

**Regional meeting on the access and prices of the ARV drugs in SEE countries**

December 15, 2020

The regional online meeting brought more than 50 clinicians, civil society participants and government representatives from South Eastern European countries and international partners to discuss progress, challenges and opportunities for improved access and pricing of antiretroviral medicines for HIV.

Organized under the Regional #SoS Project funded by the Global Fund, the meeting set the following objectives:

* To share information about country practices and challenges in access to current and future ARVs and other critical medicines for the treatment of HIV, as well as on legal and policy frameworks responsible for access to treatment including pricing, registration, and supply.
* To achieve a regional consensus on the need and potential approaches to reduce prices of ARV drugs within the SEE region.
* To provide input in country-level dialogue on price reduction strategies amongst health authorities, people living with HIV (PLHIV), civil society organizations (CSOs) and procurement agencies on ARV price reduction.

Countries: Bosnia and Herzegovina, Montenegro, North Macedonia, Romania, Serbia, also two observer countries – Albania and Kosovo\*

Final agenda, participant list and materials:

Zipped folder with all meeting materials is available for download

Organizers:

Southern Eastern Europe Regional HIV and TB Community Network (RCN)

Alliance for Public Health

100% Life

Key themes:

**Need for HIV treatment optimisation to cover treatment and prevention gaps**

**South-Eastern Europe (SEE)** **has major gaps in achieving the 90-90-90 UN goals** for HIV diagnosis and care that have been set for 2020. In 2019, only 59% of people diagnosed with HIV were on life-saving antiretroviral therapy (ART) in the selected 6 SEE countries, significantly lower than the global progress of 82%. Additionally, some 25% of people living with HIV are not yet diagnosed and therefore not on treatment in SEE, according to the WHO/Europe representative **Dr Elena Vovc**.

**Optimization of treatments and improved pricing for medicines could create savings.** These savings could fund more people to receive ART, and prevention. The three organizers highlighted this being the premise of the organizing this first meeting focused on optimization of HIV treatment costs. The meeting’s presentations, and discussions explored if they are needed and what options might be relevant for the countries.

**ART optimisation** is defined as harmonization of efforts to accelerate access to simpler, safer, more affordable HIV treatment, according to the Dr Elena Vovc from WHO-Europe*.* The optimisation utilizes new evidence, and builds on several principles such as reduced toxicity, drug interactions, and burden of pills, increased resistance barrier, harmonization for safer use across different age and different populations and lowered cost. Examples of optimization are revisiting treatment regiments, using combined, fixed-dose combination pills instead of several medications, using the streamlined regimens and corresponding monitoring and care efforts instead of highly individualized treatments. Optimisation is reflected in the WHO guidelines. For example, currently WHO recommends the use of dolutegravir (DTG), a safe, highly-effective, newer medicine with a high resistance barrier for the first treatment line. For the alternative first-line regimen it still recommends a combination that includes efavirenz (EFV), however, EFV 400 instead of EFV 600 as the first has a comparable efficacy and safety profile, however, induces fewer treatment-related adverse events. EFV 400, which contains less active pharmaceutical ingredient, is also cheaper. WHO will release its consolidated HIV treatment guidelines in early 2021 and is available to support the countries. A Ukrainian case of optimization process and impact was later presented later by Dr Hetman from Public Health Center of the Ministry of Health of Ukraine.

Other measures to reduce the cost, without compromising the quality, are

* utilizing international quality assurance during the **registration** for example, referencing and allowing simplified procedure for medicines and manufacturers that underwent the [WHO prequalification of medicines](https://extranet.who.int/pqweb/) or that has been registered by stringent agencies like European Medicines Agency (EMA) or U.S. Food and Drug Administration (FDA),
* utilization of **competition among different manufacturers** for improved pricing and **switching to generic substitutes** as the UK did where patents allow, or
* moving to more effective **procurement** mechanisms.

