Joint meeting EU Directors for Pharmaceutical Policy & Pharmaceutical Committee
8 and 9 July 2021
Online

SUMMARY RECORD

The meeting was co-organised and co-chaired by the Slovenian Presidency of the Council of the EU and the European Commission via video conference and was attended by more than 110 representatives from the Commission, 26 EU Member States, Norway, Iceland, the European Medicines Agency (EMA) Council of Europe (European Directorate for the Quality of Medicines), as well as WHO Europe and invited renowned international experts. In advance of the meeting the participants received two Policy briefs prepared with cooperation and in support of the Slovenian Presidency, namely Improving access to essential antibiotics and Repurposing of medicines in oncology – the underrated champion of sustainable innovation.

Day 1
Thursday, 8 July 2021

1. Welcome and introduction

Mr. Franc Vindišar, State Secretary, Ministry of Health of the Republic of Slovenia opened the meeting for the Slovenian Presidency of the Council of the EU. From the Commission's side Dr. Andrzej Rys, Director - Health systems, medical products and innovation, DG SANTE addressed the participants.

The two speakers stressed the importance of availability and access to medicines as a priority including the issues of antimicrobial resistance and the repurposing of old and generic medicines in oncology. Solutions can be explored in the context of a strong EU Health Union, learning from the lessons of COVID-19 and design new tools through the pharmaceutical strategy and the creation of the Health Emergency preparedness and Response Authority (HERA). The conclusions of the meeting will be presented to EU health ministers during their informal meeting in October and will feed into the Slovenian presidency Council conclusions. The Commission recognised the usefulness of the format of joint meeting for Directors of pharmaceutical policy and the Pharmaceutical Committee to focus on priority topics in a presidency.

INNOVATION, ACCESS AND AVAILABILITY OF ANTIMICROBIALS IN THE EU

2. HERA – State of play and interlink with antimicrobials

The European Commission presented the background, mission and objective of HERA including the actions under the HERA incubator. The presentation focused on the interlink between HERA and antimicrobial resistance (AMR) both in terms of technological review,

horizon scanning and development of antimicrobials as well as stockpiling of antimicrobials as countermeasures.

IMPROVING THE USE AND AVAILABILITY OF ANTIMICROBIALS AND BOOSTING ANTIMICROBIALS DEVELOPMENT IN THE EU

3. Information from the European Commission on the piloting of innovative approaches to EU R&D and public procurement for antimicrobials; and on the outcome of the survey on the restriction and optimisation of antimicrobials usage

The Commission (DG SANTE and RTD) presented the outcome of the EC questionnaire on the optimisation and restricted use of antimicrobials in humans and a pilot on the innovative approaches to EU R&D and public procurement for antimicrobials and their alternatives, notably through the Horizon Europe work programme on Health. The presentation examined the possibility for measures on prudent use (prescription-only status, dispensing rules and package sizes), the availability of current 'push' incentives as well as the development of appropriate 'pull' incentives as a feasible option that combines EU support for late stage development of antimicrobials and circumvents the current market failures.

4. Information from France - EU-funded project: Ensure the availability of antibiotics in human and veterinary medicine while preserving the environment

The French Ministry for Solidarity and Health presentation focused on an EU technical support instrument, a three-year project, co-funded by the EU and the World Health Organization, that started in November 2020. Its aim is to ensure the availability of off-patent antibiotics in France (in humans and animals, while taking into account the environment) by identifying and implementing effective countermeasures.

IMPROVING ACCESS TO ESSENTIAL ANTIBIOTICS WITH EU SOLUTIONS

5. Presentation of the Policy brief: Improving access to essential antibiotics

Dr. Christine Årdal from the Norwegian institute of public health presented the Joint Action Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI). The presentation started with the progress made in the area of antimicrobials including in the veterinary sector. Progress is seen both for innovation in the field as well as prudent use. This is possible due to national actions plans, new EU veterinary rules and through programmes like the Global Antibiotic Research and Development Partnership and Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator. Yet there are still many challenges, including fragile access to essential antibiotics.

The presentation focused on the presentation of a 'pull' incentive proposal for antibiotic procurement in the EU to address the persisting challenges of access and delayed availability of antibiotics. The proposal is designed on the successful example of a recent Swedish pilot. The proposal at EU level would essentially be an EU Joint tender. However, unlike the joint tenders seen for vaccines, this one would not be based on consumption but would be based on receiving an access right to antimicrobials, in exchange participating Member States would offer manufacturers of antimicrobials a guaranteed annual revenue for antimicrobials of interest. This way it is possible to de-link price from units bought. The presentation also analysed other pull incentives such as transferable exclusivity vouchers that could boost

antibiotics' innovation, however, at an extremely high cost and with little guarantee of access, and patent extensions assessed as ineffective due to stable low sales.

