Adopted by EAHP's General Assembly in June 2023

EAHP Position Paper on Infectious Diseases and Antimicrobial Resistance

Making a difference through prudent use to ensure efficient therapies for patients with life-threatening infections

Combatting infectious diseases requires the implementation of a comprehensive intervention package comprised of measures including but not limited to prudent anti-infective use, vaccination and stewardship. To maintain the efficacy of antimicrobial drugs and to prevent the further spread of antimicrobial resistance, the European Association of Hospital Pharmacists (EAHP) urges an interprofessional approach in the healthcare setting and during the transition of care. Hospital pharmacists in Europe are ready to champion infection prevention and contribute and promote the prudent use of antimicrobials through the enforcement of antimicrobial stewardship (AMS). To improve patient outcomes proactive steps need to be taken.

EAHP calls on national governments and health system managers to use the specialised background and knowledge of the hospital pharmacist in multi-professional antimicrobial stewardship teams or other forms of antimicrobial governance in the hospital and in the community.

EAHP requires that hospital pharmacists are an integral part in the transfer of care to ensure that the patient care started in hospitals can be continued in the community.

EAHP asks for the inclusion of concrete measures, like the outcome measures provided by the Transatlantic Taskforce on Antimicrobial Resistance, in national action plans that increase the uptake of stewardship teams.

EAHP calls for further consolidating the role of hospital pharmacists in European vaccination strategies.

EAHP recommends the universal application of prevention and control measures by the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) among healthcare professionals and the public in the fight against infectious diseases.

EAHP advocates for adequate regulatory oversight and proper implementation of measures in the veterinary sector and the environment at global, European, national and local levels.

EAHP demands increased investment to support the development of innovative proposals and the encouragement of research projects in new fields of infectious disease control such as immunotherapy and sustainability.

EAHP urges governments to make arrangements so that essential antibiotics in dosage forms and strengths appropriate for both adults and children will be maintained on the market with contingency stock level arrangements and alternative production by hospital pharmacists enabled where necessary.

STEWARDSHIP

Strengthening of prudent use of antimicrobials in human medicine

The emergence of antibiotic resistance is widely recognised as a major public health problem. According to the European Commission and the European Centre for Disease Prevention and Control (ECDC), the number of patients in the EU that die each year as a result of infections caused by resistant bacteria increased from

25.000 in 2017 to 35.000 in 2020. [1, 2] In the last decades, there has been dramatic growth in the ability of a microorganism to stop an antimicrobial from working against it. As a consequence, only a limited number of antibiotics are available for the treatment of infections caused by resistant bacteria. Other consequences for patients are that infections persist, which results in longer hospital stays, higher healthcare costs, and an increased risk of the infection spreading to others. Thus, significant inter-professional actions are needed to ensure standard treatments and prevention of serious diseases with effective and safe medicines that are quality-assured, used appropriately, and accessible to all who need them.

The escalating threat of antimicrobial resistance is a global public health concern and now seriously jeopardises the effectiveness of standard treatments, rendering some ineffective for their approved indications. AMS teams are an indispensable tool that promote the rational use of antimicrobial agents, selection of optimal drugs, dosing, duration of therapy, route of administration and the use of antibiotic susceptibility testing to reduce the use of broad-spectrum antibiotics. In Sweden, AMS has formed an integral part of the strategic programme against antibiotic resistance for the past 20 years.[3] The first European adoption of the Infectious Disease Society of America (IDSA) Practice Guidelines based on a new evaluation of the literature including European publications was performed in 2013 and published by an interdisciplinary working group from Austria, Germany and Switzerland.[4] The primary goal of AMS is to optimise clinical outcomes while minimising unintended consequences of antimicrobial use.[5, 6, 7] Consequently, **EAHP calls on national governments and health system managers to use the specialised background and knowledge of the hospital pharmacist in multi-professional antimicrobial stewardship teams or other forms of antimicrobial governance in the hospital and in the community.**

Seamless transitions between the interfaces of different health settings need to be considered during the implementation of multi-professional AMS teams or other forms of antimicrobial governance in the hospital and in the community. **EAHP requires that hospital pharmacists are an integral part in the transfer of care to ensure that the patient care started in hospitals can be continued in the community.**

As outlined by a Danish study, there is room for improvement in the use of diagnostic tests as an aid in promoting prudent antibiotic use.[8] Investments in and guidelines for rapid point-of-care tests are needed to support the appropriate use of antimicrobials.[9, 10, 11] In addition, research should be conducted to improve the evidence for the use and illustrate the value of rapid-point-of-care tests.