**Pooling (pooled) procurement**, also called as bulk or group purchasing, is pooling resources and negotiation power when “purchasing is done by one procurement office on behalf of a group of facilities, health systems of countries” (WHO, 2016). As the Global Fund’s representative explained, there are different methods of pooled procurement, ranging from pooled negotiations used in the BeNeLux countries (i.e., negotiations are joint, however, the end result of procurement is done nationally) to pooled procurement, for example, for vaccines in the Baltic States. Utilizing those methods might require changing procurement-related legislation, on one hand, and, on the other, optimizing ART, so that needs are more aligned. South-Eastern Europe is exploring pooled procurement for vaccines. For HIV medications, no pooled procurement is used in the European region, unlike Latin America, according to the WHO representative, however, there is a use of international procurement, i.e., buying of specific medicines from international procurement agencies like UNICEF or UNDP or *wambo* platform hosted by the Global Fund. Albania and Kosovo are procuring ARVs through UNICEF, while Georgia uses *wambo* system for purchasing ARVs from its domestic resources based on its successful experience of the use of this system for the Global Fund funded medicines. Countries might choose different procurement methods for different antiretroviral medicines, based on the market analysis. For example, Kazakhstan uses UNICEF procurement for certain ARVs, is expected to benefit from the Medicine Patent Pool’s voluntary license of highly potent and effective dolutegravir (DTG), which will enable to get generics into the market and lower it cost and purchases certain ARVs from domestic manufacturers. It remained unanswered. The participants were promised by the WHO and the Global Fund to share additional materials on pooled and international procurement modalities.

**Situation in SEE region and countries**

**ARV pricing in the Balkans** *(ppt by Ms. Zoia Zamikhovska, 100% LIfe)*

**ARV pricing is high and greatly differs across SEE countries**, based on the 100% Life desk-review assessment’s data presented by Zoia Zamikhovska. The difference between the lowest and the highest price paid in the four SEE countries with data could reach 10 times and more for some medicines, i.e., in case of the combination of TDF/FTC it ranges between 228 EUR per patient per year in North Macedonia and 2520 in Serbia. North Macedonia has best prices in most cases across the four countries with data, however, even its prices are significantly higher nearly for all medicines in comparison with Kazakhstan (an upper-middle income country), notably nearly 5 times higher for DTG.

**Low use of generics including because of registration-related barriers, procurement lists and procedures and their high pricing contribute to high pricing**. The regional assessment by the 100% Life provided details of the use of flexibilities in some countries but not others to ensure increased competition and therefore better pricing of state procured medicines. Different countries have different positive practices, outlined in Ms. Zamikhovska’s presentation.

Romania has a great presence of generics in the country, while in Bosnia and Herzegovina generics are registered just for one specific ARV and in Montenegro has only 4 out of 11 medicines or their combinations registered and no generics.

Simplified registration of medicines, using international quality assurance mechanisms, is best developed in North Macedonia. No country allows international procurement. Most countries use centralized procurement.

**North Macedonia** *(PPT by Andrej Senih, Stronger Together)*

The annual average cost of combination regimens is EUR 1’900 per patient. Around 51% of patients are on the cheapest treatment regimen of TDF/FTC/EFV, costing EUR 328 per year. The WHO- and EACS-preferred regimen containing DTG costs EUR 5000 annually and is therefore prescribed only to 3% of patients. Hence DTG require concentrated price reduction efforts. DTG is patented, therefore Macedonian activists start advocacy for a patent exemption for this medicine and DTG-based fixed-dose combinations.

ARVs are funded by the state budget from the annually approved HIV programme. Its budgeting is not based on the number of patients and has not increased, though the number of patients increased by 50% in the last 5 years. Some medicines procured that are not recommended by WHO and EACS but are used to fit the allocated budget for treatment. Optimisation of treatment regimens is needed.

Non-registered medicines can participate in tenders and can follow a simplified procedure of registration of those medicines that have WHO prequalification or registration in the EU or any of its member states or by other stringent authorities. However, the registered medicines are preferred. Most generics are from the EU, their prices are relatively high, e.g. 5 times higher than global prices, and could be better regulated by state for great reductions. Furthermore, the country needs to find how to incentivize registration of additional generics.

