News from the EMA

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EMA to support establishment of the African Medicines Agency

January 26, 2024

EMA will harness its unique experience in coordinating intra-regional medicines regulation to support the strengthening of the African regulatory network.

EMA has received a grant of ten million euros from the European Commission to support regulatory systems at national and regional level in Africa, and in particular for the setting up of the African Medicines Agency (AMA), in collaboration with African, European, and international actors. The European Commission's Directorate-General for International Partnerships has signed an agreement with EMA marking the official launch of the project.

AMA will be a specialised agency of the African Union (AU) dedicated to improving equitable access to quality, safe, and effective medical products in Africa. To date, 27 countries have ratified the AMA treaty, and more AU members are expected to complete the process in the coming months. The creation of AMA is a unique opportunity to facilitate the regulation and oversight of key medicines at continental level, promoting collaboration among African countries and regions.

Cooperation and collaboration are in the DNA of the European medicines regulatory network (EMRN). The EMRN is the cornerstone of EMA's work and success. The Agency operates at the heart of the network, coordinating and supporting interactions between over fifty national competent authorities for human and veterinary medicines. By sharing its unique expertise and regulatory model, the EMRN will share experience with AMA in pooling resources and coordinating work to regulate medicines efficiently and effectively, ensuring high-quality standards and use of the best available expertise, reducing administrative burden to allow medicines to reach patients faster and accelerating the exchange of information on critical issues such as medicines safety.

EMA has committed to mobilising experts to support AMA, its technical committees, and African regulators in the set-up of AMA's governance and scientific and administrative processes. EMA will also offer training to reinforce scientific and regulatory expertise in the evaluation and supervision of medicines together with experts from European Union (EU) Member States.

EMA's contribution is part of the 'Team Europe' initiative on manufacturing and access to vaccines, medicines, and health technologies in Africa (MAV+), launched by the Commission in May 2021. Under the EU's Global Gateway strategy, the initiative has mobilised so far 1.3 billion euros including around 135 million euros in grants for regulatory strengthening. Working together with EU Member States, African partners such as the African Union Development Agency (AUDA-NEPAD) and the World Health Organisation (WHO), the European Union will help to strengthen regulatory capacity in Africa with a comprehensive set of actions at continental, regional, and national levels.

New platform for collection of sales and use data of antimicrobials in animals

January 29, 2024

EMA has just launched the new Antimicrobial Sales and Use (ASU) Platform to support the collection of data by Member States on the sales and use of antimicrobials in animals. As of January 2024, all Member States in the EU and European Economic Area (EEA) must submit these data annually to the ASU Platform. This new obligation was introduced by the Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6) as one of the measures to fight antimicrobial resistance.

The collection of data on the sales and use of antimicrobials in animals has always been critical in the fight against antimicrobial resistance. The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project was in place between 2009 and 2023 as a voluntary initiative by EMA and European countries to monitor the sales of veterinary antimicrobials in Europe. It served as a blueprint for the ASU Platform that supports and enhances the EU's actions to address antimicrobial resistance. It requires that all Member States submit data on sales of veterinary antimicrobials and use of antimicrobials in animals in a standardised format, enhancing the collection of data and their integration in a robust system.

The new IT system and web interface will not only streamline the submission of data for the Member States, but it will also strengthen the analysis and identification of trends in antimicrobial consumption across the EU/EEA. Access to reliable data provides invaluable insights for participating countries on the impact of their measures to promote the prudent use of antimicrobials in animals and could help to identify potential actions at national and international levels to support an overall decrease of AMR.

EMA will publish annual reports showcasing the main results of the analysed data, with the first report expected in March 2025, after the first reporting cycle is concluded. It will also develop a public interactive database on a business intelligence interface, that will help to further disseminate the outcomes of the ASU Platform data analysis. A timeline for implementation and guidance to assist national competent authorities to implement the legislative requirements are available on EMA's website. The reporting of data on use in animal species will be implemented gradually.

