

News from the EMA

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Paving the way towards coordinated clinical trials in public health emergencies in the EU

July 25, 2023

EMA has published a report¹ from a workshop that collected insights and suggestions for possible European Union (EU)-level actions to improve the way clinical trials are set up and conducted in the EU during public health emergencies. The actions presented in the report aim to holistically address the barriers and challenges experienced during the COVID-19 pandemic and the outbreak of mpox disease in setting up adequately sized clinical trials across multiple Member States that enable rapid gathering of sufficient, high-quality evidence to support robust decision-making by health authorities across the EU.

The workshop was organised by EMA's Emergency Task Force (ETF) and the European Commission (EC) on June 9, 2023, with participation from national competent authorities (NCAs), ethics committees' representatives, and academic sponsors.

The workshop discussions emphasised the need for larger studies across several European countries, speedier recruitment, and delivery of conclusive results with accelerated timelines during a public health emergency. Proposed actions focus on two areas:

- The processing and regulatory approval of large, multinational clinical trials in the EU during public health emergencies. This includes e.g., improving coordination between regulators and ethic committees within and across Member States, speeding up assessment and authorisation of clinical trial applications, exploring flexibilities in the implementation of the Clinical Trials Regulation, facilitating the use of the EU Clinical Trials Information System (CTIS);
- The framework for funding and efficient allocation of resources for clinical trials during emergencies in the EU, including the establishment of a Coordinating Committee to support prioritisation of trials, improved mechanisms to identify and rank promising compounds, mobilising EU and Member State funding mechanisms, and measures to help speed up contracting of clinical trial sites.

According to the recommendations, ETF's essential role of providing scientific advice, reviews, and supporting large clinical trials in emergency situations, should be expanded to also include concerned ethics committees on a

voluntary basis to discuss and coordinate clinical trials protocols.

The workshop participants emphasised the need to make Europe a better place for research. The proposed actions will be taken into account by the EC, EMA, and the Member States in establishing a concrete roadmap for improved clinical trials during public health emergencies in the EU. The work on approvals of clinical trials in public health emergencies will be taken forward by the Accelerating Clinical Trials in the EU (ACT EU) initiative, the EU collaboration between the EC, Heads of Medicines Agencies (HMA) and EMA that seeks to transform how clinical trials are initiated, designed, and run. The framework for funding will be specifically discussed with the EC and Member States in the context of current efforts to improve the coordination for funded clinical research in the EU and with international actors.

Reference:

1. Report of the EMA/ETF workshop on Lessons Learned on Clinical Trials in Public Health Emergencies. First published July 25, 2023; [EMA/340269/2023](https://www.ema.europa.eu/en/press-material/press-release/press-release-2023-07).



Towards a permanent collaboration framework for EMA and Health Technology Assessment bodies

September 15, 2023

Over the past three years, EMA and the EUnetHTA 21 (European Network for Health Technology Assessment) consortium have delivered a number of milestones to prepare the EU for the entry into application of the Regulation on Health Technology Assessment. EUnetHTA 21 ceased to operate on September 16, 2023, but preparations will continue for the implementation of the Regulation, under the direction of the Health Technology Assessment (HTA) Coordination Group.

Reviewing achievements over the years at their concluding meeting on September 14, 2023, in Amsterdam, EMA and EUnetHTA 21 highlighted a number of initiatives:

- Completion of seven parallel joint scientific consultations (JSC) for medicines under the EUnetHTA 21 consortium contract. This joint work is intended to improve the generation of robust evidence that meets the needs of regulators and HTA bodies;
- Discussion on evidence needs for advanced therapy medicinal products in oncology, addressing mutual challenges such as indirect comparison and addressing evidence gaps through post-licensing evidence generation;
- Organisation of trainings for patients and healthcare professionals to facilitate their participation as experts in regulatory and HTA processes, alongside collaborative work on methodologies for engagement of patients

and healthcare professionals in assessments;

- Recommendations to optimise the assessment reports of EMA's Committee for Human Medicines (CHMP) for each medicine in order to systematically document key elements of the assessment such as the eligible patient population, choice of comparator and endpoints, as well as relevance of subgroup data.

More information on the achievements is available in a technical report.¹

The Regulation on Health Technology Assessment (EU) 2021/228 which entered into force in January 2022 and applies as of January 2025, will govern the European cooperation between medicine regulators and HTA bodies. Under the new framework, EMA and HTA bodies will collaborate in the context of joint clinical assessments, JSC, and the identification of emerging health technologies.