Need for further implementation of antimicrobial stewardship (AMS) programmes

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[1] European Commission. Factsheet - AMR: A major European and Global challenge. 2017. Available at: https://health.ec.europa.eu/system/files/2020-01/amr_2017_factsheet_0.pdf (last visited on 10 June 2023).

[2] European Centre for Disease Prevention and Control. Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020. November 2022. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/Health-burden-infections-antibiotic-resistant-bacteria.pdf (last visited on 10 June 2023).

[3] S. Mölstad, S. Löfmark, K. Carlin, M. Erntell, O. Aspevall, L. Blad, H. Hanberger, K. Hedin, J. Hellman, C. Norman, G. Skoog, C. Stålsby-Lundborg, K. Tegmark Wisell, C. Åhrén, O. Cars. Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance. Bull World Health Organ. 2017 Nov 1;95(11):764-773.

[4] K. de With, K. Wilke, W.V. Kern, et al. Strategien zur Sicherung rationaler Antibiotika-Anwendung im Krankenhaus S3-Leitlinie, AWMF-Registernummer 092/001. 2018. Available at: https://register.awmf.org/assets/guidelines/092-001l_S3_Strategien-zur-Sicherung-rationaler-Antibiotika-Anwendung-im-Krankenhaus_2020-02.pdf (last visited on 10 June 2023).

[5] ASHP statement on the pharmacist's role in antimicrobial stewardship and infection prevention and control. Am J Health Syst Pharm. 2010 Apr 1;67(7):575.

[6] Australian Commission on National Safety and Quality Health Service. Role of the pharmacist and pharmacy services in antimicrobial stewardship. Antimicrobial Stewardship in Australian Health Care 2018. Available at: https://www.safetyandquality.gov.au/sites/default/files/migrated/Chapter11-Role-of-the-pharmacist-and-pharmacy-services-in-antimicrobial-stewardship.pdf (last visited on 10 June 2023).

[7] The Institute for Safe Medication Practices (ISMP). Pharmacists' and Nurses' Role in Antimicrobial Steward-ship, Antimicrobial Resistance, and Sepsis Care. September 23, 2021. Available at: https://www.ismp.org/resources/pharmacists-and-nurses-role-antimicrobial-stewardship-antimicrobial-resistance-and-sepsis (last visited on 10 June 2023).

[8] R.V. Sydenham, U.S. Justesen, M.P. Hansen, L.B. Pedersen, R.M. Aabenhus, S. Wehberg, D.E. Jarbøl. Prescribing antibiotics: the use of diagnostic tests in general practice. A register-based study. Scand J Prim Health Care. 2021 Dec;39(4):466-475.

[9] K.L. Dooling, D.J. Shapiro, C. Van Beneden, et al. Overprescribing and inappropriate antibiotic selection for children with pharyngitis in the United States, 1997-2010. JAMA Pediatr 2014;168:1073-4.

[10] L.E. Norton, B.R. Lee, L. Harte, et al. Improving guideline-based streptococcal pharyngitis testing: a quality improvement initiative. Pediatrics 2018b;142:e20172033.

[11] E.M. Walters, J. D'Auria, C. Jackson C, et al. An ambulatory antimicrobial stewardship initiative to improve diagnosis and treatment of urinary tract infections in children. Jt Comm J Qual Patient Saf 2019;45:829-37.

