Minutes of the conference call of Eurasian Community for Access to Treatment and MSD company

April, 24th 2019, Saint Petersburg, Russia

Representatives of the company:

Paul Schaper, Executive Director, Global Public Policy

Lital Young, Regional Medical Director, Mid-Europe, Russia, Middle East, Africa

Emily Gibbons, Director, Global Public Policy

Participants:

#	Name	Country	Organization
1	Nikita Trofimenko	Ukraine	100 Percent of Life Charity Organization
2	Lyudmila Untura	Moldova	PLHIV League of Moldova
3	Sergey Biryukov	Kazakhstan	AGEP'C Non-Governmental Fund
4	Dmitry Lisenkov	Russia	Vector of Life Charity Fund
5	Lubov Vorontsova	Kazakhstan	Answer Public Foundation's Subsidiary in Almaty
6	Anahit Harutyunyan	Armenia	Positive People Armenian Network
7	Anna Galstyan	Armenia	Positive People Armenian Network
8	Elena Rastokina	Kazakhstan	Answer Public Foundation's Subsidiary in Almaty
9	Anatoly Leshenok	Belarus	People PLUS NGO
10	Ekaterina Novikova	Kyrgyzstan	Partnership Network Association
11	Irina Statkevich	Belarus	Positive Movement NGO
12	Oleg Dymaretsky	Ukraine	Wave Charity Organization
13	Diana Imamidin Kyzy	Kyrgyzstan	Partnership Network Association
14	Vladislav Denisenko	Ukraine	100 Percent of Life Charity Organization
15	Alexey Trutnev	Russia	NAVIGATOR Social Support Center
16	Ruslan Poverga	Moldova	Positive Initiative Public Association
17	Denis Godlevsky	Russia	AIDS, Statistics, Health NGO
18	Natalia Egorova	Russia	ITPCru
19	Julia Vereshchagina	Russia	ITPCru
20	Alexey Mikhailov	Russia	ITPCru
21	Maria Shibaeva	Russia	ITPCru
22	Andrey Skvortsov	Russia	AIDS Relief Fund
23	Gregory Vergus	Russia	ITPCru
24	Artem Vereshchagin	Russia	Support Group "Mayak"
25	Tatyana Khan	Russia	ITPCru
26	Vitaly Bespalov	Russia	Parni Plus
27	Sergey Golovin	Russia	ITPCru
28	Anna Garkusha	Ukraine	Consumers of Ukraine Charity Organization
29	Ilya Lapin	Russia	Canadian Legal Network
30	Anatoly Garkusha	Ukraine	Consumers of Ukraine Charity Organization

Meeting Facilitator: Sergey Golovin, ITPCru

Beginning of the conference call. Introduction of participants.

(Paul Schaper) At MSD, I focus on global policies for HIV and viral hepatitis C, and various infectious diseases in general. I have two colleagues with me, one of them is engaged in medical issues, including issues for EECA; the second colleague, Emily, works with me in the sphere of HIV and viral hepatitis C policies. We will answer questions that you sent to us and those questions which will arise in the course of the discussion.

Question 1. MSD drug products registration in EECA countries

We seek to register and obtain marketing authorization in countries where two conditions are met: the level of need and the level of demand that would justify our efforts on registration. Unfortunately, very often these two factors do not correlate. As a rule, we have the need, but there is not always the necessary demand and the required treatment programs. Considering the limited resources that we have for registering drugs in countries, we prioritize those countries where these two conditions (need and demand) are combined.

Registration of Isentress 400 mg and Zepatier

Isentress (Raltegravir 400 mg) for treatment of HIV infection and Zepatier (elbasvir/grazoprevir) for treatment of chronic hepatitis C are registered in seven countries of the region: in the three Baltic states (Latvia, Lithuania, Estonia), Russia, Georgia, Kazakhstan and Ukraine.

We have the experience of supplying drug products for treatment of HIV infection and chronic hepatitis C in countries where our company's drugs are not registered. We are able to do this when various international procurement agencies obtain regulatory waivers from national authorities to import unregistered product. In the area of HIV infection, first of all, these are generally programs supported by the Global Fund.