While aiming to improve the availability of innovative medicines and certain medical devices for patients in the EU, it will also ensure efficient use of resources and enhance the quality of health technology assessment in the EU by ensuring the sustainability of European cooperation. The establishment of the Member State Coordination Group on Health Technology Assessment, as provided by the regulation, and of a stakeholder network, will give a transparent and inclusive

framework to facilitate continued collaboration between partners and reduce duplication of efforts for national HTA authorities and industry.

For the transition period (up to January 2025), EMA and HTA organisations have established a new framework for Parallel EMA/HTA Scientific Advice for the period September 2023 until January 2025, when the HTA Regulation applies. During this transition period, developers can request the involvement of HTA bodies when applying for EMA scientific advice. The outcome of the procedure will be a scientific advice letter from EMA and individual written recommendations from participating HTA bodies. The selection criteria are available in the Guidance on Parallel EMA/HTA body (HTAb) Scientific Advice for the Interim Period.

Preparations are also continuing at EMA to pave the way for the implementation of the regulation. The agency has identified a number of priorities and opportunities for the next 15 months. These include defining a single evidence plan to facilitate development programmes, harmonising views on the strength of the evidence, and involving patients, clinical experts, and other relevant experts in decision-making.

Reference:

1. Report on the implementation of the EMA-EUnetHTA 21 work plan 2021 – 2023. First published September 15, 2023; EMA/290158/2023.

Revised transparency rules for the EU Clinical Trials Information System

October 06, 2023

EMA has adopted revised transparency rules¹ for the publication of information on clinical trials submitted through the CTIS. The simplifications introduced will give access to clinical trial information to stakeholders including patients and healthcare professionals in a faster and more efficient way.

One of the key changes of the revised rules is the removal of the deferral mechanism, which allowed sponsors to delay the publication of

certain data and documents for up to seven years after the end of the trial to protect personal data and commercially confidential information (CCI).

The updated rules strike a balance between transparency of information and protection of CCI. They benefit patients, because key clinical trial information, that patients flagged as being most relevant for them, is published early. They also introduce process simplifications that benefit

clinical trial sponsors who have to protect CCI and personal data. Finally, they benefit healthcare professionals because the resulting system is more user-friendly, facilitating access to information about clinical trials and enrolment in clinical trials, and also increasing awareness of possible treatment options.

The updates were triggered by feedback from stakeholders and experience after the launch of the system. An eight-week public consultation was held between May and June, 2023.

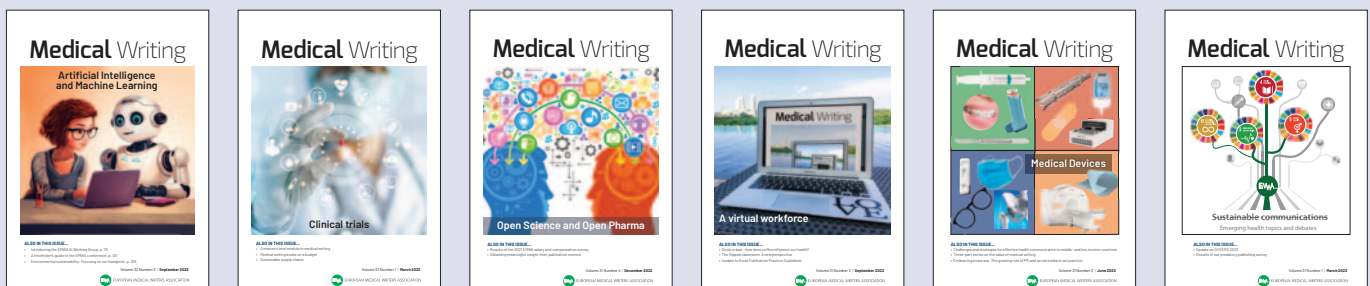
The revised transparency rules will apply after their technical implementation in CTIS, including its public portal, which is expected to be finalised in the second quarter of 2024. The effective date of completion of the process and the entry into application of the new rules will be communicated to the users of the system before they become applicable.

CTIS is the single-entry point in the EU for the submission and assessment of applications for clinical trials for sponsors and regulators. The system includes a public searchable database for healthcare professionals, patients, and the general public to deliver the high level of transparency foreseen by the regulation.

The authorisation and oversight of clinical trials is the responsibility of EU/EEA Member States while EMA is responsible for maintaining the CTIS. The EC oversees the implementation of the Clinical Trials Regulation.

