

News from the EMA

SECTION EDITOR



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First electronic product information (ePI) published for selected human medicines

November 08, 2023

The Heads of Medicines Agencies (HMA), the European Commission (EC) and EMA have published for the first-time electronic product information (ePI) for selected human medicines harmonised across the European Union (EU).

The product information of a medicine includes its summary of product characteristics, labelling, and package leaflet. These documents accompany every medicine authorised in the EU and explain how they should be prescribed and used. They can all be found, often as a PDF document, on the websites of EU regulators, with a printed package leaflet also provided in the medicine's box. Digital platforms open new possibilities to share this information electronically, keep it constantly updated and make it more accessible to end users such as healthcare professionals and patients.

The creation and testing of ePIs in real regulatory procedures is being explored through a one-year pilot initiative by HMA, EMA, and the EC to enable the transition to the electronic system for medicines evaluated both nationally and at the European level. The ePI initiative is an action under the Pharmaceutical Strategy for Europe supported by the EU funding programme EU4Health.

The published ePIs are for medicines evaluated by EMA or by national authorities in Denmark, the Netherlands, Spain, and Sweden. Companies participating in the pilot create and submit the ePI as part of their regulatory application. The pilot, which involves 25 medicines, will conclude in July 2024, and the outcomes will inform how to integrate the ePIs into common practice and expand their use across the EU.

The ePIs can be viewed at the Product Lifecycle Management Portal in English for centrally approved medicines and in the local language for nationally approved ones. Testing is ongoing to allow access to ePIs in all EU languages. In addition, ePI data can be accessed via a public application programming interface where developers can explore the potential of this new format within existing digital platforms.

These ePIs were created following the EU ePI Common Standard adopted by the European medicines regulatory network to provide a consistent structure throughout all Member States and ensure the information works across different e-health platforms. This should facilitate the use of product information to meet individual needs and access requirements. Future developments could include functionalities such as automatic update notifications, access to supportive videos or audio content, and online adverse-reaction reporting tools.



Global regulators celebrate 10 years of strategic leadership and cooperation

November 13–16, 2023

The year 2023 marked the 10th anniversary of the International Coalition of Medicines Regulatory Authorities (ICMRA). ICMRA was established in December 2013 by eight regulators to address a need for a global governance mechanism and stronger cooperation. Today, ICMRA consists of 38 members, with the World Health Organisation as an observer. ICMRA is currently chaired by the EMA with co-chairs from ANVISA Brazil and PMDA Japan.

The anniversary was celebrated during ICMRA’s annual summit and Plenary in Melbourne on November 13–16, hosted by the Therapeutic Goods Administration of Australia.¹ ICMRA members exchanged views and discussed topics such as the use of artificial intelligence and machine learning in medicine regulation, evolution of clinical trials, and

advanced medical products based on genes, cells, or tissue engineering.

In the past decade, ICMRA has made significant progress in a range of areas which are at the heart of the work of many regulators world-wide. Significant milestones include activities supporting the fight against antimicrobial resistance and the management of medicines shortages, but also topics such as clinical trials, pharmacovigilance, regulatory convergence and reliance, innovation, real-world evidence, and alignment in the global COVID-19 response.

ICMRA’s major achievement is the leadership provided by its members working together during the COVID-19 pandemic. The coalition worked to expedite and streamline development and approval of COVID-19 vaccines and treatments and helped to increase the efficiency and

effectiveness of regulatory processes and decision-making. ICMRA called for large, well-designed clinical trials to ensure regulators have solid evidence for decision-making and organised workshops on manufacturing, safety, and efficacy of COVID-19 vaccines. In June 2023, ICMRA received the Global Award for Outstanding Contribution to Health at the Drug Information Associations (DIA) Global Annual Meeting.

In the coming years, ICMRA will continue to address current and emerging human medicine regulatory and safety challenges, strengthen collaboration and communication, and enhance the quality, safety, and efficacy of medicines for the benefit of patients worldwide.

Reference:

1. ICMRA summit 2023. Available at: <https://dohac.eventsair.com/icmra-summit/agenda>

Sustainable communications

Medical journalism

Medical decision making

Mentorship

Social media

Writing for patients

Check out the back issues of EMWA’s journal *Medical Writing* at <https://journal.emwa.org>

Consumption of antimicrobials in animals reaches lowest level ever in Europe

November 20, 2023

European countries have substantially reduced sales of veterinary antibiotics, which translates into a lower risk of bacteria becoming resistant in people and animals. Overall sales of veterinary antibiotics decreased by 53% between 2011 and 2022, reaching the lowest level ever reported, according to data from 25 countries. This is one of the key findings of the 13th annual report on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), 2009–2023.

