WHO/Europe and ECDC intensify collaboration on infectious diseases and health emergencies

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Dr Zsuzsanna Jakab, WHO Regional Director for Europe, and Dr Andrea Ammon, Director of the European Centre for Disease Prevention and Control (ECDC), met at the WHO Regional Office in Copenhagen, where they expressed their commitment to strengthen collaboration on infectious diseases and disease outbreaks by establishing operational guidelines on collaborative actions. This will support European countries in reaching the sustainable development goals through addressing communicable diseases and antimicrobial resistance and strengthening immunisation.

WHO/Europe and ECDC have been collaborating on public health development in Europe via a memorandum of understanding (2005) and an administrative agreement (2011), focusing on communicable diseases surveillance, prevention and control, risk assessment and communication, health emergencies and the use of International Health Regulations to prevent and respond to health threats. A joint Coordination Group of WHO/Europe and ECDC has been set up, with annual joint activity plans, information sharing and regular interaction by staff in activity implementation.

EMA: DEFECT WITH BUCCOLAM PLASTIC SYRINGES AND PRAC RECOMMENDED SUSPENSION FOR HYDROXYETHYL STARCH (HES) SOLUTIONS

The European Medicines Agency (EMA) has reported a defect with Buccolam plastic syringes, urging parents and carers to carefully inspect the syringes before giving the medicine to children.

There have been a few cases in which the syringe cap did not come off completely, leaving a translucent tip-cap which stopped the medicine from leaving the syringe. This has sometimes resulted in the tip-cap coming off inside the patient's mouth and

being inhaled or ingested. A letter will be sent alerting doctors and pharmacists who prescribe and dispense Buccolam. The company marketing Buccolam is resolving the issue for new syringes, but syringes already on the market and those already dispensed to patients need to be carefully checked before use.

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended the suspension for HES solutions for infusion, following a review initiated on 17 October 2017.

These products are used as plasma volume replacement following acute blood loss, where treatment with alternative products known as 'crystalloids' alone is not considered to be sufficient. The review was triggered after use of HES solutions in critically ill patients and those with sepsis and kidney injury, despite restrictions introduced in 2013 to reduce the risks of kidney problems and deaths. The PRAC recommendation has been sent to the Coordination Group for Mutual Recognition and Decentralised Procedures-Human (CMDh) for consideration at its meeting on 22–25 January 2018.

FMD—CONCLUSIONS FROM THE SAFER EUROPE WITHOUT FALSIFIED MEDICINES CONFERENCE FAKE MEDICINES

In 2011, Falsified Medicines Directive introduced rules to improve the protection of public health with new harmonised, pan-European measures to ensure that medicines are safe and that the trade in medicines is rigorously controlled. To achieve this, the Directive sets out obligatory safety features on the outer packaging of medicines. Detailed rules on these features are regulated by a Delegated Regulation which lays down the characteristics of the safety features, how medicine authenticity should be verified and by whom. This Delegated Regulation will enter into force on 9 February 2019. The Safer Europe without Falsified Medicines Conference organised in November 2017 was aimed at gathering information on the current state of implementation of

the safety features at the European Union level and in Member States.

Different panels consisting out of the different stakeholders, that is, the European Medicines Verification Organisation (EMVO), the European Commission, national competent authorities, manufacturers, parallel traders, wholesalers, pharmacists and representatives from the hospital sector including hospital pharmacists exchanged their views and looked at the challenges ahead in implementing the safety features of medicinal products. Ideas on how to overcome hurdles that have been identified for the different sectors were also exchanged. While the National Medicines Verification Systems (NMVS) and the European Medicines Verification System (EMVS) are faced with connecting around 2500 manufacturing companies and many thousand end users such as (hospital) pharmacies, hospitals and wholesalers, end users and manufacturers are faced with different challenges that need to be tackled in the next 13 month.

For hospitals and hospital pharmacies the main challenge remains the lack of involvement in the activities of National Medicines Verification Organisations (NMVOs). Concerns in this regard have been raised and NMVOs have shown willingness to interact with hospital stakeholders. Moreover, national competent authorities have been made aware of their crucial role in raising awareness among hospital owners and managers in order to support and facilitate the implementation process. In addition, a hospital platform has been set-up on European level that looks into the development of communication strategies and the collection and sharing of best practices in order to better understand and solve common issues in the hospital sector.

However, not only the hospital end users are faced with challenges but also pharmacies, wholesalers and manufacturers have encountered problems. Pharmacies must upgrade their pharmacy software and products libraries, invest in new scanners and develop procedures and training for their employees. Wholesalers lack consolidated data on distribution authorisation holders in the European Union (EU) which makes it difficult to determine the number of end-users that have to be connected to the repository system. Manufacturers of medicinal products are still waiting for clarification from the European Commission and the national competent authorities on the various coding and labelling requirements and thus cannot pursue their serialisation activities.

