Minutes of the meeting of the Eurasian Community for Access to Treatment with Macleods

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Company: **Macleods**
Name, title: Mr. Shailesh Pednekar, President-International Business
Name, title: Ms. Rohini Karde, Sr General Manager-Institutional Business

Start of the meeting. Introduction of participants.

Question: Which TB drugs do you plan to register in Azerbaijan?

Answer: In Azerbaijan we tried to work with Agent. Initially, this company undertook to register some of our drugs, because they claimed to produce some products themselves. Recently, the company refused to promote products from our portfolio because they decided to promote only those products that they produce themselves. We are currently looking for a partner in Azerbaijan and we would be grateful if you could share any contacts of reliable local companies that we could work with.

Question from a community representative from Azerbaijan: What difficulties have you encountered in working with this company in Azerbaijan? The thing is that in Azerbaijan the healthcare system works differently. The Ministry of Healthcare does not solve the issues of treatment and does not have access to medical institutions. These issues are handled by the Agency for Management of Territorial Medical Institutions. That is, the Ministry of Healthcare has nothing to do with supplying medicines to medical institutions, and you will have to contact this Agency. Have you encountered any barriers in working with state structures?

Answer: I have no information about barriers in the healthcare system. The company we worked with promotes medicines on the private market (a network of pharmacies). They refused to work with us for registration because they do not participate in public procurement. At the moment in Azerbaijan no TB drugs can be sold in the commercial network. All supplies go through the Global Drug Facility (GDF) or through government tenders. That is why we are asking for your help in finding a local partner who will be interested in our portfolio and will be able to supply drugs to the public sector.

Comment from a representative of the patient community: As far as I know, we have Azerpharm and Zeytun Pharmaceuticals in Azerbaijan, which cooperate with the Ministry of Healthcare. Perhaps these companies will be interested in cooperation.

Answer: Thank you for the information.

Question: As we know, Macleods has been granted a non-exclusive license to manufacture the TB drug pretomanid under the BPaL regimen. The company will commercialize the TB drug in about 140 countries. Is Belarus included in this list? Have you applied for registration of this drug? Is there any information about what price will be offered for public procurement? Do you plan to register rifapentine in Belarus? And if yes, what is the approximate price?

Answer: We do not currently have any operations in Belarus. We have neither an office nor partners in this country. At present, we have no plans for this country either. Since Belarus is part of the EAEU, taking into account all the specifics of this region, we will need to find a local partner. If there is a demand in Belarus for our drugs to enter the market, we are ready to discuss it. Please, identify your needs.

Question: What drugs do you plan to register in Kazakhstan? You planned to start production of bedaquiline in June 2023. Did you manage to fulfill your plans?

Answer: We have an office in Kazakhstan and we plan to register our products. The problem is that now we need to conduct additional research so that we can register our products under the Eurasian registration procedure. This delays the process as we need to collect additional information for the registration dossier, so we will not be able to give you a timeline.

Question: Why do you not take advantage of the opportunity to register drugs under the national procedure? As far as we know, every EAEU country has such an option.

Answer: Colleagues, I will need your help in this matter, because according to our information that we have received from our country partners, it is no longer possible to register drugs under the national procedure in the EAEU countries. As far as we know, this procedure is provided only in Belarus. We also took part in a conference held by the EAEU countries, where it was said that now it is possible to register new products only under the Eurasian procedure. That is, if a product has already been registered, we can re-register it under the national procedure, but if it is a new product, we must register it under the Eurasian procedure.

Comment from a representative of the patient community: As of today, the situation is as follows. The EAEU member countries extended the possibility of

registration under the national procedure by separate governmental resolutions, which were valid until the end of 2023. On December 31, 2023, these Resolutions ceased to be in force. But, for example, in Kyrgyzstan, a draft governmental decree has now been submitted for discussion, which will extend the possibility of using the national registration procedure until December 31, 2024. Taking into account that it will take 2 or 3 months for this decree to be adopted, all pharmaceutical companies will have a short period of time to submit a registration dossier under the national registration procedure. It is important to note that a dossier is considered filed even if it contains any errors. Accordingly, companies simply need to be able to submit the dossier within this period.