During the same period, sales of antibiotic classes that are considered critically important in human medicine for veterinary use noticeably decreased: sales of 3rd- and 4th-generation cephalosporins dropped by 49%, polymyxins by 81%, fluoroquinolones by 25%, and sales of other quinolones dropped by 90%. While all antibiotics should be used prudently and responsibly to preserve their effectiveness, it is of particular importance for these antibiotics to mitigate the potential risk to public health, as indicated in the Antimicrobial Advice ad hoc



Expert Group (AMEG) categorisation.

EMA has been monitoring sales of veterinary antimicrobials in Europe through the ESVAC project since 2009, when 9 European countries volunteered to provide data on sales of veterinary antimicrobials. The number of participating countries has increased more than three-fold since the start, and in 2022, 31 European countries were working together in this project.

ESVAC has led to the collection of reliable data on antimicrobials sold for use in animals, providing invaluable insights for participating countries on the impact of their measures to promote the prudent use and setting targets to reduce the consumption of antimicrobials in animals.

The ESVAC project is a European success story about commitment and strong collaboration. The project is coming to an end in 2023 and EMA will publish the last ESVAC report with data from 2022. The ESVAC concept has been integrated into the EU legislation, making the collection of data mandatory for all EU countries, not only for sales of veterinary antimicrobials but in the coming years also for use of antimicrobials in animals. The first report with sales and use data from 2023 will be published in 2025.

The last ESVAC report also includes information on the progress made towards the targets set in the EC's Farm to Fork Strategy to reduce the sale of antimicrobials for farmed animals and aquaculture in the EU. In 2022, the 27 EU Member States have achieved just over half of the 50% reduction target set for 2030 compared to 2018, proving that countries are on the right track of meeting the goals of the strategy.

First version of the Union list of critical medicines agreed to help avoid potential shortages in the EU

December 12, 2023

The EC, the Heads of Medicines Agencies (HMA), and EMA have published the first version of the Union list of critical medicines.¹ It contains more than 200 active substances of medicines for human use considered critical for healthcare systems across the EU/European Economic Area (EEA), for which continuity of supply is a priority and shortages should be avoided. The European Medicines Regulatory Network (EMRN) will prioritise critical medicines for EU-wide actions to strengthen their supply chain.

The list is an important tool to support the EU's efforts in ensuring supply security and preventing shortages of critical medicines. Inclusion in the list does not mean that the medicine is likely to experience a shortage in the near future. It means that the prevention of shortages is particularly important as a shortage could cause significant harm to patients and pose important challenges to health systems. A medicine is considered critical if it is used in serious diseases and cannot be easily replaced by other

medicines, for example in case of a shortage. It is included in the Union list of critical medicines if it meets certain criteria, including being critical in more than one third of EU/EEA countries.

The list contains active substances covering a wide range of therapeutic areas and includes vaccines and medicines for rare diseases. It reflects the outcome of the review of 600 active substances taken from six national lists of critical medicines. The Union list will be expanded in 2024 and will then be updated every year.

The review was carried out with all EU Member States, and criticality was assigned based on an agreed methodology developed in consultation with key stakeholder groups, including patients' and healthcare professionals' organisations and industry associations.

Medicines on the list can continue to be prescribed and used as usual by patients and healthcare professionals. Additional reporting requirements for marketing authorisation holders and national



EU medicines agencies reflect on lessons learned from COVID-19

December 01, 2023

The European Medicines Regulatory Network (EMRN) has been at the forefront of the fight against COVID-19 with its crucial role in the evaluation and monitoring of medicines, including vaccines. A joint report¹ issued by the EMA and the HMA reviews the Network's response and highlights the main learnings for any future health crises.

This review highlights some of the unprecedented challenges related to COVID-19 that had to be addressed, the activities and areas that enabled the effective response to the COVID-19 emergency, and provides recommendations on which improvements are needed.

Accelerated procedures for the evaluation of COVID-19 vaccines and therapeutics, as well as scientific recommendations on the use of certain medicines enabled the public health response through safe and effective prevention and treatment options. Collaboration between EU and international partners was also crucial to ensure that regulators around the world adopted a coordinated approach to COVID-19 treatments and vaccines.