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Apart from discussing the challenges of the different stakeholders and proposing solutions, the conference also took stock of where we stand. So far 26 out of the 32 participating countries have created a NMVO. Even though progress has been made in the choice of the IT providers for the system, half of the NMVOs are currently experiencing delays in the start of their project implementation phase. Also, the question on access to data in the repositories by national competent authorities remains yet to be fully resolved and requires continuous dialogue between the European Commission, Member States and the EMVO.

Many things remain to be done before 9 February 2019. However, all stakeholders were confident that the current challenges can be overcome in the month ahead. The impact of the EMVS on medicines availability remains yet to be seen and is thus currently difficult to assess. Nonetheless, some stakeholders have expressed the view that the system could potentially be of use for the prevention of medicines shortages as it improves the available information for authorities and supply chain actors.

EPHA—JOINT STATEMENT AND CALL TO ACTION ON ANTIMICROBIAL RESISTANCE (AMR)

The European Public Health Alliance (EPHA) presented a Joint Statement and Call to Action on AMR at the 2017 meeting of the Health Policy Platform. Both documents go together—the Call to Action being a shorter executive summary of the Joint Statement. EAHP, alongside other European and international organisations active in the health sector, has endorsed the statement.

The Health Policy Platform is a collaborative initiative that was set-up in after the mandate of the EU Health Policy Forum ended in December 2013 to ease the communication between the European Commission services and health stakeholders. It is aimed to be inclusive and to reflect geographical and professional diversity of the participants.

The Joint Statement contains 11 key points for action that its authors and signatories (representing a diverse group of public health stakeholders including organisations representing the interests of healthcare and animal health professionals and students, patients and disease-specific groups, health groups active at the national level and many others involved in tackling AMR's many dimensions) would like to see addressed by the European

Commission and the relevant Executive Agencies working on AMR.

Some points are the involvement of civil society in AMR One Health policymaking, supporting the development and implementation of National Action Plans and allocation of adequate European funds to actions against AMR, make full use of EU legislative powers in AMR-relevant sectors and nurture and actively involve healthcare professionals, including students. The statements' objective is to highlight areas where the signatories feel that more action is required than what is outlined in the One Health Action Plan. Specifically, the 11 points include an increased involvement of civil society, students and health professionals, the sufficient allocation of EU funds to actions against AMR, the monitoring and benchmarking of AMR data throughout Europe, supporting and promoting rapid diagnostic tests and in general empowering patients and raising public awareness.

EMA RECOMMENDATIONS: CONTRACEPTION IN MEN AND WOMEN AND CMDH ENDORSES SUSPENDING THE MARKETING OF MODIFIED-RELEASE OR PROLONGED-RELEASE PARACETAMOL

The EMA has updated recommendations for contraception in men and women taking mycophenolate medicines, used to prevent rejection of transplanted organs and the CMDh has endorsed by majority EMA's PRAC December 2017 recommendation to suspend marketing of modified-release or prolonged-release products containing paracetamol.

The updated recommendations follow a periodic review of mycophenolate medicines by EMA's PRAC. Mycophenolate medicines are known to increase the risk of malformations and miscarriages during pregnancy if the fetus is exposed to them in the womb. EMA has now concluded that current evidence does not indicate a risk of malformations or miscarriages when the father has taken mycophenolate, although the risk of genotoxicity cannot be completely ruled out. For male patients, EMA now recommends that either the male patient or his female partner use reliable contraception during mycophenolate treatment and for at least 90 days after stopping treatment. For female patients, the risk is unchanged. These medicines must not be used in pregnant women unless there are no suitable alternatives to prevent transplant rejection.

The CMDh has endorsed by majority EMA recommendation to suspend

marketing of modified-release or prolonged-release products containing paracetamol (designed to release paracetamol slowly over a longer period than the usual immediate-release products).

CMDh agreed with the agency's advice that the advantages of a longer-acting product did not outweigh the complications of managing an overdose of the medicine, since the treatment procedures for immediate-release products are not appropriate for modified-release paracetamol. Products containing modified-release paracetamol alone or combined with the opioid medicine tramadol will remain suspended unless the companies that hold the marketing authorisations can provide evidence of appropriate and practical EU-wide measures to help prevent overdose with these products and adequately reduce its risks. The CMDh decision will now be sent to the European Commission which will issue a final legally binding decision valid throughout the EU.

FIP REPORT ON HARM REDUCTION

The role of pharmacists in reducing harm from drugs of abuse is highlighted in the recent report by the International Pharmaceutical Federation (FIP), which calls for increased engagement between pharmacy organisations, policymakers and health authorities, in order to remove barriers and allow increased involvement of pharmacists in harm reduction services.

In describing harm reduction services such as needle exchange and opioid substitution in different regions and countries, the report highlights that out of 158 countries reporting people who inject drugs of abuse, only 90 of them have established needle exchange programmes. The derived benefits of harm reduction include the prevention of infection by HIV and hepatitis C, fewer overdoses and less drug-related criminal activity.

