Minutes of the meeting of
Eurasian Community for Access to Treatment and Emcure

October, 3rd 2019, Yerevan, Armenia

Representative of the company:

- Balaji UD, Sr. Director, Global HIV/AIDS Initiatives, Emcure Pharmaceuticals Ltd

Participants:

	Participant	Organisation	Country
1	Igor Chilcevschi	League of PLWH of Moldova	Moldova
2	Andrei Lungu	OA "Initiativa Pozitiva"	Moldova
3	Alex Schneider	Life4me.plus	Switzerland, Russia
4	Nurali Amanzholov	Central Asian Association of PLWH	Kazakhstan
5	Lyubov Vorontsova	Central Asian Association of PLWH	Kazakhstan
6	Yelena Rastokina	PF «Answer»	Kazakhstan
7	Sergey Biryukov	PF «AGEP'C»	Kazakhstan
8	Tetyana Khan	ITPCru	Russia
9	Denis Godlevskiy	ITPCru	Russia
10	Natalia Egorova	ITPCru	Russia
11	Maria Shibaeva	ITPCru	Russia
12	Meruert Bektemisova	“Partnership network” Association	Kyrgyzstan
13	Aibar Sultangaziev	“Partnership network” Association	Kyrgyzstan
14	Sergey Uchaev	ISHONCH VA HAYET	Uzbekistan
15	Anatoli Leshanok	RPA“People PLUS”	Belarus
16	Irina Statkevich	BPA "Positive Movement"	Belarus
17	Marina Chokheli	TB People/OSF Georgia	Georgia
18	Zoya Zamihovska	100% LIFE	Ukraine
19	Evgenia Kononchyk	100% LIFE	Ukraine
20	Nadiia Savchenko	100% LIFE	Ukraine
21	Olha Klymenko	TB people UA	Ukraine
22	Mykyta Trofymenko	100% LIFE	Ukraine
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24	Anastasiia Rupcheva	100% LIFE	Ukraine
25	Maryna Kopylenko	100% LIFE	Kyiv
26	Anahit Harutyunyan	“Positive People Armenian Network” Social NGO	Armenia
27	Oleksandra Kolotyha	100% LIFE	Ukraine
28	Morgane Ahmar	ITPC Global	Morocco

Facilitator: Sergey Golovin

Beginning of the meeting. Introduction of participants.

Company presentation

I will briefly tell you about Emcure, in particular, about the activities that it conducts in the field of HIV infection treatment and about our work in this region. Further on I will provide specific information for each country and what we do there. First, we will discuss drugs, then we will talk about countries, and after that I will answer your questions.

Emcure was founded in 1983. In addition to ARVs, the company produces a wide range of other drug products. The company was founded in India, now we have 17 production sites. In addition to finished products, we produce substances (active pharmaceutical ingredients - API), which means that we have a full production cycle.

The plan of our talk is as follows. First, we will talk about drug products that have received FDA prior approval or WHO prequalification. We will talk about where we get the substance from. We will discuss key drugs, including tenofovir, lamivudine, and dolutegravir. Then we will discuss our plans for registration in this region. We will talk about the new drugs that are in the pipeline, about the innovations of Emcure, about the IMS rating in India and the social responsibility of the company.

The table below shows ARVs that have received US FDA preliminary approval. They are present on both PEPFAR and Global Fund lists. These drugs also have WHO prequalification.

(T) USFDA APPROVED

Sr. No	Product Name	Strength	(T) USFDA Approval
1	Atazanavir Sulfate and Ritonavir Tablets	300 mg / 100 mg	3/17/2014
2	Atazanavir Sulfate Capsules	300 mg	8/19/2010
3	Atazanavir Sulfate Capsules	100mg / 150mg / 200mg	02/04/2008
4	Efavirenz Tablets	600mg	12/20/2007
5	Nevirapine Tablets	200mg	09/28/2007
6	Lamivudine + Zidovudine Tablets	150mg / 300mg	08/08/2007

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In addition, we have drugs that we have submitted for both FDA preliminary approval and WHO prequalification.