The Network pooled its resources to address the increased workload and new tasks like managing medicine shortages, generating evidence on COVID-19 medicines in the real-world setting, and regularly providing reliable and

science-based information to the public. Additionally, the EU safety monitoring and risk management system was strengthened to collect and monitor the high volume of data from the mass vaccination campaigns. This allowed the Network to promptly identify, assess, and manage safety issues.

Throughout the COVID-19 crisis, the EMRN also ensured that medicines for other diseases affecting Europeans continued to be evaluated and supervised without delays.

The report suggests that more can be done in terms of the ability to set up large clinical studies in a rapid manner. In terms of real-world data, there is a need to gather multiple data sources that can generate useful evidence for regulatory assessments. The report also acknowledges the need to have a larger pool of experts that can be involved to carry out scientific assessments (such as accelerated reviews for promising medicines) when crisis situations arise.

The report has been adopted by EMA's Management Board. Several recommendations have already been implemented as part of EMA's extended mandate, with the Agency assuming an enhanced role on preparedness to be more proactive on

public health threats. HMA and EMA also continue working closely on areas such as resourcing, process improvements and communication. In addition, the ongoing review of the EU pharmaceutical legislation will also provide a vehicle to bring about other changes to the EU regulatory toolbox. The recommendations will also be considered in future updates of EMRN's strategy.

Reference:

1. COVID-19 lessons learned – Joint report on the response to the public health emergency. Updated on December 01, 2023. Available at: <https://www.ema.europa.eu/en/human-regulatory-overview/public-health-threats/coronavirus-disease-covid-19>



competent authorities will be established and become effective once the proposed pharmaceutical legislation becomes applicable.

The publication of the Union list will not impact existing or to-be-established national lists of critical medicines. However, it will support the network's efforts in drawing up national lists where these do not yet exist. In addition, it will support and expedite the EC's analysis of the supply chain of critical medicines to determine potential vulnerabilities. The EC and EMA's Medicines Shortages Steering Group (MSSG) may propose measures to address vulnerabilities in the supply of those medicines, to ultimately prevent and mitigate shortages. More information on the list, including its composition, how it was established and how it will be used, is available in a question-and-answer document on EMA website.¹

The Union list of critical medicines comple-

ments other measures adopted by the EMA/HMA taskforce on availability of authorised medicines and by the MSSG, such as good practices for industry and for patients and healthcare professional organisations for the prevention of medicine shortages, the recently created MSSG solidarity mechanism, the MSSG toolkit, and the MSSG's recommendations for actions to avoid shortages of key antibiotics used to treat respiratory infections.

Reference

1. Availability of critical medicines. December 12, 2023. Available at: <https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/medicine-shortages-and-availability-issues/availability-critical-medicines#ema-inpage-item-64278>



First gene-editing therapy to treat beta thalassaemia and severe sickle cell disease

December 15, 2023

EMA has recommended approval of the first medicine using CRISPR/Cas9, a novel gene-editing technology. Casgevy (exagamglogene autotemcel) is indicated for the treatment of transfusion independent beta thalassaemia and severe sickle cell disease in patients 12 years of age and older for whom haematopoietic stem cell transplantation is appropriate and a suitable donor is not available. This new therapy may free patients from the burden of frequent transfusions and painful vaso-occlusive crises that occur when sickled red blood cells block small blood vessels and has the potential to significantly improve their quality of life.

Beta thalassaemia and sickle cell disease (SCD) are two inherited rare diseases caused by genetic mutations that affect the production or function of haemoglobin, the protein found in red blood cells that carries oxygen around the body. Both diseases are life-long debilitating and life-threatening.

Casgevy is a cell-based gene therapy medicinal product using CRISPR/Cas9 technology to edit the patient's own blood stem cells. It is a personalised one-off treatment that involves mobilising bone marrow stem cells from a patient's blood. CRISPR gene-editing finds a specific sequence of DNA inside a cell. Using "molecular scissors" to make precise cuts, it

enables adding, removing, or altering genetic material at that specific location of the genome of the cells. With Casgevy, stem cells are edited at the erythroid-specific enhancer region of the BCL11A gene which usually prevents the production of foetal haemoglobin (HbF). These modified cells are then infused back into the patient, and the reduction of BCL11A gene transcription leads to increase of HbF production thus providing functioning haemoglobin.