> Question: Are you planning to register Zepatier in other countries?
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> Answer of the company representative: At this stage, no registration is planned in any other countries in the region, other than the seven that have already been mentioned. If there is a specific interest in our product, a necessary treatment program and corresponding demand for our product in another country, we will work with their government on this issue.
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> Question: Please tell us about registering of Isentress 600 mg.
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> Answer of the company representative: Raltegravir 600 mg is registered in four countries: the three Baltic states and Russia. In its instructions for use (USA) it is stated that it is for treatment-naïve patients, that is, it is positioned as a first-line drug. This does not correlate with the position of WHO, which recommends Raltegravir for patients who have already received the therapy. The same situation is in most EECA countries. There is little data on the use of Raltegravir 600 mg in patients who previously received ARV therapy, and there are very few countries where Raltegravir is used in the first line treatment. Taking this into account, we, most likely, will not focus our efforts on registration in these countries; however we will focus on those countries where Raltegravir is already actively used in first-line treatment.

Registration of pediatric forms of Raltegravir

There are three types of Raltegravir for pediatric use: 100 mg, 25 mg and granules for neonates. The 100 mg and 25 mg forms are registered in the same countries as the 400 mg: the Baltic states, Russia, Georgia, Kazakhstan and Ukraine. There was a proposal from the WHO to remove Raltegravir 100 mg

from the WHO's list of vital and essential drugs, in order to reduce the number of recommended doses and give priority to a dose of 25 mg. The current WHO recommendations suggest that a dose of 25 mg (chewable tablet) should be preferred. Because of administration challenges presented by the oral granule formulation, after reviewing in-vitro data, WHO recommends crushing and dissolving this tablet in water to give it in the form of a suspension to those children who cannot chew the tablet. Given this recommendation, MSD will not prioritize wide registration of granules formulation.

> Question: Is it possible to use this suspension, obtained from a 25 mg tablet, for treating neonates?
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> Answer of the company representative: There is no such recommendation in the product label for use for the 25 mg tablets, but the WHO endorses the use of the 25 mg tablet as a dispensable.

Question 2. The company's plans for the next 3 years

The company has a good portfolio of drug products in the pipeline. There are plans for future development of the pediatric form of Doravirine. There is a new drug product with a new form of action that can be used as a treatment, and it can also have the potential for prevention and for prolonged forms. This is all preliminary so far, because the studies are still at the early stages. Right now, it is too early to say something about countries, especially about EECA countries.

Question 3. Localization plans in EECA

We believe that the production at the global level is the most cost-effective way. Nevertheless, if a government strongly prioritizes localization, we are ready to discuss with governments that give priority to localization, despite the additional costs this process may entail. We have plans to localize Zepatier and Doravirine in Russia.

> Question: Are you planning to localize them in Russia with R-Pharm as before?
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> Answer of the company representative: At the moment, I cannot provide such information. I believe that it would be helpful if we could organize a separate meeting for Russia within the next 2 or 3 months with the participation of the MSD Russian office, where we can discuss in detail the questions about Russia, including plans for localization.

Question 4. Clinical trials in EECA

We conduct three types of clinical trials (CTs): CTs as part of our clinical development program, investigator-initiated studies and local data generation studies, aimed at obtaining data in a particular market.

From the countries participating in this call, only Russia was included in CTs for Doravirine. In the future, an extensive research program is planned, including Doravirine combinations with a new MK-8591 molecule. Very likely, the program will be held also in Russia, possibly in other EECA countries. At this stage, we cannot say more precisely. We will be able to provide information later when we have it.

There is an investigator-initiated studies program that MSD supports. This procedure can work in any country. A doctor or investigator can submit an application, which will be reviewed by a special committee within our company. At the same time, it is possible to submit applications both for studies that include our company's drugs, and for studies of a treatment cascade and other studies in the field of HIV infection. Such application can be submitted by a doctor or investigator from any country.

> Question: How many countries have participated in such trials from our region?

Answer of the company representative: Unfortunately, we receive very few applications for such trials from countries participating on this call. There was an HIV study in Russia, and one study on hepatitis C which is currently carried out in Kazakhstan.