North Macedonia has a good collaboration between infectious disease clinic that leads the ARV procurement and the patient association. In the last 7 years, this collaboration gave greater strategizing of the formulations of tenders and more reliable, predictable and improved treatment options.

**Bosnia and Herzegovina** (*PPT by Dr Siniša Skočibušić*)

Fragmented and complex health system, governance and procurement result in the uneven availability and cost of medicines within the country. Sarajevo has 13 medicines in comparison only with 5 in Banja Luka and 6 in Tuzla. In 2020, a joint task force with delegated experts from the two entities of the country was established to update the national HIV treatment guidelines, which have not been revised since 2013. Testing for HIV is insufficient in the country; most people are diagnosed late. Currently, just 25% of people living with HIV receive the first line ART. Brands dominate the medicines procured. The price is an issue. There has been a major increase of nearly 25% in the cost paid for medicines between 2016 and 2017 by the Health Insurance and Reinsurance Institute of Federation of Bosnia and Herzegovina, while the number of patients has remained unchanged. This increase was the result of the switch of patients to newer medicines and changes in schemes used. Three singular or compound medicines– raltegravir (RAL), rilpivirine+tenofovir disoproxil fumarate+emtricitabine and efavirenz – all procured from originator manufacturers, contribute to 2/3 of the ARV cost paid by the Health Insurance in the Federation of Bosnia and Herzegovina. Notably, the set of medicines for procurement are decided not by the Institute but by the Ministry of Health and clinics. More than one third of the expenditure for ARVs from the Insurance Fund of the Republic Srpska is spent for one combination of medicines, tenofovir disiproxil fumarate+emtricitabine.

**Montenegro** (*PPT by Dr Brankica Dupanovic*)

Currently, 302 people living with HIV are enrolled in ART and 96% of them achieve viral suppression, indicating good treatment adherence. HIV care is centralized in one infectious disease hospital (which is currently turned to the COVID-19 center). The national guidelines approved utilize the WHO and EACS guidance. The country uses individualized treatment approach with limitations, as fewer number of drugs and monitoring tools are available. The Health Insurance Fund finances ARVs. The pricing of specific medicines ranges between EUR 54.99 per month (tenofovir+emtrocibine) to more than EUR 532 for DTG per month. All medicines procured are brands. Newer medicines need to be put on the list of reimbursed medicines. There is a need to increase the interest of pharmaceutical companies to deliver new medicines. Currently 5 patients are on unlisted, unregistered treatments, the approval of the use of such medicines is done by the Ministry of Health, on the recommendation of the clinic for infectious diseases and the National Insurance Fund.

**Romania** (*PPT by Nicoleta Dascalu prepared by ARAS, Accept, RAA and UNOPA*)

Significant improvement in HIV management and modern medications have been observed in the last 6 years. Romania does not have legally binding guidelines but follows the EACS ART guidance. The country’s report called ‘[The Romanian HIV National Program: Description of a Maze](https://health-observatory.ro/wp-content/uploads/2019/11/The-Romanian-HIV-National-Program_Description-of-a-Maze_Policy-Report.pdf)’ outlines the complex approaches to funding and organizing the program including the procurement of ARVs. ARV financing and procurement is taking place from two sources – centrally from the national HIV program and by hospitals that receive funding from this national program and can procure medicines. The system has not faced major stockouts in the last year, however from time to time there are stockouts in some regions. Framework agreements are signed centrally with some suppliers for three years. External reference pricing is used in the country to define prices for brand medicines and is calculated as the lowest available price in the basket of the selected 12 countries within the European Union. Among the 116 pharmaceutical products available in Romania for HIV treatment, only 5 have been identified as having a slightly higher price in Romania than in the other European Union countries in 2019. Additionally, the generic prices are shaped by an internal reference pricing - it has to be not more than 65% of the brand medicine price, however, this is set only once, normally when approving the price for the first generic medicine on the market.