Launch of new HMA-EMA catalogues of real-world data sources and studies

February 15, 2024

EMA and the Heads of Medicines Agencies (HMA) have launched two public electronic catalogues: one for real-world data (RWD) sources and one for RWD studies.

The catalogues help medicines regulators, researchers, and pharmaceutical companies to identify the most suitable data sources to address specific research questions and support the assessment of study protocols and results. They aim to promote transparency, encourage the use of good practices, and build trust in research based on RWD. The initiative builds on more than 15 years of operation of the former databases, developed by the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP):

- The catalogue for RWD sources enhances and replaces the ENCePP Resources Database, an EMA-coordinated index of resources of available research organisations, networks, and data sources in the fields of pharmacoepidemiology and pharmacovigilance within Europe.
- The catalogue for RWD studies expands and replaces the European Union electronic register of post-authorisation studies (EU PAS Register®).

As part of this initiative, the ENCePP website has been renewed. While some data sources and all centres and networks have migrated to the new catalogues replacing the ENCePP Resource Database, other content, such as ENCePP Guide on Methodological Standards in Pharmacoepidemiology and the ENCePP Code of Conduct, will remain available on the renewed ENCePP website.

The catalogues introduce various improvements to the previous ones. Using FAIR (Findable, Accessible, Interoperable, and Reusable) data principles, they use an agreed set of metadata to describe and connect data sources to studies. It is based on the list of metadata published by the HMA-EMA Big Data Steering Group in May 2022. A revised list will be published soon. In addition, search on a wider set of metadata, enhanced view, export, and data submission functionalities have been implemented in the catalogues.

The publication of the RWD catalogues brings the EMRN closer to more data-driven regulation. Improving discoverability of data is one of the priorities set in the HMA-EMA joint Big Data Task Force final report (phase two), reflected in the European medicines agencies network strategy to 2025 and implemented through the joint HMA-EMA Big Data Steering Group workplan. Ultimately, these developments will help European patients receive better medicines faster and promote safe and effective use of the medicines on the market.

All European data holders, marketing authorisation holders, networks, researchers, and institutions who are interested in having their data used for medicines regulation or are obligated by policy on non-interventional post-authorisation safety studies (PASS), are encouraged to use these catalogues.

New recommendations to strengthen supply chains of critical medicines

April 23, 2024

EMA has published a number of recommendations to address vulnerabilities in the production and delivery of medicines included in the Union list of critical medicines and strengthen their supply chain (Reference Number: EMA/44164/2024).

These recommendations have been developed by EMA's Medicines Shortages Steering Group (MSSG) and will facilitate the availability and supply of critical human medicines for which vulnerabilities in the supply chain have been identified. Measures considered by the MSSG will be selected according to the risks posed to the supply chain and the type of medicine, and include:

- Possible recommendations to marketing authorisation holders (MAHs) to increase manufacturing capacity and diversify the suppliers in the supply chain (for example through the addition of alternative manufacturing sites), and to monitor forecasts of supply and demand of medicines and available stocks in the entire supply chain.
- Recommendations to certain actors in the supply chain, such as MAHs, and the European Commission to stockpile medicines to protect against fluctuations in demand or supply.
- The possibility to request a MAH to establish a shortage prevention plan for medicines in the Union list of critical medicines. EMA will publish guidance and templates for shortage prevention plans in June 2024.
- Provision of scientific and regulatory support to address vulnerabilities in the supply chain, including assistance to small and medium-sized enterprises.

Use of work-sharing procedures or other types of reliance on assessments conducted by another recognised authority, and accelerated timetables for required variations to address supply chain vulnerabilities of critical medicines.

The MSSG will work closely with the European Commission's Critical Medicines Alliance (CMA). The MSSG will develop regulatory and governmental policy recommendations focused on short- to medium-term actions, while the CMA will focus on long-term measures in the field of industrial policy to address vulnerabilities in the supply chain of critical medicines.