AMS is still a long way from being routine in European hospitals. This is despite the scientific results of efficient reduction of antibiotic overuse, positive contributions to resistance development and even cost savings through AMS.[12] ECDC also supports the strengthening of the fight against antimicrobial resistance i.e. through an AMS toolkit with a special section including hospital pharmacists' involvement.[13] The European Commission strongly supports AMS as an important tool in their publications, e.g. EU Guidelines for the prudent use of antimicrobials in human health.[14] Besides the positive effects on patient treatment and sustainability of antibiotic therapy, there is also a cost-benefit described in the literature.[15] **EAHP asks for the inclusion of concrete measures, like the outcome measures provided by the Transatlantic Taskforce on Antimicrobial Resistance, in national action plans that increase the uptake of stewardship teams.**

The composition of AMS teams varies and could be adapted to the resources and infrastructure of the hospital. An AMS team must include at least one hospital pharmacist with expertise in infectious diseases, an infectious disease physician and a clinical microbiologist.[16] Involving other healthcare professionals is very beneficial, and in some cases, AMS teams have included a diverse team of professionals including IT specialists and nurses.[17] The interdisciplinary nature of the team is essential in order to use to the fullest the different expertise available within the hospital and to nurture interdisciplinary cooperation and ownership of the program. For example, the knowledge of the hospital pharmacist is indispensable for substitution decisions, dosage recommendations and therapeutic drug monitoring.

Development of antiviral and antifungal stewardship

AMS is known widely due to its benefits for patient care but the work of these teams is primarily focused on antibiotics. Antiviral or antiretroviral stewardship programmes are less prominent despite their effects on medication error rates and other outcomes.[18] Similarly, also antifungal stewardship is not yet available widely to address the effects of new resistant species among yeasts (eg, *Candida auris*) and the use of antifungal products in agriculture. Efforts should be made to further promote interdisciplinary antiretroviral and antifungal stewardship teams within the AMS context. Antiviral or antiretroviral teams should ideally comprise a pharmacist specialist, an infectious diseases physician and associated learners who have the ability to assist in the identification and correction of inpatient antiretroviral-related errors.[19]

ONE HEALTH APPROACH

Investing in prevention strategies, infection control measures and immunisation

Public health interventions, preventive measures and changes in human behaviour have proven to be effective tools against infectious diseases over many decades.[20] The COVID-19 pandemic has put the spotlight on vaccination strategies, vaccine development and other preventative measures. To curb the spread of infectious diseases, the efforts of prophylaxis like vaccination and hygiene are important and need to be further enhanced. Prevention of infectious diseases should be strengthened by integrating vaccination

[12] H.J. Wickens, et al., The increasing role of pharmacists in antimicrobial stewardship in English hospitals. Journal of Antimicrobial Chemotherapy. 2013. 68(11): p. 2675-2681.

[13] European Centre for Disease Prevention and Control. European Antibiotic Awareness Day – Key messages for hospital pharmacists. 2021. Available at: https://antibiotic.ecdc.europa.eu/en/get-informed/key-messages/professionals-hospitals/hospital-pharmacists (last visited on 10 June 2023.

[14] Commission Notice – EU Guidelines for the prudent use of antimicrobials in human health (2017) OJ C 212, p.1-12. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_.2017.212.01.0001.01.ENG&toc=OJ:C:2017:212:TOC (last visited on 10 June 2023).

[15] N.R. Naylor, N. Zhu, M. Hulscher, A. Holmes, R. Ahmad, J.V. Robotham. Is antimicrobial stewardship cost-effective? A narrative review of the evidence. Clin Microbiol Infect. 2017 Nov;23(11):806-811.

[16] K. de With, F. Allerberger, S. Amann, et. al. Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious - Diseases. 2016. Available at: https://link.springer.com/content/pdf/10.1007%2Fs15010-016-0885-z.pdf (last visited on 10 June 2023).

[17] F. Allerberger, R. Gareis, V. Jindrák and M.J. Struelens. Antibiotic stewardship implementation in the EU: the way forward, Expert Review of Anti- infective Therapy. 2019. 7:10, 1175-1183.

[18] S.M. Michienzi, A.F. Ladak, S.E. Pérez, D.B. Chastain. Antiretroviral Stewardship: A Review of Published Outcomes with Recommendations for Program Implementation. J Int Assoc Provid AIDS Care. 2020 Jan-Dec;19:2325958219898457.

[19] A.M. DePuy, R. Samuel, K.M. Mohrien, E.B. Clayton, D.E. Koren. Impact of an Antiretroviral Stewardship Team on the Care of Patients With Human Immunodeficiency Virus Infection Admitted to an Academic Medical Center. Open Forum Infectious Diseases, Volume 6, Issue 7, July 2019.