EMA based its recommendation on two ongoing, single-arm trials in patients aged 12 to 35 years. In the first one, 42 patients, including 13 adolescents, with transfusion-dependent beta thalassaemia who received a single dose, were included in the primary efficacy set. Of these 42 patients, 39 were transfusion-free for at least one year. In the second trial, 29 patients, including six adolescents, suffering from severe SCD, were included in the primary efficacy set. Of these 29 patients, 28 were free of vaso-occlusive crises (VOC) episodes for at least 12 consecutive months. Characterised by severe pain and organ damage, VOC is the leading cause of emergency department visits and hospitalisations for patients with SCD.

The safety of Casgevy was evaluated in the same two ongoing, single-arm trials and one long-term follow-up study, in which 97 adolescent and

adult patients with transfusion-dependent beta thalassaemia or SCD were treated with the medicine.

The most common side effects are low white blood cell counts including febrile neutropenia, low level of platelets, liver disease, nausea, vomiting, headache, and mouth sores. These events are due to the medicines required for the modified blood cells to engraft and replace the unmodified stem cells.

Casgevy was supported through EMA's PRiority Medicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs. Casgevy is recommended for a conditional marketing authorisation, one of the EU's regulatory mechanisms to facilitate early access to medicines that fulfil an unmet medical need. This type of approval allows the Agency to recommend a medicine for marketing authorisation with less complete data than normally expected, if the benefit of a medicine's immediate availability to patients outweighs the risk inherent in the fact that not all the data are yet available.

In order to confirm the efficacy and safety of Casgevy, the company will have to submit the final results obtained from the currently ongoing



pivotal trials by August 2026, as well as results from the ongoing long-term follow-up study and other studies that will be conducted with the product. Patients treated with Casgevy will be followed up for 15 years, to monitor the long-term efficacy and safety of this gene therapy. To further characterise the long-term safety and efficacy of the medicine, the company will also have to conduct and submit the results of a study based on data from a patient registry.

In its overall assessment of the available data, the Committee for Advanced Therapies (CAT), EMA's expert committee for cell and gene-based medicines, found that the benefits of Casgevy outweighed the possible risks in patients with beta thalassemia and SCD. The CHMP, EMA's human medicines committee, agreed with the CAT's assessment and positive opinion, and recommended approval of this medicine.

The opinion adopted by CHMP is an intermediary step on Casgevy's path to patient access. The opinion will now be sent to the EC for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role or use of this medicine in the context of the national health system of that country.



Artificial intelligence workplan to guide use of AI in medicines regulation

December 18, 2023

EMA and the HMAs have published an artificial intelligence (AI) workplan to 2028, setting out a collaborative and coordinated strategy to maximise the benefits of AI to stakeholders while managing the risks.

The workplan will help European Medicines Regulatory Network (EMRN) to embrace the opportunities of AI for personal productivity, automating processes and systems, increasing insights into data, and supporting more robust decision-making to benefit public and animal health. The AI workplan, prepared under the joint HMA-EMA the German Federal Data Protection Act (BDSG), ensures the EMRN remains at the forefront in benefiting from AI in medicines regulation. The workplan was adopted by EMA's Management Board at its December, 2023, meeting.

The field of AI is developing swiftly. Pharmaceutical companies increasingly use AI-powered tools in research, development, and monitoring of medicines. National competent authorities are responding to the new opportunities and challenges by starting to use and develop AI tools. The workplan focuses on four key dimensions:

● **Guidance, policy, and product sup-**

port: Actions focus on continuous support to products in development as well as the development and evaluation of appropriate guidance for the use of AI in the lifecycle of a medicine. Work has already begun with the ongoing public consultation on the AI reflection paper, open until the end of December 2023. Furthermore, in 2024 preparations to support the implementation of the EU AI Act will start.

- **AI tools and technology:** The aim is to identify and provide frameworks across the network to use AI tools to increase efficiency, enhance understanding and analysis of data, and support decision-making. Full compliance with data protection legislation will be ensured.
- **Collaboration and training:** Initiatives are designed to continuously develop capacity and capability of the network, partners, and stakeholders to keep ahead of the evolving field of AI.
- **Experimentation:** The workplan acknowledges the fundamental role of experimentation in accelerating learning and gaining new insights. Several actions are proposed to ensure a structured approach to experimentation across the network.

As AI technology is fast evolving, including the ethical and policy aspects related to it, the BDSG will regularly update the workplan. Regulators, medicine developers, academics, patient organisations and other interested parties will be informed and engaged throughout the implementation of the plan.