Minutes of the Meeting of the "Eurasian Community for Access to Treatment" with ViiV

September 27, 2023

Representatives of the organization:
- Anjali Radcliffe - Director of International Government Affairs, Policy and Access
- Tia Vincent - Head of Medical Affairs, International Region
- Jim Thompson – Commercial Director, International Region
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- Sophie Tamblyn - Associate, Government Affairs, Policy and Access

Meeting Commencement. Introduction of Participants.

Comment: First and foremost, we would like to thank you for the opportunity to participate in this meeting. We meet with you every year, and although our opinions do not always align, constructive dialogue is important to us.

Question: Please tell us about your plans to include countries in the Eurasian Economic Community (EurAsEC) not currently covered by the voluntary license for cabotegravir.

Answer: The voluntary license for cabotegravir for pre-exposure prophylaxis (PrEP) is intended for countries least developed countries, low income countries, lower middle-income countries as defined by the World Bank as well as Sub-Saharan Africa. It will take some time for generic versions to enter the market. Until generic versions become available, ViiV will supply cabotegravir- LA for PreP to national programs. We are also collaborating with donors such as PEPFAR, the Global Fund, and community organisations such as AVAC, and national PrEP programs to enable access to this product. Currently, our focus is on implementing this license rather than expanding it.

Question: Have you already initiated shipments of cabotegravir? If so, at what price?

Answer: The first shipments through PEPFAR are expected to be made later this year. Unfortunately, the price is confidential.
Additional comment: The first shipments via PEPFAR did occur before the end of 2023.

Question: Do you have any additional information about the agreement with MSF beyond what is publicly available?

Answer: We will inquire with our colleagues and get back to you later.

Additional comment: *We very much support MSF's mission for CAB LA for PrEP access. Our current priority is to continue discussions so we can enable supply for the programmes MSF our running but we do not share more detail about contractual terms in the agreement publicly*.
*An agreement with MSF has since been reached.

Question: At what level will your price for cabotegravir be compared to other products?

Answer: As cabotegravir is a sterile, injectable medicine, it is a much more complex molecule to manufacture than, for example, dolutegravir. Therefore, it wouldn't be realistic to compare the associated costs. We believe you may have reviewed the study conducted by the CHAI foundation, in which an estimated price for CAB (14-18 USD per patient per year for supply volumes from 800,000 users per year - note ECAT) was assessed.

Question: Recently, Cepheid and Danaher announced their readiness to undergo an independent audit to confirm that they are supplying their product at a non-profit price. The results of the audit will be made public. Are you willing to take similar steps?

Answer: Please provide us with additional information, and we will discuss with our colleagues to see how feasible it is to implement.
Additional Comment: *If there is a specific initiative or organisation that is conducting these audits, we would be willing to review this to consider what value such an audit may deliver in terms of enabling access.*

Question: What is the rationale behind your policy to keep certain provisions of license agreements confidential? For example, confidential provisions are included in the special agreement for dolutegravir for above-average income countries and in the proposed MSF agreement for cabotegravir. Do you not consider this practice to contradict the social aspect of your mission?

Answer: Price information is often considered confidential, and this practice is not unique to the pharmaceutical industry. We understand your question and concerns, but we have no plans to make this information publicly available.

Question: Access to dolutegravir in Belarus is unstable, which is due to the high price of the drug. The special license agreement for Azerbaijan, Belarus, Kazakhstan, and Malaysia (hereinafter - the special agreement) did not eliminate price inequality in the EurAsEC region (the price in Belarus is currently about six times higher than in Armenia, Moldova, and Ukraine). Dolutegravir disproportionately consumes a significant portion of the national budget for ART compared to other ARV drugs (82% of the total ART budget in 2022). The patient community in Belarus plans to continue advocating for a price reduction for dolutegravir. How was the price of dolutegravir for Belarus calculated when concluding the license agreement with MPP on November 30, 2020? Do you plan to make the pricing rationale publicly available to the patient community in Belarus? Do you plan to reduce the current price, for example, by including Belarus in the general dolutegravir license of April 2014?