NGOs see that more prices are negotiated behind closed door and not public. However, a question remains how NGOs can engage in monitoring and influencing in practices. Ms Zamikhovska explained that a similar challenge is currently also discussed in Kazakhstan and the options explored are getting a legal advice what is feasible and explore if transparency of pricing and the public need to know outweighs the need for the protection of negotiation results. There might be some precedents by the EU Court of Justice that could be used.

**Strategies to improve pricing and access to ART**

**Serbia** (*PPT by Goran Radisavljević, TOC & Maja Stosic*)

Pricing is the issue, particularly for branded ARVs. The country team implements a strategy with the three objectives: (1) reduction of brand ARVs prices, (2) analysis of procurement practice and exploring feasibility and start a dialogue for better prices; and (3) the optimization of ART schemes. The country team conducted assessments and a series of consultations. They explored feasibility of options including generic substitution among different stakeholder groups. The team assessed several scenarios of potential savings and optimization of the HIV budget: pooled procurement of ARVs (estimated savings of 25% of the current budget); international procurement using UNICEF pricing (savings of more than 1 million USD); optimization of ARV scheme in line with the EACS and WHO guidelines (12% savings). The analysis showed that if the annual reduction of medicine budget reached 20%, the amount of funds for prevention could be doubled in the next two years. Price reduction efforts are not new in the country and are already used in other areas, like cancer and TB.

The work and the policy brief, produced based on the assessments, have already received a positive feedback from the Office of Prime Minister.

The country team has not been successful to engage clinicians and some patient groups; attitudes towards generics were that their ingredients are not good and therefore not acceptable for HIV treatment. Clinicians have a great influence on patients and therefore their attitudes might extend to patients. The team plans to intensify capacity building among clinicians and bring experiences from other countries to facilitate better collaboration with clinicians. Developing the national ART guideline, as planned under objective (3) will also help. Availability of HIV clinicians to engage might have been restricted by the COVID-19 response.

**Generics – myths vs. reality** (*PPT by Dr Alex Schneider, PhD in chemistry*)

Germany, the country with the highest state budget for healthcare, has greatly increased the use of generics in 2005-2015. However, back in 2000s the country faced negative attitudes towards generics from clinicians and other groups. The authorities addressed those attitudes through the awareness campaign among clinicians, NGOs and the public, by explaining what originators and generics mean.

Active pharmaceutical ingredients (API) are the chemical compounds produced in chemical factories. There are no generic or brand APIs. APIs together with excipients are formed into medicines in pharmaceutical factories and in those factories, depending on who owns them, become brand medicines or generic medicines. However, generic and brand medicines use APIs produced in the same factors, for example, in case of lopinavir, APIs for generic and brand medicines are produced in three factories in India and one factory in China. Side-effects from medicines mainly come from APIs, not from excipients which are non-active ingredients like sugar or celluloses, or impurities. If one experiences side effects, the action of medicine will not change if the person is switched from generic to a brand medicine or vice versa. Sergii Dmitriiev from 100% Life shared his personal experience that he has not experienced any change after he was switched from branded Truvada to generic version during the Ukrainian treatment optimization processes.

Manufacturing costs for medicines can be easily estimated based on API costs, e.g., Truvada production costs is 5.3-6 USD per package, while they sell often for 50 EUR. The high margin of profit could be used for advocacy work and negotiations for price reduction.

Dr Skočibušić highlighted the need for balancing the interests and investment in innovation of new medicines and making medicines affordable. The price of originators is high because of the research and development (R&D) costs, which might reach as high as 1 billion USD for developing one successful medicine. Therefore, the monopoly of originators in the market is allowed and during that monopoly period the brand companies include the innovation costs in the price. However, as Dr Schneider pointed after 10 years they recuperate the investments in R&D (or as in case of some medicines, their price paid for innovation labs that discover medicines, as Mr Dmitriiev added). There is need for transparency pricing of both brand and generic medicines and the costs of R&D. It is important to fund research. In case of antibiotics, which are less profitable area and do not imply long-term use, there is a lack of interest in creating new antibiotics, therefore the scientific community is looking for funds for clinical trials with the vision of making them available without patents, as generics.