[20] A. Mercer. Protection against severe infectious disease in the past. Pathog Glob Health. 2021 May;115(3):151-167.

planning developed for the fight against them and providing all healthcare professionals with access to vaccine records.[21, 22]

Hospital pharmacists – as part of the vaccination team across healthcare sectors – are raising awareness about vaccine safety, supporting vaccine administration processes and sharing clear information with citizens who have questions. They play a significant role in providing information to their fellow healthcare professional colleagues on vaccines, their development, differences and administration patterns and, in that way, influence the perception of vaccines and their importance for combating diseases. Hospital pharmacists, because of their specialised training are able to guarantee the safe handling of vaccines and are in a position to support the traceability and vigilance of vaccines. In the context of national vaccination awareness programmes the involvement of the expertise of hospital pharmacists as trusted sources of information is important for adequately informing the public. They are also essential societal pillars that lead by example by being vaccinated themselves and that provide objective and trusted information to improve public health. **EAHP calls for further consolidating the role of hospital pharmacists in European vaccination strategies.**

Similarly to vaccination, existing prevention toolkits and hand hygiene as the single most important prophylactic measure need to be boosted. The prevention toolkit for healthcare professionals in hospitals and other healthcare settings of ECDC – to which EAHP contributed from the perspective of the hospital pharmacist – is for example a measure that should be promoted.[23, 24] **EAHP recommends the universal application of prevention and control measures published by ECDC and WHO among healthcare professionals and the public in the fight against infectious diseases.**

Targeted use of antimicrobials in veterinary medicine and intensive livestock farming

There is strong evidence, that the use of antimicrobial drugs in animals also induces antimicrobial resistance in human pathogenic bacteria. The European Commission has taken significant measures in the veterinary sector[25] and defined guidelines which address the need for preventive measures on European, national and local levels.[26] More action is, however, needed to protect vital life-saving antimicrobials for human health. Safeguards for patients with severe infections need to be put in place. Colistin, an antimicrobial of the class of polymyxins that is one of the few treatments available for some severe drug-resistant infections in humans, is for some of them the last line of defence. **EAHP advocates for adequate regulatory oversight and proper implementation of measures in the veterinary sector and the environment at global, European, national and local levels.**

Lowering the exposure and enhancing sustainability

Some medicines are not metabolised and inactivated by the body of both humans and animals and then end up in the environment and – through their impact on agriculture, aquaculture and livestock – in the food chain. Hospital pharmacists are an indispensable source of information and interpretation for monitoring the amount and pattern of the usage of antimicrobials in hospitals. They should support the use of quality indicators for the judgement of the success of AMS programmes.[27] Their knowledge should be utilised to lower the exposure to antimicrobials and enhance sustainability in hospitals.

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[21] Vaccines Europe priorities for vaccination policies in Europe. June 2017. Available at: http://www.vaccineseurope.eu/wp-content/uploads/2017/06/VE-paper_priorities_vaccination_policy-22-05-2017.pdf (last visited on 10 June 2023).

[22] The Review on Antimicrobial Resistance. Vaccines and alternative approaches: reducing our dependence on antimicrobials (Chaired by Jim O'Neill). 2016. Available at: https://amr-review.org/sites/default/files/Vaccines%20and%20alternatives_v4_LR.pdf (last visited on 10 June 2023).

[23] European Centre for Disease Prevention and Control. Communication toolkit for healthcare professionals in hospitals and other healthcare settings. 2017. Available at: https://antibiotic.ecdc.europa.eu/en/communication-toolkit-professionals-hospitals-and-other-healthcare-settings (last visited 10 June 2023).

[24] World Health Organization. Evidence of hand hygiene to reduce transmission and infections by multidrug resistant organisms in healthcare settings. 2014. Available at https://cdn.who.int/media/docs/default-source/integrated-health-services-(ihs)/infection-prevention-and-control/mdro-literature-review.pdf?sfvrsn=88dd45c7_2 (last visited on 10 June 2023).

[25] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. Consolidated version. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02019R0006-20220128 (last visited 10 June 2023).

[26] Commission Notice – Guidelines for the prudent use of antimicrobials in veterinary medicine (2015) OJ C 299, p. 7-26. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1523547946385&uri=CELEX:52015XC0911(01) (last visited on 10 June 2023).