Answer: We are very proud that we have developed the UMIC Voluntary Licence for certain Upper Middle Income Countries countries which has contributed to expanding access. We believe that Upper Middle Income countries, can and should contribute more to the cost of developing innovative medicines than the world's poorest countries The governments of the mentioned countries have welcomed this license agreement. The royalty is determined based on how many people are transitioned to dolutegravir: the higher the percentage of people on dolutegravir as part of the total number of people on ART, the lower the royalty, and therefore should enable a lower price to be charged by the generic company. Currently, we are working with the Medicines Patent Pool to implement two more royalty levels. These two additional levels will be added to the existing three-tier royalty system. They will also depend on the percentage of people on ART receiving dolutegravir-containing regimens. We do not plan to include Azerbaijan, Belarus, and Kazakhstan in the standard dolutegravir license.

Additional Comment: The additional two royalty tiers were added prior to the end of 2023, in advance of local procurement cycles.

Question: Can you provide more details about the three-tier royalty system?

Answer: The figures below are for illustration purposes only and should not be considered as accurate. For example, if the percentage of people receiving dolutegravir is 10%, then the royalty per package might be $[X]0, for instance. If the percentage of people on dolutegravir is 25%, then the royalty per package would be lower, and so on. However, we are not prepared to disclose specific figures. The two additional levels will allow generics to further reduce prices, but this depends on a higher percentage of people using dolutegravir and larger purchases of dolutegravir. We want to emphasize that we cannot control the prices of generics. If you do not observe a decrease in generic prices in your countries as coverage increases, you should engage with generic manufacturers and suppliers. In response to the question about Belarus, I can only say again that our view is that upper-middle income countries can and should make a greater contribution, and therefore, the price of the drug there should be higher than in the world's poorest countries.

Question: The license for above-average income countries has existed since 2020 and has not led to the expected expansion of access to dolutegravir in Belarus. At the moment, no more than a quarter of those who need it have transitioned to dolutegravir. When we talk about fairness, we are talking about fair access for patients to medications, and you are talking about the fairness of pricing. How many people should be on dolutegravir, as formulated by the World Health Organization? This includes all people in need of first-line therapy. By your logic, the price should decrease as the percentage of people on the drug increases, while WHO says it should be the opposite. In other words, we should ensure coverage without thinking about the price. How was the price of dolutegravir for Belarus calculated in the license agreement?

Answer: For us, it's important to strike a balance between an affordable price and the need to ensure a sustainable return on investment in the development of new drugs. Developing an injectable form is a complex and costly process, and we need to recoup our investments. Therefore, it's crucial for us that countries with above-average income pay more. However, we understand the concerns regarding access, and that's why reduced royalty rates have been developed. Right after the conclusion of the special agreement, the price of dolutegravir decreased by about 50%. We currently see that approximately 60% of Adults living with HIV who are on treatment in these countries have gained access to the drug. We may interpret these numbers differently, but for us, this is a success.

Question: Where can we find information about how you calculated this? To ensure accountability of the manufacturer to the patient community, we need the ability to review these calculations, assess them, and agree or disagree with them. If these calculations are not available, we are left in the dark.

Answer: We cannot provide specific information about prices (which are the responsibility of the generic licensees) or royalty rates, but we understand the concern of activists. We believe the agreement has worked, and a balance has been achieved.

Question: What humanitarian supplies have been sent to Ukraine? What are the plans for further work in Ukraine?

Answer: We strongly condemn the military actions and are deeply concerned about the humanitarian crisis they have caused. Ukraine is covered by the standard voluntary license, and generic drugs can be supplied there. Over 10,000 packs of ARV drugs, including pediatric

formulations of "Tivicay," were provided to Ukraine and host countries as a donation. Together with GSK, we donated £2 million through the Global Fund to support testing and treatment programs in Ukraine. We have also supported initiatives of other organizations, particularly Save the Children , and and GSK's £3 million donation to the Red Cross's Ukraine crisis work. We provided £850,000 through the Positive Action initiative for 12 community organizations engaged in humanitarian activities and providing services and care. We are adapting our humanitarian programs as the situation evolves.