During the discussion all participants shared the importance of access and availability to antimicrobials and agreed that this is an issue of priority both in terms of stimulating innovation as well as finding ways for prudent use and dealing with the market failures. It was noted that end-to-end action, possibly with global characteristics and in line with the one health principle, to tackle this silent pandemic is overdue. It was recognised that it is important to build on and benefit from knowledge and collaboration developed so far. The Pharmaceutical Strategy for Europe, Europe's Beating Cancer Plan, the announced HERA and the European Health Data Space offer the opportunity for common actions at EU level in response to public health needs.

Member States were mostly supportive of a common action or pilot on antimicrobial procurement which has the de-linkage characteristics presented by EU-JAMRAI. It was suggested that such a project could be led by the European Commission , but must be voluntary for Member State and industry involvement in order to respect the clear division of competences between Member States and the Union. The possibility of extending this model to participation beyond the EU as part of a global actions was also mentioned. In any case the model needs to be further elaborated to clarify its implications on the market and the costs it would incur for public finances.

It was also discussed whether the development of new essential antibiotics could be incentivised by a regulatory approach comparable to privileged treatment of Orphan Drugs at Union level.

Some Member States supported the need for reshoring production of antibiotics and for EU stockpiling as some of the possible countermeasures to be further explored, also in the context of the potential future role of HERA which remains to be clarified in autumn.

Even though public production or not-for profit production could be examined as options most Member States stressed the need to ensure the involvement of the private sector in the process. At the same time there needs to be appropriate coordination of all actions in the area both in terms of incentives and procurement while taking into account the market effects of any public measures and ensuring stewardship, a cooperation with the veterinary sector and having due regard to the environmental impact of antibiotics.

The opportunity brought by the pharmaceutical strategy and the revision of the general EU pharmaceutical legislation is an opportunity to revise the system of incentives for medicines. Some delegations supported the need for AMR specific incentives while others stressed the importance for incentives to be general, i.e. covering all medicines without making specific exceptions for antibiotics. The need to examine bacteriophage therapies; to take into account children-specific formulations; and, availability of those products were also mentioned.

The Commission confirmed the importance of these discussions in the development of the options in the revision of the legislation. It mentioned that this discussion follows a series of thematic workshops on different areas of priority and recalled the revision process which includes a public consultation on the matter in the autumn as well as future meetings including in the pharmaceutical committee.

Day 2
Friday, 9 July 2021

REPURPOSING OF GENERIC AND/OR OLDER MEDICINES IN ONCOLOGY

1. Repurposing of medicines – The hidden champion of sustainable innovation

DG SANTE presented the opportunities and challenges regarding repurposing in the EU. It stressed that repurposing is the hidden champion for innovation with potential in savings and in research. It made the links to the current regulatory incentives for innovation in the EU and outlined the work conducted on repurposing in the context of the expert group on Safe and Timely Access to Medicines for Patients (STAMP) which led to a pilot project, presented by Spain. The presentation touched on relevant programmes and projects such as the Strengthening Training of Academia in Regulatory Science (STARS) and the project Exscalate4Cov which use of supercomputing. Finally, the presentation covered the future funding possibilities through Horizon Europe and EU4Health and outlined the role for repurposing within Europe's beating cancer plan and the pharmaceutical strategy.

2. Repurposing drugs in oncology

The Anticancer Fund explained the rise of repurposing in science and political focus. The presentation analysed how both hard repurposing (using a medicinal product in another therapeutic area) and soft repurposing (within the same therapeutic area), e.g. one cancer to another cancer, can be achieved through the existing and future policy tools in Europe's beating cancer plan and other EU initiatives such as the ones foreseen in the context of STAMP. The presentation drew from lessons learned from COVID-19 which showed that large well designed clinical studies, including platform trials, are important to validate research results. It also presented the regulatory challenges and suggested to strengthen the role of the European Medicines Agency (EMA) as a regulator that could advise companies to expand a medicine label noting however that this cannot be imposed currently as an obligation to a marketing authorisation holder. Finally, the presentation highlighted the practice of off-label use (especially for paediatrics), which is not regulated at EU level, concluding that a European solution through regulatory review and broader role of EMA and an EU-wide health technology assessment (HTA) as well as public investment in infrastructure for multi-arm trials in clinical assessment of off-label use could be the building blocks to support repurposing in the EU.