Answer: Our consultants tell us that products registered under this scheme can only be in circulation until Dec 2025. Then these products must be re-registered under the Eurasian procedure, otherwise they cannot be used.

Comment from a representative of the patient community: Yes, there is such a peculiarity. However, each country has a so-called national list of essential drugs. If a company registers its product under the national procedure, and this product is on this list, it will not need to be re-registered under the Eurasian procedure.

Answer: Perhaps you can share these legislative acts with us.

Comment from a representative of the patient community: On the ITPC EECA website there is an analysis of the EAEU legislation in Russian, which was published in March this year. Here is the link to the analysis (in Russian): https://itpc-eeca.org/2024/03/19/analiz-izmenenij-v-lekarstvennoj-politike-eaes-i-stran-chlenov-eaes-v-2022-2023-godah/analiz-izmenenij-v-lekarstvennoj-politike-eaes-i-stran-chlenov-eaes-v-2022-2023-gg/

Question: You said that you have no partners in Belarus. We know that several years ago you had an experience of registration of your drug Aluvia (lopinavir/ritonavir) in Belarus, and the drug never appeared on the market. At that time your partner was Ekzon OJSC, which registered the drug in Belarus. What was the problem?

Answer: We spent a lot of effort and money to register the drug in Belarus, and as a result not a single package of the drug was sold. Therefore, we are not considering the Belarus market at the moment, as we, as a commercial organization, do not see any economic potential in it.

Question: Do you plan to register pretomanid and clofazimine in Kyrgyzstan? This company is widely represented in the country's market with first-line TB drugs. But almost all the drugs were registered in 2019-2020, which means that the marketing authorizations will expire in 2024-2025. Will the marketing

authorizations be extended taking into account the EAEU legislation? Are there any plans to apply for registration in the country in case of issuance of a compulsory license for bedaquiline? If yes, what will be the approximate price of the drug?

Answer: As for bedaquiline, taking into account the recent statements by Innovator , we believe that patents may not be concern. We are ready to supply the drug if Kyrgyzstan requests interest in supplying our bedaquiline. We are ready to supply the drug and there are no difficulties for us.

Question: Do you plan to register bedaquiline in Kyrgyzstan?

Answer: Yes, we plan to do so. As I have already said, we want to use the Eurasian registration procedure.

Comment from a representative of the patient community: It will take you two years.

Answer: Yes, we are aware of that.

Comment from a representative of the patient community: At the moment, Kyrgyzstan allocates quite a large amount of money from the state budget for procurement of TB drugs, and the state has the opportunity to procure bedaquiline on its own. We also have a state enterprise Kyrgyzpharmacia, which can conclude contracts for the supply of any drugs without tenders through direct contracts. Would you like to negotiate with them?

Answer: Yes, we are negotiating with them on some of our HIV drugs. I cannot disclose the details, but I can say that we are waiting for them to finalise the contact and contractual conditions us so that we can produce and supply the drugs.

Question: In your opinion, what barriers prevent pharmaceutical companies from producing substances/active substances in Russia?

Answer: This is a complex issue. It is a very interesting market with a fairly well-developed industry of its own. Part of your question is related to the synthesis of the active pharmaceutical ingredient, and why this is not done in Russia. This is quite a complex process, which on the one hand requires a large number of developed production facilities, and on the other hand it requires ingredients and precursors. It is a whole ecosystem that is built around the synthesis of an active pharmaceutical ingredient. On the other hand, we see that this process has already been launched in small quantities and for some drugs the process of synthesizing the active pharmaceutical ingredient is already underway. We assume that in the current situation, taking into account all factors, including sanctions, this process will develop and more will be synthesized.

Question: If you register your drugs under the Eurasian procedure, will you work with the Russian market? Is there any understanding of what the price of the drugs will be?

Answer: Yes, we have such a plan in general, but we will do it through local partners. We are not ready to talk about prices yet, as we are fully focused on registration. We are a bit confused about registration processes, as there was a Eurasian procedure, then national ones. We want to register the drugs first, and then we can talk about prices.

Question: At the moment, the situation looks like that in at least two countries the partners turned out to be unreliable. Have you analyzed the Russian market in order to register drugs under the Eurasian procedure? This market is also ambiguous. Do you have partners in Russia? Through which country are you planning to register drugs under the Eurasian procedure? What is your strategy.