Reference:

1. Revised CTIS Transparency Rules.
First published October 5, 2023;
EMA/263067/2023.



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and machine learning

Clinical trials

Open Science and
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Medical Devices

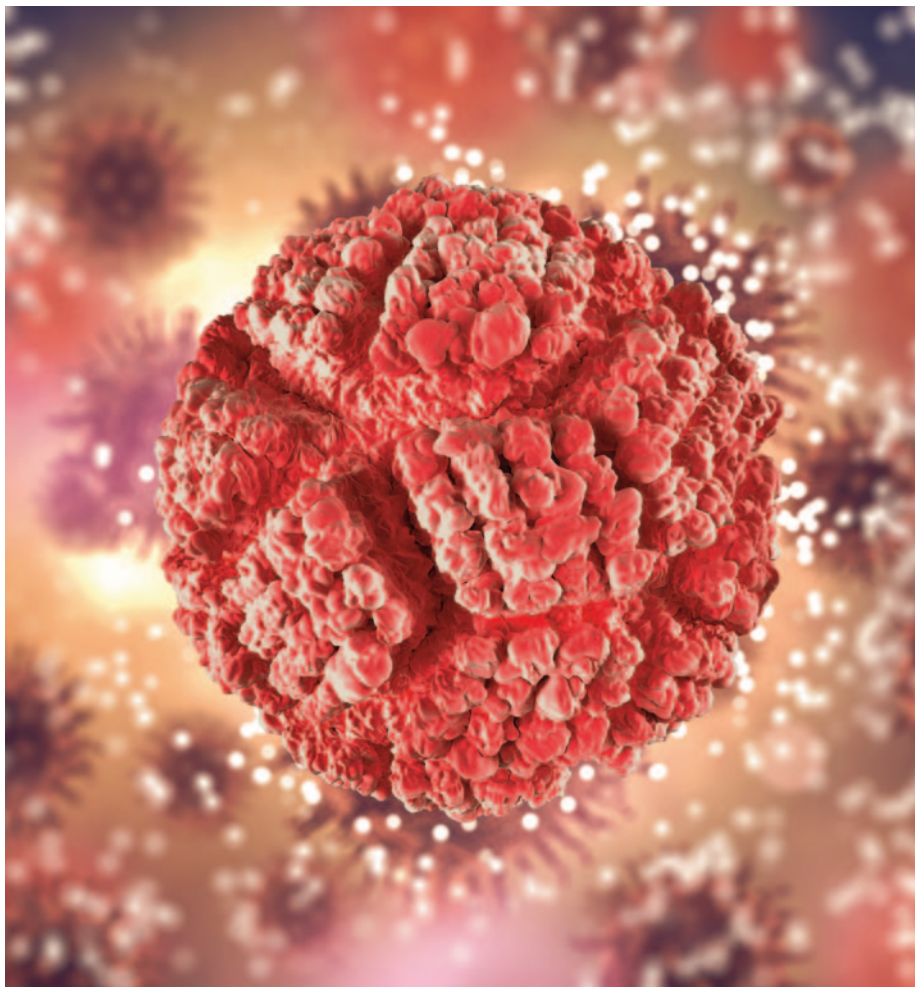
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New treatment option for heavily pre-treated multiple myeloma patients

October 13, 2023



EMA's human medicines committee (CHMP) has recommended a conditional marketing authorisation in the EU for Elrexio (elranatamab; Pfizer Europe MA EEIG) as a monotherapy (used on its own) for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies and whose cancer has worsened since they received their last treatment.

Multiple myeloma is a rare cancer of the plasma cells, a type of white blood cell that produces antibodies and is found in the bone marrow. In multiple myeloma, the proliferation of plasma cells is out of control, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. When plasma cells become cancerous, they no longer protect the body from infections and produce abnormal proteins that can cause problems affecting the kidneys, bones, or blood.

A range of new medicines for the treatment of multiple myeloma have been developed and

approved in recent years, leading to a steady overall improvement in patient survival. However, new medicines are needed for patients who have already been treated with the three main classes of medicines (immunomodulatory agents, proteasome inhibitors, and monoclonal antibodies) and who no longer respond to them.

Elranatamab, the active substance in Elrexio, is a monoclonal antibody that targets two proteins simultaneously. By attaching at the same time to a protein called B-cell maturation antigen (BCMA), which is present on the surface of the multiple myeloma cells, and to CD3, a protein that is present on the T cells (cells in the immune system), the medicine activates the T cells to kill the multiple myeloma cells.

The CHMP based its recommendation for a conditional marketing authorisation on an open-label, single arm, multicentre, phase 2 clinical trial. The part of trial that was considered as pivotal investigated the efficacy of Elrexio monotherapy in 123 participants with

refractory multiple myeloma who had received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, but who had not received prior BCMA-directed therapy. 61% of patients enrolled in the trial responded to the treatment with Elrexio and more than 70% of the responding patients have a probability to live without their disease getting worse for an average of 15 months.

