia, Gilead drugs are sold by Pharmstandard. If we hypothetically imagine that in 3-5 years the EAEU will conduct purchases among Russia, Kazakhstan and Belarus, who will supply the drugs?

Answer: We think it is worth waiting for this to happen. It is unproductive to discuss a hypothetical situation now.

Question: Could you provide a table with the registration status of the company's drugs (for treatment of HIV, HCV, TB) in the EECA markets (Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Uzbekistan and Ukraine)?

Answer: We will now provide you with this information.

- Viread (tenofovir) is registered in Azerbaijan.
- Epclusa and Viread are registered in Armenia, the registration certificate for Truvada has expired.
- Sovaldi, Harvoni, Vosevi, Epclusa and Viread are registered in Georgia.
- Harvoni, Viread, Eviplera and Odefsey are registered in Kazakhstan, the registration certificate for Truvada has expired.
- Harvoni is registered in Kyrgyzstan, the registration certificates for Truvada and Viread have expired.
- Truvada and Viread are registered in Moldova.

- In Tajikistan, the registration certificates for Truvada and Viread have expired.
- Viread is registered in Turkmenistan, the registration certificate for Truvada has expired.
- Sovaldi, Epclusa and Viread are registered in Uzbekistan, the registration certificate for Truvada has expired.
- Sovaldi, Harvoni, Epclusa, Eviplera, Genvoya, Truvada and Viread are registered in Ukraine.
- Sovaldi, Harvoni, Epclusa, Atripla, Biktarvy, Eviplera, Genvoya, Truvada and Viread are registered in Russia.

Comment of the representative from Russia: Gilead received an appeal from patient organizations, including Life4me+, urging the company to relinquish its patent rights to Truvada, given the importance of PrEP in the country. This is an important letter, and we would like to receive a response thereto.

Comment of the Company's representative: Indeed, this is an important appeal, and it is now being discussed within the company. We propose to follow up this issue at a meeting with patient organizations which will be held on December 10.

Comment of the moderator: Yes, that will suit.

Question: Does the company plan to renew previously expired registration certificates in EECA countries?

Answer: We can provide an answer later.

End of the meeting.