Answer: We plan to register either through Russia, and then in other countries under the mutual recognition procedure, or in Kazakhstan.

Question: You do not have an absolute understanding at the moment? Or will you be filing registration dossiers in two countries?

Answer: We have an office in Kazakhstan, and the original plan was to file everything in Kazakhstan. But now we are preparing dossiers, some of which will be filed for registration in Russia, and the other part in Kazakhstan.

Question: Why was this strategy chosen? Do you want to split your portfolio and not to file everything in Kazakhstan?

Answer: We don't have any specific strategy. Since this is a new process for us, we decided to try to approach it from both sides.

Comment from a representative of the patient community: Please be informed that Russia does not always recognize dossiers filed in other countries, and vice versa, Kazakhstan does not recognize dossiers filed in Russia in all cases. There is some fairly serious opposition there.

Answer: This is a new process for us, so we are prepared for anything.

Question: What TB drugs do you plan to register in Tajikistan? Do you plan to participate in small tenders?

Answer: We supply our drugs to Tajikistan through GDF. We follow what national tenders are announced, but we do not participate in them and do not

supply anything. We want to register our products in Tajikistan. We need to check the information regarding the timing. But we have a plan to register products for both drug-sensitive and drug-resistant TB.

Question: I think the registration process in Tajikistan is quite simple. You can start the registration process through the Pharmacovigilance Agency. We have been trying to reach manufacturers in Tajikistan for many years, but there is no progress in this direction yet.

Answer: In fact, the dossier is almost ready and we expect the drugs to be registered by the end of the year.

Question: Pretomanid was included in the state nomenclature of Ukraine back in 2020. Have you succeeded in public procurement of this drug in Ukraine and, if not, why not? And what can be done, in your opinion, to include it in public procurement (even if it is financed by the Global Fund)? Has your company applied for state registration of pretomanid in Ukraine? If not, when can we expect to enter the Ukrainian market and at what price?

Answer: We have applied for registration of pretomanid at the end of 2023, and we expect the drug to be registered at the end of 2024. At this point, no one has come up to us with an expressed need.

Question: What is your estimate of the number of patients who may need pretomanid and bedaquiline, and do you have a mutual understanding with medical officials in Ukraine?

Answer: We are not currently communicating with medical agencies in Ukraine. We have already submitted a dossier for registration of pretomanid, and we also want to register bedaquiline. As for the need, unfortunately, since all procurement to Ukraine goes through the GDF, we cannot see within these procurements o which specific countries and what volumes of drugs are going to which countries. We do not even know approximately what the need is in each country. We see only the general picture. We cannot see the need in your region as a whole, and governments do not tell us about it. It is difficult for us to estimate the potential size of the market. If we knew what each country needs, it would help us a lot.

Question: You talk about getting orders from the GDF, but these are mostly countries that are procuring drugs from the Global Fund. As you know, the Global Fund is now changing its policy and there is pressure on countries to start procuring more directly from their own budgets. I think it would be useful for you to study the need in countries, because in the future countries will be procuring drugs directly.

Answer: We are always interested in understanding the government's need, but that requires an open tender, or we need to be told directly about the need. We need to be proactively contacted. As far as Ukraine is concerned, we have seen that a large number of tenders have been announced in the past, which we also participated in. But in the last two years the number of these tenders has been obviously decreasing, and the drugs are mainly procured through GDF. We do not understand the need because most countries do not have open tenders.

Comment from a representative of the patient community: In order to assess the capacity of countries to procure TB drugs, if you don't have general data from GDF, you can look at the Global Fund proposals. There is a plan for the next 1–3 years for ordering drugs in each area. If this information is not enough, you can contact the country and they can give you the data. If you give a price lower than the GDF, then you can negotiate with the country in the future.

Answer: Thank you for the information. We are trying to collect information from different sources and we are not looking only at countries' proposals. Right now we are focusing on the data we get from global agencies.

Question: In December 2022, WHO started recommending rifapentine in drug-sensitive tuberculosis (DS-TB) regimens. In January 2023, the DS-TB regimen with rifapentine also appeared in the Ukrainian national protocol. Your company has both a combination drug with rifapentine (isoniazid/rifapentine 300 mg/300 mg) and a mono-drug (rifapentine 300 mg). According to the State Register of Medicinal Products of Ukraine, your company's preparations with rifapentine are not registered in Ukraine. At the same time, a combination drug rifapentine/isoniazid of your production was registered in Ukraine earlier. Do you plan to enter the Ukrainian market with these drugs, if yes, when and at what price?