The overall safety profile of elranatamab was established by analysing data from 265 participants. The most common side effects are a decrease in blood cells, infections, and cytokine release syndrome (CRS) (i.e. a condition causing fever, vomiting, shortness of breath, headache, and low blood pressure). One of the main risks associated with elranatamab use is neurological toxicity including immune effector cell-associated neurotoxicity (ICANS), as these events have the potential to be life-threatening or fatal if not properly managed. Monitoring and mitigation strategies for CRS and ICANS are described in the product information and in the risk management plan that is an integral part of the authorisation.

Elrexio 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. Elrexio is now recommended for a conditional marketing authorisation, one of the EU 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 results obtained from the pivotal trial, the company will have to submit data from a randomised phase 3 trial comparing the efficacy and safety of elranatamab monotherapy and elranatamab used in combination with daratumumab versus the treatment regimen daratumumab, pomalidomide, and dexamethasone in adults with relapsed or refractory multiple myeloma who have received at least one prior line of therapy, but not more than three, including lenalidomide and a proteasome inhibitor. The company is also required to submit the final results of the pivotal phase 2 clinical trial.

EMA alerts EU patients and healthcare professionals to reports of falsified Ozempic pens

October 18, 2023

The EMA has been notified by relevant national competent authorities that pre-filled pens falsely labelled as the diabetes medicine Ozempic (semaglutide, 1 mg, solution for injection) have been identified at wholesalers in the EU and the UK. There is no evidence that any falsified pens have been dispensed to patients from legal pharmacies and there are no reports of harm to patients in relation to the falsified medicine.

The pens, with labels in German, originated from wholesalers in Austria and Germany. The pens have batch numbers, 2D barcodes, and unique serial numbers from genuine Ozempic packs. In the EU, each medicine pack has a unique 2D barcode and serial number so that it can be tracked in an EU-wide electronic system. When the packs of the falsified Ozempic were



scanned, the serial numbers were shown to be inactive, thereby alerting operators to a potential falsification.

There are differences in the appearance between the falsified pen and the original pen. A picture of the falsified pen has been published by the German medicines agency (please note that the picture of the falsified pen is an example and

falsified pens with other features are also likely).

The issue is currently being investigated by EU medicines regulatory authorities and the police. EMA is assisting national authorities in their investigations. Wholesalers and pharmacies in the impacted countries have been warned about the suspicious offers of Ozempic to wholesalers. In addition, parallel distributors across the EU have been alerted.

In the meantime, the German and Austrian regulatory authorities have issued statements of non-compliance with good distribution practices (GDP) to the concerned wholesalers in their countries for not following required procedures, including compliance with security measures. EMA is monitoring the situation closely and will provide updates as appropriate.

The latest reports of falsification come in the wake of an increase in demand for Ozempic which has also led to a shortage situation.

EMA takes further steps to address critical shortages of medicines in the EU

October 24, 2023

Today, EMA published details of the newly created solidarity mechanism developed by the EMA Medicines Shortages Steering Group (MSSG). This voluntary mechanism allows Member States to support each other in the face of a critical medicine shortage.

The solidarity mechanism, which is based on an informal setup during COVID-19, will enable any Member State facing a critical shortage that has been escalated to the MSSG for coordination at European level to request assistance from other Member States in obtaining medicine stocks. This mechanism can only be used under very

limited conditions and was developed as a last resort for Member States after they have exhausted all other possibilities.

The solidarity mechanism complements a number of actions that the MSSG can carry out to address critical shortages in the EU. These were also published today as part of the MSSG Toolkit.¹ The toolkit includes recommendations for monitoring supply and demand, an approach that was used to tackle the widespread critical shortages of antibiotics in the autumn and winter seasons of 2022/2023. The toolkit also provides guidance on interactions with marketing

authorisation holders and manufacturers to increase and redistribute existing stocks and the implementation of regulatory flexibilities, such as the exceptional supply of certain medicines that may not be authorised in a particular EU Member State, or full or partial exemptions to certain labelling and packaging requirements for medicines.

The two documents published today are part of a clear set of actions announced by the EC today to protect Europe against medicines shortages in the future.

The MSSG was established under Regulation (EU) 2022/123, which reinforces the role of the Agency in crisis preparedness and management for medicines and medical devices in order to monitor shortages and ensure a robust response to major events or public health emergencies and to coordinate urgent actions on the supply of medicines within the EU. The regulation formalises and strengthens the governance structures EMA had put in place to ensure swift and coordinated action during the COVID-19 pandemic.

Reference:

1. MSSG Toolkit on recommendations on tackling shortages of medicinal products. First published October 24, 2023; EMA/899955/2022. Available from: https://www.ema.europa.eu/en/documents/other/mssg-toolkit-recommendations-tackling-shortages-medicinal-products_en.pdf