In case of critical shortages of medicinal products included in the Union list, the MSSG Toolkit on recommendations on tackling shortages of medicinal products would apply.

New treatment for rare motor neurone disease recommended for approval

February 23, 2024

EMA has recommended granting a marketing authorisation in the EU for a new therapy for the treatment of adult patients with amyotrophic lateral sclerosis (ALS), a rare and often fatal disease that causes muscles to become weak and leads to paralysis. Qalsody (tofersen) is indicated for the treatment of adults with ALS, who have a mutation in the superoxide dismutase 1 (SOD1) gene.

In patients with ALS the nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing increasing loss of muscle function and paralysis of voluntary muscles, including respiratory muscle, which ultimately leads to respiratory failure. ALS is a devastating disorder. The mean survival time with ALS is two to five years.

The exact causes of ALS are unknown but are believed to include genetic and environmental factors. In approximately 2% of people living with ALS, the condition is caused by a genetic mutation (change) that leads to the production of defective SOD1 enzymes, causing nerve cells to die.

Currently, there is only one treatment for ALS (riluzole) authorised in the EU. Patients are offered supportive treatment to relieve the symptoms of the disease, such as physical, occupational or speech therapy and breathing support. There is a large unmet medical need for effective therapies that preserve muscle function and prolong the life of patients with ALS.

Qalsody is an antisense oligonucleotide that binds to the mRNA of the SOD1 gene to reduce the production of SOD1 protein. By reducing the amount of defective SOD1 protein, this medicine is expected to improve the symptoms of ALS.

The opinion by EMA's committee for human medicines (CHMP) is based on the totality of evidence, including the targeted way the drug works, effects observed in a SOD1 animal model, biomarkers, and clinical data.

Clinical data were obtained from a 28-week, randomised, double-blind, placebo-controlled clinical study in 108 patients aged 23 to 78 years with weakness attributable to ALS and a SOD-1 gene mutation confirmed by a central laboratory. The study randomly assigned 108 patients in a 2:1 ratio to receive treatment intrathecally (through a spinal injection) with either Qalsody or placebo for 24 weeks. Plasma neurofilament light chain (NfL) was measured during the study as a marker of damage and deterioration of axons (thread-like structures attached to nerve cells that send out signals away from the cell). Reductions of approximately 60% in plasma NfL concentrations were observed in patients who received Qalsody compared to the placebo group, suggesting reduced neuronal injury. There was also a numerical improvement noted in the physical abilities of patients who received Qalsody compared to the study participants who received placebo, as measured by the standard rating scale known as "ALS Functional Ratings Scale–Revised" (ALSFRS-R).

