European Union governments call for a more ambitious approach on antimicrobial resistance

Richard Price

The European Union's (EU) 28 member state governments have reached an important set of new conclusions on the actions they must take together to help combat antimicrobial resistance (AMR).

The Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance represent the culmination of intense efforts by the six-month Dutch presidency of the Council of the European Union to forge a fresh political resolution on the topic.

'Council conclusions' on any topic give the European Commission a mandate to take initiatives secure in the knowledge that it represents the will of the EU's member state Governments.

New EU AMR Action Plan required

A key highlight of the conclusions is the call from Governments for the development of a new EU Action Plan on antimicrobial resistance, that should go further than previous versions. The new action plan should include 'measurable (clearly defined quantitative or qualitative) goals, benchmarks and effective measures to achieve these goals', something lacking from the previous action plan.

National AMR Action Plans before mid-2017

The conclusions also call for national AMR action plans to be in place in all EU countries before mid-2017. These should include measurable goals to reduce infections in humans and animals, and the use of antimicrobials in the human and veterinary sector. The conclusions urge all EU member states to include within their national AMR action plans measures to improve prescribing practices, and means of monitoring progress.

EU Guidelines on prudent use of antimicrobials in human medicine

The European Commission is further instructed by the Conclusions to develop EU guidelines on prudent use of

antimicrobials in human medicine in order to support national guidelines and recommendations.

Commenting on the 2016 Council Conclusions on AMR, Tajda Miharija Gala, EAHP Vice-President and lead spokesperson on antimicrobial resistance, said:

EAHP has argued strongly of the necessity for a new EU action plan on AMR, but also one with more 'teeth' than the previous version. The Council's recommendation for both a new plan, and the inclusion of hard measures by which the plan's success can be judged, is therefore very welcome.

LANDMARK COUNCIL CONCLUSIONS SIGNAL CHANGE AHEAD FOR EUROPEAN PHARMACEUTICAL SYSTEM

A busy Dutch presidency of the EU Council has also published conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States. The conclusions represent the collective view of the EU's 28 national governments on where combined attention is required to improve the operation of the pharmaceutical system.

In a document that commentators are noting as being unusually forthright by EU Council standards, parts of the pharmaceutical industry are criticised for 'inappropriate market behaviour' and sub-optimal compliance with post marketing authorisation regulatory obligations. In addition, the Council conclusions state: "patients' access to effective and affordable essential medicines is endangered by very high and unsustainable price levels".

Other criticisms of the current operation of the European pharmaceutical system include expressed concerns about 'orphanisation' of the pharmaceutical market that is, exploitation of Orphan Drug Regulation to achieve higher prices. Greater transparency in the construction of early market authorisation schemes is also called for.

Attention is also provided in the conclusions to the problems experienced by smaller member states in providing access to medicines for patients, and the

need for the a share of the profits from public-private research partnerships to be better directed (ie, to further research).

The document suggests that the pharmaceutical system in the European Union 'may be imbalanced', in part due to "the lack of leverage of individual member states in negotiations with industry". Amongst the remedies suggested include increased forms of cooperation between member states, such as in the fields of:

- ▶ joint procurement,
- ▶ 'joint horizon scanning',
- ▶ further cooperation in health technology assessment (HTA)—including potential mutual recognition, and
- ▶ collection and exchange of price data.

Overall, the missive from EU Governments identified a need for 'further analysis to examine the current functioning of the pharmaceutical system in the EU' and gives the European Commission instructions to take a lead on this 'as soon as possible'. The conclusions specifically instruct the Commission to prepare a timetable and methodology for conducting this analysis 'by the end of 2016'.

EDQM PUBLISHES TWO NEW RESOLUTIONS ON PHARMACY PRODUCTION AND RECONSTITUTION

The European Directorate for the Quality of Medicines & HealthCare (EDQM) has published two new resolutions related to production and reconstitution of medicines in pharmacies.

EDQM is a Directorate of the Council of Europe (not to be confused with the European Union) that contributes to the protection of public health by elaborating harmonised standards to ensure the quality of medicines.

New EDQM Resolution CM/Res (2016)2 relates to good reconstitution practices in health care establishments for medicinal products for parenteral use.