Regarding the third type of trials, we have an example of such a study in Ukraine, in which patients with HIV infection and diabetes took part. This trial was presented at the conference in Glasgow in 2018. There are trials in Russia involving patients with HIV infection. In Serbia, trials were carried out for patients with hepatitis C.

We conduct local research in different countries of the region, including in Russia on Zepatier.

Question 5. Pricing policy of the company, prices reducing in EECA countries

We do not comment on the strategies of our future pricing. We regularly analyze our prices and try to revise them when a number of factors change: including the demand and changes in treatment protocols, in market dynamics, in other drugs. In addition, we seek to cooperate with all stakeholders: i.e. the procurement agencies, the governments. The priority is given to those who express their commitment and the idea of increasing treatment coverage.

There are examples of price reductions in the region, though. For example, Ukraine, after broad consultations on expanding the treatment program, where a reduction in price was recorded to expand access, as well as negotiations with the participation of Global Fund in the countries of Central Asia.

Question: Do you plan to reduce the prices for Raltegravir in Russia, given the increase in the number of people using the drug, etc.?

Answer of the company representative: Unfortunately, I cannot comment on the situation in Russia. In general, we are ready for such a discussion, and we are ready to consider price reduction, given the changing picture of demand and market dynamics.

Question: In Russia, we have seen a dramatic increase in sales of Raltegravir by $15 million. Has an additional analysis been carried out for the sharp rise in the volume of procurement in Russia? Given such a large order, the price should have already been changed, but this never happened. Why is that?

Answer of the company representative: I repeat, that I cannot comment on the Russian example specifically, especially the question of future pricing. I will try to organize or assist in organizing a meeting between Russian activists and the Russian MSD office to discuss this situation. If we see the desire of the state to increase the volume of procured drug products, then we are ready to properly conduct a dialogue on improving the access to our drug products.

Question 6. Zepatier in Russia: plans to submit the drug to the VED List

We do plan to submit Zepatier to the List of Vital and Essential Drugs. The pricing will be arranged so that the drug was included in this List.

Question: If Kazakhstan does not match both MSD criteria for Raltegravir (neither need, nor demand), is it possible to give the country a voluntary license for the drug in this case?

Answer of the company representative: We have 4 voluntary agreements. We issued four licenses to four companies for Raltegravir 400 mg (I would prefer not to mention the companies' names). None of them brought the drug to the market. They decided that the development costs, obtaining WHO prequalification or preliminary FDA approval expenses would not be justified given the position taken by WHO and the current demand for Raltegravir in countries.

Question: What countries are included in these agreements?

Answer of the company representative: These are low-income countries in sub-Saharan Africa and India. In addition, we had a license issued to the Medicines Patent Pool for all pediatric forms of Raltegravir. None of the companies that received the Patent Pool license brought the drug to the market

Question: Maybe in this case it is better to issue a license to the countries of Central Asia, including Kazakhstan, so that they bring the drug to their markets?

Answer of the company representative: We will work with companies that are ready to be approved by strict regulatory authorities. We want to ensure that products manufactured under our license comply with international quality standards. Therefore, companies will have to guarantee that they will receive WHO prequalification or FDA approval.

Question 7. The voluntary license strategy for Raltegravir 600 mg and elbasvir/grazoprevir

We are open to discussing this issue with major manufacturers of generics. Taking into account the fact that Raltegravir 600 mg and elbasvir/grazoprevir are not included in the WHO recommendations, we do not consider the voluntary license strategy for these drugs to be a viable strategy to enhance access. Especially, given the negative experience of the voluntary license for Raltegravir 400 mg.

Question 8. Voluntary License Strategy for Doravirin

We are still considering this possibility for Doravirine and are negotiating the possibility of issuing a voluntary license. Right now I cannot share any specific information; we will provide it at the next meetings.

Question 9. Gardasil 9 (vaccine against human papillomavirus), registration in the region

Paul Schaper: Unfortunately, this is beyond my scope. I noted this question and will consult with the Vaccine Department. At the next meeting I will answer the question about this drug product.

End of conference call