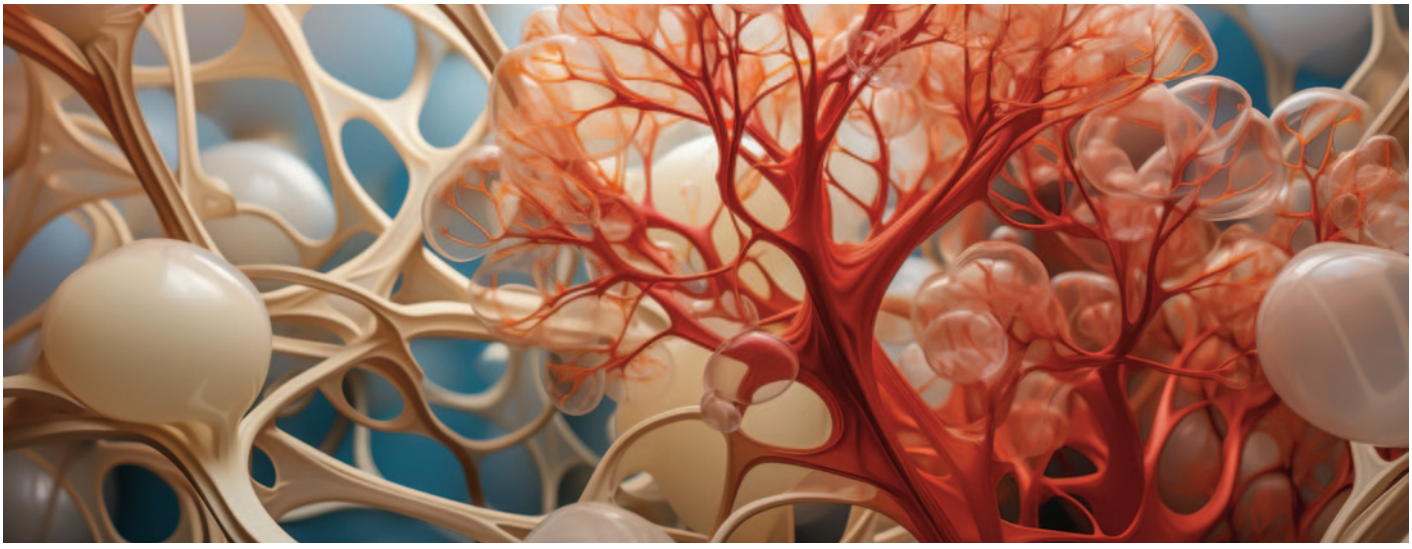
The CHMP requested the applicant to submit data post-authorisation to further characterise the long-term efficacy and safety of Qalsody, on the basis of an open-label long-term extension study, collaboration with two disease registries, and an observational registry-based study. In addition, it will be investigated if the use of tofersen can delay or even prevent emergence of clinically manifested ALS in presymptomatic SOD1-ALS patients.

The most commonly reported side effects were pain, fatigue, pyrexia (fever), arthralgia (joint pain), myalgia (muscle pain), and increased levels of white blood cells and proteins in the cerebrospinal (brain and spinal cord) fluid.

The CHMP consulted patient representatives during the assessment of benefits and risks of Qalsody to ensure that patients' needs and their perspective are taken into account in the regulatory decision-making process.

The recommendation made by the CHMP is for a marketing authorisation under exceptional circumstances. This route of authorisation allows patients access to medicines for which comprehensive data cannot be obtained under normal conditions of use, either because there are only very few patients with the disease, the collection of complete information on the efficacy and safety of the medicine would be unethical, or there are gaps in the scientific knowledge. These medicines are subject to specific post-authorisation obligations and monitoring.

The opinion adopted by the CHMP is an intermediary step on Qalsody's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on the 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.



New antibiotic to fight infections caused by multidrug-resistant bacteria

March 22, 2024

EMA has recommended granting a marketing authorisation in the EU for Emblaveo (aztreonam-avibactam), indicated for the treatment of complicated intra-abdominal and urinary tract infections, hospital-acquired pneumonia, and infections caused by certain types of bacteria (aerobic Gram-negative) where treatment options are limited.

Infections due to Gram-negative bacteria that are resistant to many currently available antibiotics are a serious public health problem since patients have limited or sometimes no treatment options. Infections due to multidrug-resistant bacteria are estimated to cause 35,000 deaths in the EU every year.

Emblaveo will be available to be given by infusion into a vein. It is a fixed-dose combination of two active substances, aztreonam and avibactam.

- Aztreonam is already authorised for use in the EU on its own and avibactam is authorised for use in combination with another antibiotic (ceftazidime). Aztreonam is an antibiotic that belongs to the group "beta-lactams". It works by attaching to proteins on the surface of the bacteria. This prevents the bacteria from building their cell walls, which kills them. Aztreonam has been shown to be effective at treating a range of serious infections.
- Avibactam blocks the action of many of the bacterial enzymes called beta-lactamases. These enzymes enable bacteria to break down beta-lactam antibiotics, such as aztreonam, making them resistant to the antibiotic's action. By blocking these enzymes, avibactam restores the activity of aztreonam against aztreonam-resistant bacteria.