[27] Transatlantic Taskforce on Antimicrobial Resistance (TATFAR). Summary the modified Delphi process for common structure and process indicators for hospital antimicrobial stewardship programs. June 2015. Available at: https://www.cdc.gov/drugresistance/pdf/summary_of_tatfar_recommendation_1.pdf (last visited on 10 June 2023).

INCENTIVES

Addressing the lack of antibiotic development

Increasing resistance, particularly of carbapenem resistance and vancomycin resistance in Europe, means that specific funding actions are necessary for the benefit of the patient.[28] Despite the commitments of the European Commission and others in relation to the support of research and developments further incentives are needed.

It is crucial that the revision of the EU's general pharmaceutical legislation addresses the increase of European production sites to lower dependency on international markets and the development of new antibiotics. It is, however, questionable if transferable exclusivity vouchers are the right incentive to increase development, especially since any option of such upfront nature has not been tested before. Unpredictable results, including costs and also the lack of tailored conditions ensuring access to the new antibiotics, could be the consequence. At the same time, a prolonged exclusivity period for the medicines to which the voucher is applied puts respective patients at a potential risk of diminished competition in the market, both in terms of supply chain fragility (resulting in secondary shortages) and also higher costs. In addition, quality metrics to discourage the development of unnecessary or ineffective antibiotics would need to be put in place. **EAHP demands increased investment to support the development of innovative proposals and the encouragement of research projects in new fields of infectious disease control such as immunotherapy and sustainability.**[29]

Keeping old and established but still essential antibiotics on the market

In addition to the development of new antibiotics, universal access to old and established antibiotics that are being used in new ways needs to be maintained. The growing and more frequent shortages of antimicrobials are an additional contributing factor to antimicrobial resistance affecting the effectiveness of antimicrobials worldwide.[30] The shortage of amoxicillin and amoxicillin/clavulanic acid has severely impacted treatment options for patients across Europe.[31] Shortages of antimicrobial drugs compromise their prudent use and must be avoided. Surveys conducted by EAHP in 2019[32] and 2020[33] showed that antibiotic shortages ranked among the top three medicinal product shortages. Measures need to be taken by countries, including national governments, pharmaceutical industry, healthcare professionals, patients as well as other stakeholders at the pan-European level, to lower the risk of antibiotic shortages, especially since substitution supported by the AMS team is not always possible. Sweden and the UK are already piloting subscription-based models that provide a sufficient antimicrobial product supply guarantee.[34] Studies that gather further information on this, including those securing access to essential legacy/establish antibiotics, should be supported.[35] **EAHP urges governments to make arrangements so that essential antibiotics in dosage forms and strengths appropriate for both adults and children will be maintained on the market with contingency stock level arrangements and alternative production by hospital pharmacists enabled where necessary.**

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[28] World Health Organization and the European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2022. 2020 Data. 2022. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/Joint-WHO-ECDC-AMR-report-2022.pdf (last visited on 10 June 2023).

[29] O.A. Dar, et al. Exploring the evidence base for national and regional policy interventions to combat resistance. The Lancet , Volume 387 , Issue 10015 , 285 - 295.

[30] N. Shafiq, A.K. Pandey, S. Malhotra, et al. Shortage of essential antimicrobials: a major challenge to global health security BMJ Global Health 2021;6:e006961.

[31] European Medicines Agency. Shortage of amoxicillin and amoxicillin/clavulanic acid Various presentations including paediatric formulations and presentations. 2023. Available at: https://www.ema.europa.eu/en/documents/shortage/amoxicillin-amoxicillin/clavulanic-acid-supply-shortage_en.pdf (last visited 10 June 2023).

[32] N. Miljković, A. Batista, P. Polidori, et al. Results of EAHP's 2019 Medicines Shortages Survey. European Journal of Hospital Pharmacy. 2020;27:202-208.

[33] L.D. Vinci, P. Polidori P, N. Miljković, et al. Lessons learnt from the COVID-19 pandemic: results of EAHP survey on the future crisis preparedness of hospital pharmacies. European Journal of Hospital Pharmacy. 2022;29:242-247.

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[35] C. Pulcin et al. Ensuring universal access to old antibiotics: a critical but neglected priority, Clinical Microbiology and Infection 23 (2017) 590-592.