3. Framework to support not-for-profit organisations and academia (institutions and individuals) in drug repurposing by STAMP

Spain started its presentation by making the distinction between repurposing led by the marketing authorisation holder (MAH) of the medicine in question versus that led by another actor. The latter case poses administrative difficulties in terms of leading to a line extension or a variation to the product and making the new indication available to patients. This challenge contributes to off-label use in EU which can lead to problems down the line such as access issues due to withdrawal of the medicine from the market and complex responsibility issues. EU regulators in STAMP established a multi-stakeholder Repurposing Observatory Group that designed a pilot for repurposing of medicines. This pilot supports not-for-profit stakeholders,

termed Champion (e.g. academic organisations and not-for profit organisations) through the facilitation of scientific advice at regulatory level aiming at supporting evidence generation and interaction with MAHs. The aim is that research conducted by organisations other than the MAH could lead to a variation or extension of the marketing authorisation with a new approved indication. After a slight delay due to COVID-19 it is expected that the pilot will be ready to launch before the end of the year and will have taken on board valuable lessons from the pandemic.

REPURPOSING OF MEDICINES – FUTURE SOLUTIONS

4. Presentation of the Policy brief: Repurposing of medicines in oncology

Dr. Sarah Garner from the World Health Organisation EURO analysed the rationale, the opportunities/ and the risks in terms of cost/barriers mentioning that development pathways need to think about HTA and payers as well to achieve access to the repurposed medicine. The presentation stressed the need for large phase II studies and analysed the financial and regulatory barriers. Potential solutions include the use of real world evidence and early involvement of payers and HTA authorities. It was noted that regulatory simplification and assistance is key to achieve commercially repurposed products and suggested the EU should consider establishing a 'list of priority indications' which represent unmet medical needs which can be supported through funding, public-private partnerships and regulatory assistance. The role of the Europe's beating cancer plan and the pharmaceutical strategy in this respect was also mentioned.

5. Artificial intelligence for drug repurposing

Dr. Marinka Žitnik, Assistant Professor of Biomedical Informatics, Harvard Medical School presented the possibilities brought by artificial intelligence (AI) in the area of repurposing including in-silico approaches. New medical instruments in pharmaceutical research will be virtual ones such as modern AI and advanced computing. The mechanism with which AI helps discover drug disease relationships through protein pairing and interactions was presented. The presenter stressed the importance of good datasets and meaningful definitions of therapeutic tasks. Examples of drug repurposing for which algorithms rank their relevance to represent promising therapeutic opportunities were presented. It also noted the activities of AI repurposing for emerging diseases (e.g. COVID-19). The presentation finished with the future outlook which will allow not just ranking but to engage with interactive AI systems which will allow researchers to ask questions as input to algorithms and receive replies and clarifications. Such iterative interactive models on efficacy and safety research that can be used to understand causal sense in treatment mechanism and better predict drug combinations in poly therapy settings and help avoid unexpected adverse drug interactions as well as potential beneficial effects of drug interactions. Such techniques could also help predict drug effects on special population groups.

During the discussion the Commission mentioned that given the pharmaceutical strategy, this is the time to consider all possibilities both legislative (revision of general pharmaceutical acts) and non-legislative ones.

Most interventions supported a centralised coordination at EU level for repurposing although more detail is needed on how this would work. Some delegations supported the idea of establishing a 'priority list' of target indications for repurposing, however discussion showed that this is not without disadvantages as it would potentially draw research to only the indication appearing on the list and achieving such a list would be challenging. There was broad support for exchange of best practices (the French model was mentioned as an example).

It was stressed that through the current system it is not possible to ask that a marketing authorisation holder apply for a variation even if the research is there to support that and that care was needed when considering commercial and non-commercial products. The level of evidence must remain the same. A MAH has obligations which might be difficult for non-commercial organisation to take on. The importance of involvement of regulatory bodies along for the life-cycle was noted.

Some delegations supported the use of differentiated labelling for repurposed medicines. Other ideas were to introduce monographs for repurposing off-patent medicines similar to monographs for herbals. Another idea was the use of a clause similar to that under Article 126a of Directive 2001/83/EC for companies willing to take on an indication or to consider regulatory procedures specific for repurposing in the context of legislation.

Delegations supported the planned pilot for the interaction of not-for-profit organisations with regulators and MAHs and mentioned that any future system should take into account the need for robust scientific advice, it should be administratively simple and use existing possibilities in terms of data sharing (European Health Data space, SPOR system (substances, products, organisations and referentials) etc.) as far as possible. Finally, the need for repurposing in paediatric indications was stressed as these products are frequently used off-label.