Answer: Rifapentine is currently in the process of registration. We expect that the drug will be registered in the 4th quarter of 2024. As for the 3HP regimen (isoniazid/rifapentine 300 mg/300 mg for three months), we supplied it to Ukraine through GDF, so you could see the remaining supply of GDF in the country. This supply was not carried out through a national tender.

Question: Perhaps you have data on how to use the combination drug isoniazid/rifapentine for treatment of DS-TB? Or is the drug used solely for prophylaxis?

Answer: The 3HP regimen is used in IPT as a preventive drug for TB, froom what we understand as per latest Expression of Interest (EOI) published by WHO, regimens containing rifapentine may be used to treat TB, but different ones. For example, HPMZ (isoniazid, rifapentine, moxifloxacin and pyrazinamide) during

the active phase and then HPM (isoniazid, rifapentine, moxifloxacin) in the ongoing phase wewill know more in future as guidelines get published.

Question: Is production of rifapentine likely to be disrupted due to increased demand following WHO recommendations that it be used not only for treatment of latent TB infection but also in regimens for treatment of DS-TB?

Answer: We would like to understand the exact increase in demand in terms of numbers. Because we have been manufacturing rifapentine for 3 years, we are able to meet any demand that comes to us now. It is important to understand how much the projected demand will grow. It is not clear at this point how quickly countries will switch from existing rifampicin-based treatment regimens to treatment regimens that contain rifapentine. We expect that this transition will not take place overnight, which means that the growth in need will also be smooth. At the moment we are ready for any increase in demand and we are capable of producing the drug.

Question: Are there any barriers to state registration of drugs in Ukraine?

Answer: We have not encountered any problems with drug registration in Ukraine, except for patent barriers.

Question: Has your company applied for state registration of bedaquiline in Ukraine? If not, when can we expect it to enter the Ukrainian market and at what price? It is worth emphasizing that the Ukrainian market is guaranteed to be open for generic bedaquiline, as Janssen has waived patents for bedaquiline in Ukraine during the court proceedings.

Answer: As we mentioned earlier, there are plans for registration. We expect the dossier to be filed in near future.

Question: Does your company have plans to register new drugs (pretomanid and bedaquiline) in Moldova?

Answer: We will apply for registration of these drugs in Moldova, but much will depend on WHO prequalification. We have already received all the documents. We will send you detailed information on the timing.

Question: Are there any changes in the work of your company's representative office in Ukraine due to the war?

Answer: We are facing the same consequences of the war as other companies. In general, we have representatives in the country and they continue their work. And we will continue to work to make sure that the drugs are available in the country.

Question: In July 2023, the head of GDF announced that your company is one of the licensees of the agreement with Janssen, i.e. has the right to produce and supply generics of bedaquiline. Please, tell us, has production been set up? What are the volumes? Have there been first supplies? Who will be the first recipients in the EECA region?

Answer: Unfortunately, recent tenders have not gone our way , so we don't know the demand yet . We are in the process of synthesizing our own active pharmaceutical ingredient. Once we develop it, we can produce the drug and put it in stock. In future we will be able to go out to tender again. And then may be we will be able to see the volumes.

Question: When do you expect to complete the process of synthesizing your own active pharmaceutical ingredient?

Answer: I think we will have the synthesis of the active pharmaceutical ingredient completed in with in 2024followed by FDF production. And if by that time we receive an inquiry for price quotation, we will keep in mind that we can make quick shipment if we have stock.

Question: Are the prices for the drugs (bedaquiline and pretomanid) expected to decrease? Including taking into account the current price-volume mechanism?

Answer: I can answer you from a strategic point of view. Both of these drugs, compared to other drugs, including those for HIV and hepatitis C, are at an early stage of market entry. All drugs go through several life cycles. And right now pretomanid and bedaquiline have relatively small volumes, and as they grow and the process of synthesizing the active pharmaceutical ingredient and the process of synthesizing the tablet itself is optimized, there will be price changes. And, if we base it on the price trend that other products have had, which is if the demand grows, the volumes increase and the price goes down, then these drugs should not be an exception.