In this regard, the FIP report specifies the need for a comprehensive service which includes syringe and needle exchange (with the provision of low-dead space syringes where possible), opioid substitution therapy (preferably with pharmacist prescribing or dose adjustment), naloxone supply for overdoses (including pharmacist-initiated supply) and health promotion (including advice on sexual health).

Furthermore, in the context of changing policies on marijuana around the world, the report addresses the issue of supply from pharmacies of marijuana or cannabinoid-containing products for the purpose of medicinal use or recreational use or both. The report considers that the sale of

marijuana in pharmacies could be argued on harm reduction principles, however, pointing out that such policies should be developed in conjunction with pharmacists in an informed process of public policy development, taking into consideration the potential damage to pharmacists' standing in the public eye.

EMA: ESMYA REVIEW PROCEDURE, XOFIGO INVESTIGATED AND PROLONGED-RELEASE PARACETAMOL RECOMMENDATION

The EMA's PRAC has started a review on Esmya, an investigation on Xofigo and has confirmed its recommendation to suspend prolonged-release paracetamol from marketing.

Esmya (ulipristal acetate) is a medicine used to treat uterine fibroids (non-cancerous tumours of the womb). Its review started after four reports of serious liver injury in patients treated with Esmya, with one case requiring a liver transplant. The in-depth review by PRAC will evaluate all available data and determine if the use of Esmya carries implications. It is relevant to note that ulipristal acetate is also the active substance of a single-dose medicine authorised for emergency contraception, ellaOne, for which no cases of serious liver injury have been reported.

The investigation on Xofigo (radium-223 dichloride) arose from reports of increased risk of death and fractures in an ongoing clinical trial. The clinical trial compares Xofigo with placebo, with both being administered in combination with Zytiga (abiraterone acetate) and prednisone or prednisolone. The patients in this study include patients with prostate cancer with mild symptoms such as pain or no symptoms at all.

Xofigo is currently authorised for use in patients whose prostate cancer has spread to the bones and is causing symptoms. Zytiga is used in men with metastatic castration-resistant prostate cancer, and prednisone or prednisolone provides relief for inflamed areas of the body. In response to developments, patients involved in the

clinical trial are being monitored closely and are no longer being treated with Xofigo. While a full PRAC investigation is ongoing, doctors are asked not to use Xofigo in combination with Zytiga and prednisone/prednisolone to treat patients with metastatic castration-resistant prostate cancer.

The confirmation of PRAC's recommendation that modified-release or prolonged-release paracetamol containing medicines should be suspended from marketing follows a re-examination of the previous recommendation that was made in September 2017 by the Committee.

The conclusion by the Committee and experts in the field of pain management and treatment of overdose was that the advantages of a longer-acting product did not outweigh the disadvantages in the case of overdose. This is primarily due to the fact that usual treatment procedures for immediate-release products are not appropriate for modified-release paracetamol. Therefore, immediate-release paracetamol products are not affected by this review and continue to be available. The PRAC's final recommendations will now be sent to CMDh, which will adopt a position.

EUROPEAN COMMISSION RELEASES Q&A INFORMATION ON BIOSIMILARS FOR PATIENT AND DATE FOR THE NEXT BIOSIMILAR STAKEHOLDER WORKSHOP

For three consecutive years, the European Commission has been organising a stakeholder conference on biosimilar medicines which serves as a platform for the exchange of clinical experience and best practice. Participants of these events included representatives of patients, healthcare professionals, authorities and pharmaceutical companies. The 2018 multistakeholder workshop on biosimilar medicines will focus on oncology, public procurement and the role of nurses and pharmacists in the uptake of biosimilars. It will take place on 14 September 2018.

Since the start of their evolution in the 1980s, biological medicines have become indispensable in the treatment of patients.

Such medicines (including biosimilars) come from living cells that have been modified using biotechnology. A biosimilar medicine is almost identical to an existing biological medicine. It is approved for the European market by the EMA. Both biologics and biosimilars are used to treat severe diseases such as cancers. Biosimilars have the potential to create competition in the biological medicine market and provide patients with broader affordable access to the newest medicines.

The outcomes of the 2017 workshop—which was held on 5th May 2017—are now available online and include the final report, presentations, a QuintilesIMS report on the impact of biosimilar competition and the consensus information paper from 2013. The information guide for healthcare professionals of the European Commission and the EMA which was launched during this event is expected to be available in six additional languages in the first half of 2018. The guide provides EU healthcare professionals with information on the science and regulation supporting the use of biosimilars in the EU.

Together with the 2017 workshop documents, the European Commission also released comprehensive information for patients on biosimilar medicines in 23 languages, expanding from the original English version which was made available in May 2017.

Section 6: Education and Research

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