Question: Why did you block the supplies of Macleods and other generics for Ukrainian refugees in EU countries? Will the supplies be unblocked, and if so, when?

Answer: Since the start of the military conflict, in collaboration with UNAIDS and host governments, we collected information about the need for ARV treatment among Ukrainian refugees in receiving countries. We provided donations that were intended to ensure people receive therapy during the transitional period until they were included in national HIV treatment programs. The donations amounted to around 10,000 packs, as requested by host governments. The supply of generics would have had a significant impact on our intellectual property rights in Europe, and therefore a significant knock-on impact to the sustainability of the business, which is why the company was not able to support this.

Question: Thank you for the donation. As we understand, this is approximately 800 courses. However, in Ukraine, after three months of military action, the Health Center is missing about 20,000 patients – people who did not come for their medication. Several generic companies offered donations of dolutegravir to the government because 90% of HIV-positive people in Ukraine are on dolutegravir-based regimens. The European WHO Bureau took on the coordination of supplies, and we found warehouses in Poland that could accept these drugs strictly for HIV-positive Ukrainians in Poland and Germany. These drugs were not intended for sale, and we do not see any patent problems. Your company blocked these supplies for 20,000 people, and now these people will switch to a different treatment regimen because there was no planned quantity of dolutegravir in EU countries. And the budget of Ukraine will suffer from this.

Answer: It seems there have been two different messages coming from the receiving countries, or there may have been a misunderstanding. We asked the governments for the specific quantity of dolutegravir needed, and we were given a specific volume which we supplied. If additional volumes had been requested, these requests would have been considered. UNAIDS and the governments reacted positively to the donation. We did not want to risk infringing intellectual property rights.

Question: These donations do not threaten patents.

Answer: We believe there is a risk. Any entry of generics into a country where there are patents threatens patent rights in that country.

Question: According to available statistics, as of today, approximately 6,000 Ukrainian citizens abroad may still need dolutegravir. Can you consider additional donations?

Answer: We have an internal policy for providing donations in crisis situations. We cannot promise additional donations, but we are open to dialogue, including if governments approach us with specific requests.

Question: What difficulties do you observe in registering drugs in the EECA region, including in the EAEU countries?

Answer: The only problem in the field of drug registration is that rules in countries often change, and we have to adapt to new regulations.

Question: What challenges exist in translating to national languages in ECEA countries (instructions and others)?

Answer: We usually encounter the following difficulties: translation specificity, translating abbreviations, and quality reduction when translating through global agencies, which may not fully consider national nuances.

Question: Are there plans to issue a voluntary license for long-acting cabotegravir + rilpivirine for HIV treatment? If yes, when is it planned, and which ECEA countries may potentially be included?

Answer: This combination is not on the WHO's priority list for combined therapy, so a voluntary license has only been issued for cabotegravir for pre-exposure prophylaxis. If there is unstable demand due to the absence of a WHO position, generics have no incentive to invest in drug development because the return is uncertain.

Comment: Waiting for WHO's position can take an indefinite amount of time, as in the case of the dolutegravir/lamivudine combination. In the Russian Federation and Kazakhstan, there are many patients on dual therapy, and WHO has still not included it in their recommendations.

Answer: Janssen is responsible for making the long-acting cabotegravir + rilpivirine combination available in low-income and lower-middle-income countries. It would be their responsibility to negotiate with the Medicines Patent Pool for a license. A license would be needed not only for cabotegravir but also for rilpivirine. We have not heard about negotiations between Janssen and the Medicines Patent Pool regarding this.

Question: How often do you receive complaints about adverse events related to the use of ARV drugs through the existing pharmacovigilance system in ECEA countries? Are there any "problematic" countries?