Mr Senih commented that generic prices also require intervention and advocacy. Tenofovir/emtricitabine costs 300 EUR/month a package in South-Eastern Europe despite becoming off-patent 2-3 years ago, i.e., it has seen only 25% reduction from the previous price. More generic presence in the market is needed for a greater competition and price reduction. When it comes to prejudice and myths around the generics, it is important to remind that most medicines in our markets are generics. Some generics come from PLIVA and KRKA, the well-known manufacturers in the SEE countries.

Efficacy and safety of medicines of U.S. FDA, EMA, WHO prequalification – are all guarantee efficacy and safety at the point of procurement. Once medicines are used in the country, countries should conduct pharmacovigilance (reporting of adverse, side effects by doctors and patients) to authorities and manufacturers as part of quality assurance mechanisms of both brands and generics present in the market.

**Ukraine case: treatment optimization in 2017-2020** *(PPT Larysa Hetman)*

Ukraine underwent optimisation of their large HIV treatment, moving away from highly individualized approach that used multiple combinations of HIV medications to more public health approach. They used newer regimens recommended for the first line in the WHO guidelines offering newer treatments, notably expanding the use of DTG. At the same time, Ukraine worked on reducing of prices for all HIV medicines and in particular those that are preferred treatment and has high impact on the general ARV budget. Particular price reductions have been achieved for first two treatment lines. For example, the annual cost of DTG-based regimen TFC/FTC + DTG was cut from US$ 1854 in 2016 to US$ 121 in 2018.

The process has been complex with its challenges. To plan the optimization, they engaged assistance from WHO and its experts such as Jens Lundgen from the Copenhagen University and WHO Collaborative Center for HIV Care. Significant efforts of the optimization process were extensive consultations, education and awareness raising among clinicians and patients. The partnership of the Ukrainian Public Health Center, patient community from the 100% Life and external expertise from the international organizations and donors were critical both for changes in clinical regiments and price reduction. There several results of the optimization seen. The forecast and procurement of medicines including planning budgets and medicines for further scale-up has become significantly easier. Treatment initiation has become faster (56% initiated ART on the day of diagnosis) and simplified opening possibilities for engaging primary care (family doctors) in treatment provision. More patients are on fixed-dose combinations, i.e., combined pills instead of separate pill cocktails. Because also of the major savings in medicine procurement, the country manages to take over ARV funding from international donors, scale up ART and free funds for domestic support for HIV prevention. Challenges remain nevertheless and should be considered by other countries planning similar processes. For one, planning scale up of ART as part of optimisation means that more people need to be diagnosed and those efforts should be intensified.

Dr Hetman highlighted the critical role of the patient community and civil society, particularly their leadership in the price reduction. It was important to work with the patient community that the optimization is the right direction for the patients and the country.

**Patient community and civil society role and tools: Ukraine and Eastern Europe** (*PPT Sergii Dmytriiev*)

Several tools are used by patient communities in Eastern Europe and Central Asia. At international level those include:

* Medicine Patent Pool, following the advocacy issued several voluntary licenses for Ukraine including for DTG; while traditionally it issues such voluntary licenses from patent-holders to low-income and lower-middle income countries, more recently a precedent was achieved and MPP issued a license for upper-middle income countries in Eastern Europe and Central Asia
* Engaging with UNICEF and UNDP in procuring medicines in the market has enabled getting significant reduction in prices for medicines or for fixed-dose combinations
* ITPC global is a global coalition of activists for better access to treatment. Engaging there helped to highlight the issues faced by the region in the global HIV advocacy and its dialogue and advocacy with brand, generic companies and international development partners. It also helps to gather intelligence about prices in other countries and practices of pharmaceutical companies
* WHO has been important partner for expert advice to countries and patient community on treatment optimization and efficacy of ARVs

Through the partnership with the public sector, patient community managed to become part of expert working groups that discuss plans of scale of ART, participation in shaping the forecast and needs defined for procurement and watchdogging the implementation of the procurement process.