The resolution recommends that all countries (currently 37) that are signatories to the Convention on the Elaboration of a European Pharmacopoeia should implement measures to guarantee that best practices are in place in health care establishments for the reconstitution of a medicinal product into a ready-to-use or ready-to-administer dosage form.

New EDQM Resolution CM/Res (2016)1 focuses on the quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients. It represents an amendment to the pre-existing Resolution CM/ResAP (2011)1 to ensure consistency

with the provisions of new Resolution CM/Res(2016)2 relating to medication reconstitution (see above).

The ultimate goals of the two new resolutions are to promote public health through the harmonisation of requirements for medicinal preparations, support health professionals with appropriate guidance to prevent risk of health damage caused by drug preparation errors, and ensure that patient needs are fully met.

EMA AND STAKEHOLDERS EXPLORE HOW TO IMPROVE PATIENT ACCESS TO ATMPs

The European Medicines Agency (EMA) has published a report with conclusions on how the regulatory landscape for access to Advanced Therapy Medicinal Products (ATMPs) could be improved, including in respect to hospital manufacture dimensions.

The report summarises the deliberations of stakeholders at a one-day meeting in May 2016. Anne Black, a hospital pharmacist based at Newcastle upon Tyne Hospitals NHS Foundation Trust (UK), with specialist background in ATMPs, represented the European Association of Hospital Pharmacists.

A specific EU regulation for ATMPs has existed since 2007 and was intended to facilitate their development and introduction to market, via centralised authorisation procedures overseen by the European Medicines Agency. However, it has been noted that the number of ATMPs coming through the regulation's procedures has been low. There have been seven EU-wide marketing authorisations provided for ATMPs since 2007, two of which have been subsequently withdrawn or suspended.

A major proposal at the meeting was for licensing requirements to take account of the particularities of ATMP manufacture. For example, participants noted that

ATMP manufacture can take place at various sites and that, for some products, the later stages of production might need to take place close to the bedside. The implication is that all sites involved—hospitals included—would need to hold a manufacturing licence. A lack of harmonisation at national level was also noted, as some member states allow hospitals to hold a manufacturing licence while others do not. Stakeholders therefore requested more information and harmonisation.

The meeting took place in the context of a European Commission consultation on new guidelines for ATMP Good Manufacturing Practice (GMP). Stakeholders considered that GMP requirements should be applied more flexibly for ATMPs at early development stages, as well as enable innovative manufacturing technologies such as bedside manufacturing and decentralised manufacturing.

Stakeholders also called for greater efforts towards international harmonisation of regulation, using the International Council for Harmonisation (ICH) as a means of achieving this.

A section of the report deals with the application of Article 28 (2) of the EU ATMP Regulation, the so called 'hospital exemption' clause. This permits member states to use ATMPs in their territories without the need for marketing authorisation. This clause applies only to custom-made ATMPs used in a hospital setting for a specific patient. Such products are produced under the responsibility of a physician and are only to be used within the member state where it is produced. In addition, a competent authority must authorise hospital exemption for ATMPs and they must comply with the same national requirements concerning quality, traceability and pharmacovigilance that apply to authorised medicinal products.

Stakeholders present at the meeting called for transparency on the use of

exemption products in the EU, so that industry, academia, regulators and even patients, can find out more easily which products are being used and for which indications. Specific proposals were for easily accessible registries and other electronic databases.

Subsequent to the meeting and the publication of the report, Anne Black, EAHP's representative at the meeting, commented:

Whilst discussion at the meeting did focus on potential flexibilities in application of Good Manufacturing Practice requirements in the area of ATMPs, I emphasised that healthcare professionals and patients have an expectation that any product provided to a patient is of appropriate safety, efficacy and quality. This should never be compromised.

On improving research and development of ATMPs, it is vital that clinical trial pharmacists are involved at an early stage as their expertise can greatly facilitate safe introduction.

Finally, careful consideration is needed to the availability of stability data for ATMPs as in my experience many trials require preparation in the clinical area due to the short expiry.

EAHP Statement 6: Education and Research

Competing interests None declared.

Provenance and peer review Commissioned; internally peer reviewed.

CrossMark

To cite Price R. *Eur J Hosp Pharm* 2016;**23**:304–305.

Eur J Hosp Pharm 2016;**23**:304–305.
doi:10.1136/ejhp-2016-001080