PRODUCTS AWAITING APPROVAL

No	Product	USFDA	WHO PQ
01	TDF 300mg + FTC 200 mg FDC Tablets	ANDA # 206213	Ref no.: HA726-0
02	TDF 300mg + FTC 200mg + EFV600 mg FDC Tablets	ANDA # 206584	--
03	Dolutegravir 50 mg Tablets	ANDA # 210036	Ref no.: HA701
04	TDF 300 mg + 3TC 300 mg + DTG 50 mg FDC Tablets GLOBAL FUND ERP RECEIVED	ANDA # 211868	Ref no.: HA722
05	Tenofovir 300mg + Lamivudine 300mg + Efavirenz 600mg Tablets	--	Ref no.: HA728
06	Abacavir 600 mg + Lamivudine 300 mg + Dolutegravir 50 mg Tablets	ANDA # 212181	--
07	Tenofovir Alfanamide 25 mg + Emtricitabine 200 mg + Dolutegravir 50 mg Tablets	NDA # 212108	--

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I would like to make a few points on the drugs indicated in this table. Tenofovir/emtricitabine is also indicated for use as PrEP. The drug tenofovir/lamivudine/dolutegravir has the status of the Global Fund (GF) ERP; this is the approval of the GF expert group. This status means that this product is currently undergoing approval by both the WHO and the FDA. To speed up the access, a special GF expert group reviews the drug product dossier, paying particular attention to quality issues, and either grants this status or not. This information is listed on the GF website. Thanks to this, with the Global Fund status, countries can purchase this drug, even if it has not received WHO or FDA approval. The GF expert panel has authorized the supply of such products. This can be called a temporary permission, so to speak, a temporary prequalification. There is a comment: the right column shows the dossier numbers submitted for consideration.

Question: Can these drugs be bought only with GF money?

Answer: Yes, that's right. In country Procurements who refer to Global fund Quality assurance document may also use this ERP approval for their procurements.

For tenofovir/emtricitabine/efavirenz 600 mg, abacavir/lamivudine/dolutegravir, TAF/emtricitabine/ dolutegravir, we are awaiting the decision from WHO within 1 month, and from the FDA within 2-3 months. They do not have WHO prequalification because WHO did not include them in their model list, but this is only a matter of time.

Question: Can we include these drugs in national protocols?

Answer: Yes. For example, these drugs are already present in American DHHS treatment guidelines. They will be included in WHO treatment guidelines only in the future.

One of the drugs that we supply to over 75 countries is the tablet form of atazanavir/ritonavir. We started with 5,000 packs of 30 tablets per batch in 2014 to produce 150,000 packs per month. We compared our drug with other similar atazanavir/ritonavir generics that are FDA approved and found that our drug tablets are 25% less in weight and size, and also have a significantly longer shelf-life (36 months versus 24 months). The tablet size affects adherence, as a smaller pill is easier to swallow. Over time, we have increased our production capacity to 640,000 tablets with option to further increase the production capacity to 700,000 packs of 30 tablets per month to rank Emcure among the largest manufacturer of atazanavir/ritonavir tablets in the world.

As I understand it, there are challenges to supply ATV/r tablets to many countries in the region due to ritonavir HME patent protection which needs to be addressed.

As for the fixed-dose combinations, we have the following drugs: tenofovir/lamivudine/efavirenz 600, tenofovir/emtricitabine/efavirenz 600 mg, tenofovir/lamivudine/dolutegravir and TAF/emtricitabine/ dolutegravir.

As you can see, there is a dramatic decrease in tablet size. This is an important thing that has happened lately. You can clearly see that the TAF/emtricitabine/dolutegravir tablet is 2 half the size of other triple drug tablets. Such a dramatic decrease in tablet size for a triple drug was not possible in the last 10 years and perhaps may not happen in the next 10 years.

Question: Do you have any plans for a combination of TAF/lamivudine/dolutegravir? This would be a very good option for people with hepatitis B.

Answer: This is a good suggestion, we will consider it, but the combination TAF/emtricitabine/ dolutegravir should also work in patients with hepatitis B co-infection. TAF is present in the USA DHHS guidelines; it is believed to be better due to lesser tenofovir associated nephrotoxicity and bone mineral density loses. TAF acts against hepatitis B, and emtricitabine and lamivudine are interchangeable drugs. We have already introduced this drug to the commercial market of India, and received good feedback.

Question: What is the price for TAF/emtricitabine/dolutegravir in India?