EMA's human medicines committee (CHMP) considered that the benefits of Emblaveo outweigh its risks for patients with infections caused by Gram-negative bacteria when they have few or no therapeutic options to fight the disease. Microbiology data indicate that aztreonam in combination with avibactam will be effective in infections caused by many multidrug-resistant aerobic Gram-negative pathogens and the combination could therefore address an unmet medical need.

Emblaveo was evaluated under EMA's accelerated assessment mechanism because it is considered to be of major public health interest. EMA's recommendation is based on the safety and efficacy data already available for each active substance and the results of two phase III randomised studies submitted by the applicant. The studies were not designed to demonstrate efficacy but do provide safety and complementary data for the combination. This is in line with EMA's guideline that allows for a flexible approach in the development of new antibiotics for human use targeting multidrug-resistant pathogens for which new treatments are needed.

The most frequent side effects in patients treated with Emblaveo were a decrease in the number of red blood cells, elevated levels of liver transaminase, and diarrhoea. This is in line with the documented safety information available for each individual substance.

The opinion adopted by the CHMP is an intermediary step on Emblaveo's path to patient access. The opinion will now be sent to the European Commission 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.

EU recommendations for 2024/2025 seasonal flu vaccine composition

March 26, 2024

Influenza viruses continuously change and evolve. The periodic replacement of the virus strains contained in influenza vaccines is therefore necessary to keep the vaccines effective. The recommendations for the influenza season 2024/2025 were endorsed by EMA's human medicines committee (CHMP) at its March 2024 meeting.

EMA has issued recommendations for the influenza virus strains that vaccine manufacturers should include in vaccines for the prevention of seasonal influenza from autumn 2024. Every year, EMA issues EU recommendations for the composition of seasonal influenza vaccines on the basis of observations by the WHO which are informed by regular monitoring activities on the prevalence and characteristics of different influenza viruses worldwide.

Based on this data EMA's Emergency Task Force (ETF) has issued a statement recommending a transition from quadrivalent to trivalent vaccines that do not include the B/Yamagata component. Currently, most authorised influenza vaccines are quadrivalent, which means that they are formulated to protect against the four main strains of influenza responsible for seasonal flu, A(H1N1)pdm09 and A(H3N2), B/Victoria and B/Yamagata. However, the B/Yamagata strain of the influenza B virus has not been detected in circulation since March 2020. This is thought to be due in part to the public health measures put in place to limit the spread of COVID-19 during the pandemic. Influenza B viruses are responsible for a quarter of annual influenza infections.

Given that the B-Yamagata virus strain no longer seems to pose a threat to public health, it is not necessary to include it in the formulation of influenza vaccines. The ETF recommends that this strain should ideally be removed from all live-attenuated vaccines from the 2024/2025 season. In the interest of guaranteeing vaccine supplies for the coming vaccination campaign, the transition to a trivalent composition for all other influenza vaccines should be completed for the 2025/2026 season.

Taking into account the statement from the ETF and the insights and recommendation from the WHO, the EMA's ad hoc Influenza Working Group, has issued the following strain recommendations for this year. Manufacturers of live-attenuated vaccines, or egg-based trivalent vaccines should include these three virus strains for the 2024/2025 season:

- A/Victoria/4897/2022 (H1N1)pdm09-like virus
- A/Thailand/8/2022 (H3N2)-like virus
- B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

Manufacturers of cell-based trivalent vaccines should include these three virus strains for the 2024/2025 season:

- A/Wisconsin/67/2022 (H1N1)pdm09-like virus
- A/Massachusetts/18/2022 (H3N2)-like virus
- B/Austria/1359417/2021 (B/Victoria lineage)-like virus

Manufacturers of inactivated vaccines can consider producing a quadrivalent vaccine containing two influenza B virus strains for the 2024/2025 season. In that case a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus in addition to the strains mentioned above is considered appropriate.

The Agency recommends that marketing authorisation holders submit applications to change the composition of centrally authorised seasonal influenza vaccines by June 17, 2024.