Answer: We have a robust pharmacovigilance system where we receive reports from practicing doctors and patients, and all of them are collected in a central database which is managed by us. In addition, the voluntary license also requires licensees to provide us with information collected through pharmacovigilance regarding potential issues with the drugs. There are no "problematic" countries in the region in terms of the number of reports.

Question: Are there countries from which no reports are received, and it seems that everything is perfect? This could serve as an indicator that the pharmacovigilance system is not working there.

Answer: The reporting pattern in each country is unique and depends on several factors. Lack of reporting to the MAH may not be indicative of issues with the country pharmacovigilance system.

Question: Please provide the latest data on GSK3036656.

Answer: ViiV focuses on HIV drugs, and this question should be directed to GSK. We do not have information beyond what is publicly available. However, we can say that GSK announced

a commitment to invest in tuberculosis research for high-burden countries this year. All developments are in early stages, with a focus on shorter treatment regimens and more easily tolerated and effective drugs. Additionally, GSK, in collaboration with the Gates Medical Research Institute, is developing a tuberculosis vaccine that showed promising results in phase 2 trials. If you need more details, we can connect you with colleagues from GSK.

Comment: Our region is heavily affected by tuberculosis, and it would be important for us to have this research conducted in ECEA countries as well.

Question: In the future, can you participate in these meetings together with GSK, if there are no legal barriers?

Answer: We will consider your request. Sometimes joint meetings may be beneficial.

Question: We request that you connect us with colleagues from GSK so that we can arrange a separate meeting regarding tuberculosis, involving those working on vaccines and those working on drugs. Which company is involved in the development of HIV vaccines – ViiV Healthcare or GSK?

Answer: We need to clarify the information regarding vaccines. We will pass on the request to our colleagues.

Additional Comment: Search is still in progress

Question: What research and clinical trials of new drugs is the company conducting or planning to conduct? Which ECEA countries are included in multicenter clinical trials?

Answer: We have several drugs in development, including combination therapies. There are specific criteria for selecting trial sites. At this stage, ECEA countries are not included in these clinical trials, in part because the early phases are currently in progress. Decisions about including ECEA countries in later phases of the trials will be made later.

Comment: There are many countries in the region that need the development of the clinical trial market for various reasons, including the actual cessation of international research in Russia. There is a developed research market in countries like Kazakhstan, Uzbekistan, and others in the region. We request that you consider including these countries in your clinical trial plans.

Answer: Thank you for the feedback. We understand the need and the gap that has emerged. When the second and third phases begin, we will keep this information in mind.

Question: We are currently establishing a group that will provide feedback on clinical trial protocols for tuberculosis and then plan to expand this practice to HIV, so that at the study design stage, we have the ability to provide you with comments on what we believe needs improvement, and so on. We invite you, under conditions of confidentiality, to share study protocols with us so that we can provide you with feedback.

Answer: Thank you very much. We are also interested in this, and with your permission, we will pass on the information to colleagues.

Question: We are concerned about the lack of data on the use of cabotegravir + rilpivirine during pregnancy, in children and adolescents, as well as in those with hepatitis B co-infection. Will there be additional research?

Answer: Firstly, we acknowledge that there is a gap in data on the use of CAB-LA and CAB+RPV during pregnancy. Since November 2020, clinical trials have had the option to continue CAB+RPV LA dosing in pregnancy, which has allowed us to gather more information. We are working with the Antiretroviral Pregnancy Registry, a special registry for pregnant individuals, as well as the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC). There are several studies where we are assessing the safety and tolerability of long acting cabotegravir + rilpivirine and cabotegravir for pre-exposure prophylaxis (PrEP) before, during and after pregnancy. There will also be joint studies on cabotegravir for PrEP, including monitoring of birth, maternal and infant safety outcomes. At this time, there are no concerning signs, but we need more data to be able to make statements for outcomes. Studies involving children take more time. Currently, there is the MOCHA study, evaluating the safety of long acting cabotegravir + rilpivirine in children and adolescents with suppressed viral loads aged 12-18. Additionally, the Crayon study will start soon, examining the safety and tolerability of long acting cabotegravir + rilpivirine in children with suppressed viral loads aged 2-12 and will determine the weight band dosing regimen.