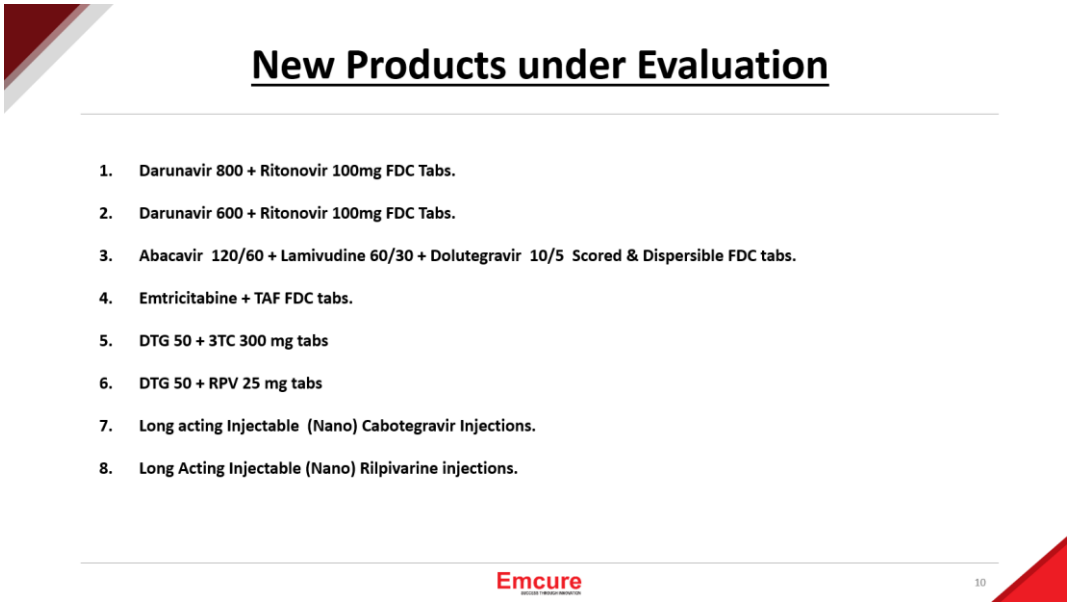
Answer: You must keep in mind that the price includes various additions (commercial, retail). In total, it's about $40 for one month's course.

Our current production capacity for triple combinations of tenofovir/emtricitabine/efavirenz, tenofovir/lamivudine/efavirenz, tenofovir/lamivudine/dolutegravir is 1,200,000 packs per month. There are 30 tablets in each package. The planned increase in capacity is up to 3,000,000 packages of 30 tablets per month.

In this regard, since we work in the field of public health, we must be sure that we can provide the necessary quantity of drugs. Therefore, it is important for us that there are two or more sources of raw materials. This table shows the drug products. Substances 1 through 7 are already manufactured by Emcure. 8, 9 and 10 will be also produced at our facilities. For each of these 10 substances, we have a second and even third source, because we need continuous and uninterrupted supply of the substance. I want to draw your attention to the fact that we produce our own maraviroc substance.

The next slide shows the volume of raw materials produced and the amount of the finished product. Every month we can produce the necessary amount of raw materials (MT or metric tons = 1000 kg): 5 MT of atazanavir, 2 MT of ritonavir, 2.5 MT of TAF, 5 MT of dolutegravir. If you convert all this into the number of packages of 30 tablets for 1 month of treatment, then you will get the following result: 0.55 million packages of atazanavir, 0.66 million packages of ritonavir, 3.32 million packages of TAF, 3.32 million packages of dolutegravir.

The table below shows the drugs that are in the developmental pipeline. Products 3 is pediatric ARV drug while7 and 8 are long acting injectables subject to obtaining product licenses.



Question: According to your calculations, when will the drug for pediatric use at number 3 be ready?

Answer: In at least two years after WHO and PADO have concluded the appropriate ratio of the components of the options shown – namely 120/60/10 mg or 60/30/5 mg.

Question: And when are drugs 7 and 8 (long acting injectables) planned?

Answer: We are currently negotiating their licensing.

Question: A question on drugs darunavir 600/ritonavir and darunavir 800/ritonavir. Both of these drugs are patented. What are your plans for them?

Answer: We will talk about patent issues a bit later.

When we were developing these projects, we aimed at 90% of the treatment coverage of people living with HIV. For example, in ATV/r tablets the Medicine patent pool's license permits supply for 112 countries, of which we have received approvals in 23 countries and in another 10 countries it is expected. Our goal is 95% coverage. Our regulatory teams work with national regulatory authorities to make this coverage possible.