Question: How much are you interested in carrying out the production and supply of pretomanid? The fact is that now TB Alliance has issued licenses to five companies, which have to share the market among themselves. We are concerned about the price plateau, because despite the presence of several manufacturers, the price does not decrease and is approximately the same for all manufacturers.

Answer: I cannot comment in any way on TB Alliance's strategy and their decision to license several manufacturers. I assume that they have a strategy to increase the availability of the drug on the market and they are sticking to it. I think it's too early to talk about price, and when we have large volumes, we'll be able to talk about it more specifically.

Question: As far as we know, Viatris received a license for pretomanid in 2019. Is our information that you did not receive the license until 2022 correct?

Answer: I do not have detailed information about this license. I will need to verify this information.

Question: Does your company have any programs that you are implementing to increase the availability of TB treatment in Eastern Europe and Central Asia?

Answer: Our goal as a generic company is to supply as many drugs as possible to international and national tenders at the lowest possible cost. This is the model we are working on, and it does not imply any additional programs aimed at adherence, etc. Our contribution is that we make cheap and affordable treatments, unlike the originators. As far as I know, historically no generic company has ever worked with communities to support patient programs. That is a different business model.

Question: We have heard that your company approached Otsuka to produce a generic version of delamanid. According to the information we have, Otsuka re-directed you to Viatris for reference samples, which were to come from Ukraine, to conduct a bioequivalence study. Could you tell us how the situation is now? Have negotiations been held?

Answer: We do not have any information regarding the fact that the samples were to come from Ukraine. But the situation is that Otsuka did send us to one of the other generic company for samples. We have contacted them, but response was awaited . As of now, we have not received the samples. But I need to verify this information. And any help in getting samples would be appreciated.

Question: Are you developing any pediatric forms of the drugs, perhaps in partnership with anyone? Are there plans to develop combination forms?

Answer: Some of the information regarding the development of new drugs is confidential because we are working on different drugs and dosages. If we talk about the TB drugs portfolio, we have developments on pediatric forms of drugs that we want to bring to the market. We want to make pediatric forms for all drugs for which it is possible to do so. We always engage with partners such as TB Alliance to develop newer FDC's. As soon as we have more specific information on the fixed-dose combination, we will share it with you in future.

Question: Do you plan to develop pediatric soluble formulations of bedaquiline and pretomanid? And if so, when?

Answer: No, we need to discuss this with the development department.

Question: If doctors from the EECA region order TB drugs from your company to treat patients with extensively drug-resistant TB (XDR-TB), will it be possible to get these drugs, including pretomanid, for compassionate use? The fact is that there are patients who are resistant to bedaquiline, and accordingly, we would like to try combining pretomanid with other drugs to treat XDR-TB patients.

Answer: No, we do not have compassionate use programs. To conclude the meeting, I would like to add that the Eurasian drug registration procedure is quite complex and chaotic. We, as a company, see a very strong need to simplify the registration processes, which will allow us to bring drugs to market faster. We are interested in any dialog, and we are ready to take an active part.

Question: Does Macleods plan to produce combinations with pretomanid?

Answer: This may be the future, currently demand of Pretomanid is what we are looking for.

Question: What are the adverse event data for bedaquiline?

Answer: We are yet to commercialize the product.

Question: How is the safety of the company's drugs monitored?

Answer: We have a global PV department, that monitors safety thru our own office and Partners.

Question: Do you receive reports of adverse events of your drugs? Or about interactions of your drugs with other drugs?

Answer: We make a no of drugs, is there any specific drugs you are interested in then we can check with Medical and PV team.

Question: Which TB drugs have WHO prequalification, when is prequalification expected for the drugs that do not yet have it?

Answer: As a process all TB products go thru WHO PQ process.

Question: How do you work with patient communities, activists and the public in other regions? How do you assess the use of digital health tools in improving management and monitoring of TB treatment?

Answer: We are a generic company and access is our prime objective. Affordable quality generics for all patients in LMIC countries.

Question: Are there partnership programs with other manufacturers?

Answer: No, we work independently as a Generic player.

Wrapping up the meeting.