Question: Can you provide more information about the registry for pregnant individuals on antiretroviral therapy?

Answer: The Antiretroviral Pregnancy Registry is an international initiative at the expert community level. It allows for the collection of data on the antiretroviral regimens taken by pregnant individuals and whether there were any adverse events related to pregnancy or in the child after birth. Please refer to the APR website for more information as this is independent of ViiV.

Question: Will there be information on the use of the cabotegravir/rilpivirine regimen for people with hepatitis B co-infection?

Answer: Since cabotegravir/rilpivirine is not effective against hepatitis B, we have no plans to collect new data on this co-infection. However, we do monitor all reports related to hepatitis B within the standard pharmacovigilance system.

Question: Tell us about the Positive Action program.

Answer: This program focuses on vulnerable populations. Calls for grant proposals are regularly announced. We suggest following our social media channels where this information is available. In 2021, there was funding for "digital" prevention campaigns for seven countries in our region. ViiV is also part of a separate working group for the EECA region for donors, recognizing that the region has the fastest-growing HIV epidemic in the world. In light of various events, including military conflicts in 2022, it is also important for us to support communities in Ukraine. At the moment, the Positive Action program for 2024 is in planning stages and I do not have visibility of what calls for proposals will be issued. We also have small projects aimed at supporting the scientific community and engaging communities to maintain the priority of HIV.

Question: Do you have plans to fund tuberculosis programs? You did not support the TB People Ukraine application with a formulation stating that this area is no longer supported. Do you consult with the community when determining funding priorities?

Answer: GSK is responsible for tuberculosis, so you should contact them. We believe that feedback from communities is important. We have a commission that deals with such issues, but we also encourage you to directly communicate your needs to us.

Question: Is there an opportunity to provide free or sponsored assistance in the form of medicines to patients in Tajikistan?

Answer: We have a donations program. In crisis situations when access is limited and intervention is needed, we can provide donations. Tajikistan is covered by the standard voluntary license for dolutegravir and a license for cabotegravir. We also have early access programs for unregistered drugs.

Question: What resources and programs do ViiV provide for patient education and awareness about HIV/AIDS and available medicines?

Answer: It depends on the type of programs you refer to. In most countries, we cannot directly discuss our products with those who use them, i.e., patients. However, we develop informational materials and can provide them to community organizations, and we can also respond to requests from organizations. We can also support general educational programs that do not pertain to specific products.

Question: Is it correct to understand that the educational platform Step Up, previously supported by Gilead, is now sponsored by ViiV?

Answer: We will get back to you regarding Step Up later. Typically, initiatives to support such programs come from patient communities, not us.

Additional Comment: *The STEP Up programme is part of our core funding with EATG. We are aware that Gilead is also funding EATG but we do not know specifically if STEP Up is entailed into that agreement.*

Question: Does the company have experience in public-private partnerships in the development of new drugs?

Answer: Yes, we have public-private initiatives related to drug development. For example, we have a drug whose development is supported by the U.S. government. We also previously had a joint initiative with the University of North Carolina in the U.S. for developing a cure for HIV (Qura Therapeutics). We collaborate with the University of Liverpool on the development of long-acting drugs for the treatment and prevention of HIV.

Comment from a community representative: If you conduct clinical trials in the EAC region, please consider the possibility of establishing special national CABs or a regional CAB to ensure the participation of patient communities in this process. Similar experiences exist with other companies.

Additional question from Sergey Biryukov (Kazakhstan), submitted after the meeting: Will the special license be expanded to allow TLD to be sold in the retail pharmacy network in the Republic of Kazakhstan?

Additional comment: *The UMIC Voluntary Licence allows generics companies to supply to the public market. I am unsure of the problem that would be addressed if TLD were sold in the retail pharmacy network. Is the concern that these sales not reimbursed by government? If you can provide some more information, then on what issue/concern is then I would be able to discuss this with colleagues.*