Now let's move on to innovation. We are the first company to invent the atazanavir/ritonavir fixed dose combination tablet. We also manufacture a combikit containing two combinations at once: atazanavir/ritonavir tablets and tenofovir/emtricitabine tablets. Thanks to this, the patient takes two tablets, receiving four drug products as per treatment guidelines. We also have combined packaging with atazanavir/ritonavir tablets and lamivudine/zidovudine tablets. And for countries which follow lamivudine, we made a combined package of atazanavir/ritonavir tablets and tenofovir/lamivudine tablets.

Maraviroc is manufactured by Pfizer, Germany. We were the only manufacturer (in addition to Pfizer, Germany) to produce maraviroc tablets.

Question: As far as I know, maraviroc is prescribed only after the test for R5 tropism. Do you have these tests? What is the price of maraviroc and the test?

Answer: In India, this test costs about $100. If the patient is resistant to both the first and second lines of ARVs, then a third line drug is needed. It is necessary to have a resistance test and see what other drugs are effective for this patient. In such instances, maraviroc will play a critical role. The price of the drug is about $150 per month.

Question: Do you test for R5 tropism? How much will they cost for Kazakhstan?

Answer: We do not produce this test kit. When we received the license for maraviroc, we were helped to find a laboratory and calibrate it for the R5 tropism test. If you intend to supply the country with this medicine, then you need to find one laboratory that will receive this test protocol, since this drug should be prescribed only after testing.

We produce sustained release nevirapine 400 mg (one tablet per day). In addition, we produce combined packaging with 400 mg nevirapine tablets and tenofovir/lamivudine tablets.

Question: Does your company see the potential for sustained release nevirapine 400 mg in our region?

Answer: As drug manufacturers, we must make the product affordable (accessible). And it is the doctor who decides what is good for the patient. Considering that many drugs develop resistance to HIV, this drug is one of the options.

Question: Is this form of nevirapine 400 mg single dose protected with a separate patent? What is its current value? Is it possible to freely replace nevirapine 200 mg with a double dose of this one? And how much more will this treatment cost?

Answer: No, there will be no change in price. The price for a monthly course of nevirapine 400 mg will be comparable to the price for a monthly course of nevirapine 200 mg. As for the patent, I do not think that this patent is valid. We will study this issue.

Question: Have you already negotiated with PEPFAR, the Global Fund, procurement agencies about nevirapine 400 mg?

Answer: They have been aware of this since when we developed this drug. We are waiting for US FDA approval for our nevirapine 400 mg tablets.

Comment: Nevirapine was excluded from WHO recommendations. Therefore, the Global Fund is unlikely to procure it.

Answer: Nevirapine is still in WHO recommendations. The procurement volumes are simply decreasing, as in Africa and Southeast Asia there are other options, e.g. combinations with efavirenz and dolutegravir.

We produce a combination of darunavir 600/ritonavir 100 to be used twice a day in the third line treatment. Now we are developing the drug darunavir 800/ritonavir 100 single tablet to be used once a day in the second line treatment.

In general, if you look at the rating of the private ARV market in India, Emcure has more than 50% of the market share.

I am going to talk for a while about the corporate social responsibility of our company. On World AIDS Day, we hold awareness-raising events like street walks or roadshows. We work together with NGOs and doctors in the field of HIV. The community of HIV-positive people in India has opened pharmacies called TAAL (Treatment Adherence Advocacy and Literacy program) that sell exclusive HIV medicines. In these pharmacies, patients not only receive medicines at subsidized prices but also meet with other HIV-positive people to communicate and share their life experiences/challenges. At these meetings, they make efforts to increase patients' adherence and literacy, which is the foundation of HIV treatment. There are five such centers operational. Emcure supports these activities as the profits from the pharmacy belong to community of HIV-positive people of India. We are the only company that responded to such a request by PLHIV. This is a stable model, it includes a doctor and a pharmacist, there are also people who teach patients different skills, provide assistance to widows, and conduct computer literacy classes for children. This venture is not owned by Emcure, but belongs to the network of HIV-positive people.

Our company makes presentations at various international conferences on HIV/AIDS. We thank the Medicines Patent Pool and such innovator companies as AbbVie, BMS, Gilead, Tibotec, ViiV, MSD, Janssen and many others that we are in partnership with.