The third area is the HIV-positive patient community and civil society work to increase the competition in the market. The organizations led by people living with HIV, like 100% Life, directly interact with representatives of brand and generic producers to encourage and support them to come to the Ukrainian and other Eastern European and Central Asian markets, to access information about preliminary prices possible for Ukraine and to push for better prices for the countries.

**Way forward – in countries and at the regional level**

The three organizers are ready to collaborate with the countries and support them under the Regional #SoS Project, seeing this as the first meeting for generating and inspiring ideas. Their commitment is to the five countries of the Project – Bosnia and Herzegovina, Montenegro, North Macedonia, Romania and Serbia, and potential regional activities. As a follow-up, the organizers will hold the second meeting to continue the discussion in February 2021. The SEE Regional Community Network will provide a platform to exchange information about availability, pricing and other information about HIV treatments in a private and confidential way. The 100% Life is ready to support the shaping of the ideas with their expertise as needed. The Alliance for Public Health, the manager of the SoS Project, plans to seek for the continued support for the Global Fund beyond 2021 and would be open for collaboration with the countries on these issues beyond 2021.

The participants from the following countries confirmed their readiness to engage in the next steps with national planning and advocacy and their interest in the next meeting: Bosnia and Herzegovina, Montenegro, North Macedonia and Serbia. Romanian participants would come back, after consulting with the national partner of the SoS Project in the country by 25 December. The countries interested in the collaboration will submit one-page document by January 10 with preliminary ideas for the context, the focus of potential work and technical assistance needs for 2021. This could be also used for planning regional-level activities, defining technical assistance needs and also discussing potential collaboration with such partners as WHO/Europe.

Below are ideas shared by the participants for moving forward:

* Montenegro would be interested in exploring pooled procurement in the region.
* The preliminary plans for North Macedonia include engaging in the formulation of the procurement tenders, encouraging more generic manufacturers to participate in tenders and getting patent exception for DTG. In mid-term, they might explore if the state regulations for setting the prices of generic medicines could be improved. Civil society would be interested in closer collaboration with state procurement agency how to frame tenders in a more strategic ways and explore how to improve the law on public procurement. The ideas are to be discussed with the participants from North Macedonia from the Ministry of Health, Health Insurance Agency and the Clinic of Infectious Diseases.
* Bosnia and Herzegovina will continue working on updating the national HIV treatment guidelines and plans to reduce disparities in availability of ARVs in different cities and entities. Technical assistance might be needed on some issues that are new, for example, if to work on shaping the terms of reference of tenders. Since most countries are accessing the European Union, it is also suggested to consider advocacy for simplified registration of medicines registered by the EU medicines agency, EMA. Furthermore, the country is interested in improving testing.
* The Albania representative representing Association of persons living with the disease, encouraged to collect information on medicines used and their price in all the countries, also adherence with the WHO guidelines. It could help national advocacy and address the very diverse regimens used. A study at the regional level could be helpful not just to expose on epidemiological issues, ARV access, the HIV care cascade but also the impact of COVID-19 in the region including on people living with HIV. Further discussions on generics and their impact on the cost for HIV treatment but also on patients. Albania, which like Kosovo are not part of the SoS Project, would be interested in joining the effort and engaging doctors and service providers in the next phases.
* Serbia will continue discussions with the office of the Prime Minister. In the next phase, they plan the new national guidelines and plan education for clinicians and patients (who are not yet aligned with the ongoing advocacy).
* The participants recommended that in the next steps it is important to engage the Health Insurance Funds who hold and shape funds. There is a challenge in some countries and entities, like the Republic Srpska, to have activists from amongst people living with HIV who could engage in the processes.
* Joint work on advocacy for good pricing for medications for PrEP could be an area of shared interests.