Let's talk about the countries our company works with and the challenges we face.

Here is a table in which countries and drugs are presented and their patent status is indicated.

In Ukraine, we started the registration process of tenofovir/emtricitabine/efavirenz and tenofovir/lamivudine/dolutegravir. We can also start the registration of abacavir/lamivudine/ dolutegravir and TAF/emtricitabine/dolutegravir. In Ukraine, there is a problem with the patent for ritonavir, so we registered only 300 mg atazanavir capsules. There are no patent problems with tenofovir/emtricitabine as PrEP and dolutegravir monocomponent. One of the key issues is the ritonavir patent, which interferes with the supply of the atazanavir/ritonavir combination. Now we are working in two directions: on the one hand, we are motivating the Patent Pool for expansion of ritonavir countries while we are also talking directly with AbbVie.

Question: What is the progress in negotiations with AbbVie?

Answer: AbbVie comes to all our conferences, they listen to our suggestions attentively and understand the need but a definite answer on territory expansion still not received. As you understand, the same problem will arise in the supply of a combination of darunavir/ritonavir.

Question: My question is about ritonavir. Will the company be ready to supply it if a compulsory license is issued? Do you have any plans to dispute the ritonavir patent? I know that this is mainly a Eurasian patent, which means that if a patent is disputed in one country, then it will be easier to dispute it in other countries.

Answer: Emcure's goal is to increase access, whether it is a voluntary or compulsory license. We are ready to negotiate to make the drug available to patients. Two challenges, two problems are shown in this table: dolutegravir and ritonavir in Kazakhstan, Belarus and Azerbaijan. In fact, thanks to Emcure, a BMS license for atazanavir in Russia was issued although the license from the Patent pool for atazanavir does not include Russia. BMS gave us a separate license for atazanavir capsules in Russia, and we registered the drug. As soon as there is good news about ritonavir license, no matter if it's voluntary or compulsory, we are ready to register it and supply it.

Question: Why does this table say that efavirenz is patented in Belarus?

Answer: There was a problem with one license, and I have to check it. I informed the Patent Pool about this problem, and it should check with this issue. What is your opinion?

Question: Generic efavirenz has been in Belarus since long time ago.

Answer: Thanks for the information. Which combination do you buy: tenofovir/emtricitabine/efavirenz or tenofovir/lamivudine/efavirenz?

Question: We buy tenofovir/emtricitabine/efavirenz.

Answer: Thank you.

Question: This a question about Kazakhstan, including tenofovir/emtricitabine/efavirenz. In our country, only relatively old ARV drugs, such as nevirapine, etc., are registered by you. When do you plan to enter our market with combinations of fixed dosages? The registration of tenofovir/emtricitabine/efavirenz 400 is also interesting. Do you have this drug? And another interesting combination is tenofovir/lamivudine/dolutegravir. I hope that it will appear in Kazakhstan soon.

Answer: Regarding efavirenz 400 mg, we have not yet developed it. Any new product development will take at least two years. Maybe it will be a better option to solve the problem with the dolutegravir patent.

Question: There are many suppliers of tenofovir/emtricitabine/efavirenz 600 in Kazakhstan. We will be glad to see tenofovir/lamivudine/dolutegravir drug product, and in two years to tenofovir/ emtricitabine/efavirenz 400.

Answer: As soon as the issue with the patent for dolutegravir is resolved, there will be no problems with tenofovir/lamivudine/dolutegravir supplies.

Question: Perhaps you know that the compulsory license process in Kazakhstan has already begun. If you started the registration process early, then we could finish both processes at the same time. The sooner the drug is registered, the more opportunities you will have to participate in tenders.

Answer: Thank you. This is very important and new information for me. For example, in Uzbekistan we already supply heat-resistant atazanavir 300/ritonavir 100, and there is no problem with the patent there.

Question: If we, Kyrgyzstan, provide you a letter of compulsory license for ritonavir, can you supply atazanavir/ritonavir to us?

Answer: Of course!

Question: (Kyrgyzstan) If we contact you and ask for a letter stating that in the case of a compulsory license you will be ready to deliver the drug to us, can you give us such a letter?

Answer: There should be no problem with this. If you give us a letter stating that a compulsory license has been issued, we will forward it to the Patent Pool to issue us a sublicense.

Question: Your products are not registered in Kyrgyzstan. Do you have plans to come to our country?

Answer: Yes, of course. We are registering drugs in Kyrgyzstan; we have already filed a dossier for dolutegravir. We have country-specific tables, including Kyrgyzstan, where we have a representative office. For such drugs as tenofovir/lamivudine/dolutegravir, abacavir/lamivudine/dolutegravir, TAF/emtricitabine/dolutegravir, tenofovir/emtricitabine, we have sent dossiers to our representative office in Kyrgyzstan, and we can submit them for registration at any time.

Question: Do you know that in Kyrgyzstan prequalified drugs and drugs approved by the FDA have a fast-track registration procedure of 45 days?

Answer: No, I did not know about it. Thanks for the information.

Question: (Kyrgyzstan) We can give a supporting letter so that the Ministry of Health and the Department of Drug Supply speed up the registration of these drugs, because they are vital.

Answer: Of course! I will convey this information to our representative office in Kyrgyzstan.

Question: What other countries do you have representative offices in?

Answer: In Russia, Ukraine, Belarus, Kazakhstan, Kyrgyzstan, Uzbekistan, Moldova, and even in Armenia and Macedonia. After you informed me of the many details of registration in countries, we can speed up these processes in these countries.

Question: Do you have any understanding how to work in the field of PrEP? Do you have any ideas, thoughts? You have mentioned tenofovir/emtricitabine as PrEP several times. How do you see the work in this direction in this region?

Answer: It is a hard job. This is a segment of people who do not have HIV, but who should take an ARV drug. This differs from the traditional approach, the patient's code for diagnosis reveals HIV, and then

medications are prescribed. The only way to achieve this is to raise awareness. When we attended the WHO meeting, they had ambitious plans to increase the number of people on PrEP: to increase them 10 times over the next two years. We asked WHO the question that you have just mentioned. The only solution is over-the-counter drugs. WHO has plans to engage celebrities to advertise on social networks, the press and other media.

Question: We talked little about Russia. The following information is intended for you and your Russian representative office. Perhaps Russia is the only country where tenofovir/emtricitabine is under patent. We hope that tenofovir/emtricitabine generics will be registered in Russia, and it will be available both for treatment and PrEP.

Question: This is a question about buying the drug in pharmacies in India. Do I understand correctly that anyone can come and buy this drug?

Answer: Not quite so, a prescription is needed.

Question: You said that there is a doctor in these pharmacies.

Answer: No, the doctor comes there from time to time. There is a consultant who tells the buyer (patient) to go to this pharmacy.

Question: Are you considering creating such points in other countries? Can you supply ARVs for retail sale in Kazakhstan so that they are available in pharmacies?

Answer: I can introduce you to the Network of HIV-Positive People in India. It all depends on the protocol in Kazakhstan, or to be precise, on the availability of drugs in the protocol. In some countries, this is done through a government distribution system.

Question: If you will have the opportunity to sell the drug in a retail network, will you supply it or refer to the fact that there is a state distribution system? We have patients who are not citizens of Kazakhstan. Many of them need the opportunity to purchase ARV drugs prescribed by a doctor at the pharmacy, including those in your portfolio. If we tell you exactly which ARVs are needed, can you make at least one pharmacy where you can supply a certain quantity of drugs so that an ordinary buyer can buy them. It is also very important for PrEP.

Answer: Yes, we can do that.

Question: (Kyrgyzstan) As for tenofovir/emtricitabine/efavirenz, tenofovir/emtricitabine/dolutegravir, TAF/emtricitabine/dolutegravir, TAF/lamivudine/dolutegravir: what price are you ready to announce?

Answer: Deliveries of TAF have not been started yet; the prices of tenofovir/lamivudine/efavirenz and tenofovir/emtricitabine/efavirenz have already been published.

Question: For tenofovir/lamivudine/dolutegravir, everything is clear; we have a price of $7 to $10 per package. If there is a combination of TAF/lamivudine/dolutegravir, how much will the price change?

Answer: The price will be approximately the same or even lower.

Question: Thank you. Then we will request to include combinations that may be with TAF in the treatment protocol. WHO has not yet recommended TAF, but we can try to include it in the protocol.

I am ready to send your country-specific information to every one of you. I can also give you contacts of our country managers.

End of the meeting.