

News from the EMA

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Making the best use of big data for public health: Publication of the Big Data Steering Group workplan for 2020–2021

September 14, 2020 – The Big Data Steering Group set up by EMA and the Heads of Medicines Agencies (HMA) has published its workplan which sets actions to be delivered in 2020–2021. With the European Medicines Regulatory Network focused on the response to the COVID-19 pandemic, the workplan aims to progress evolution to data-driven regulation through smart working, leveraging collaboration with stakeholders and the use of remote expert workshops.

In the past three years, EMA and HMA have led a thorough assessment of the challenges and opportunities posed by big data in medicines' regulation. This culminated in January 2020 with the publication of recommendations for regulators to evolve their approach to data use and evidence generation. Following this preparatory work, the Big Data Steering Group was established in February 2020 to advise the EMA

Management Board and HMA on implementing ten priority recommendations.

Its first workplan, published on September 14, 2020, aims to increase the utility of big data in regulation from the quality of data through study methods to assessment and decision-making. It foresees closely involving patients and is guided by advances in science and technology. Other stakeholders will also be involved and the workplan intends to leverage international collaboration. Stakeholders will have the opportunity to discuss the workplan and its implementation in the context of a virtual multi-stakeholder forum scheduled for late 2020.

Big data are extremely large, rapidly accumulating datasets captured across multiple settings and devices, for example through wearable devices and electronic health records. Coupled to rapidly developing technology, big data can complement the evidence from clinical

trials and fill knowledge gaps on a medicine, and help to better characterise diseases, treatments, and the performance of medicines in individual healthcare systems. The rapidly changing data landscape forces regulators to evolve and change the way they access, manage, and analyse data and to keep pace with the rapid advances in science and technology.

The work carried out by the Big Data Steering Group builds on the Regulatory Science Strategy to 2025, published in March 2020, and will support the European Medicines Agencies Network Strategy to 2025, currently under development. The European Medicines Regulatory Network has to prioritise the unprecedented public health challenge of the COVID-19 pandemic and implementation of the Big Data Steering Group workplan will need to be flexible and certain actions may need to be re-scheduled depending on the development of the pandemic.



September 18, 2020 – EMA has recommended granting an extension of indication for Velphoro (sucroferric oxyhydroxide) to include control of serum phosphorus levels in children aged 2 years or older with chronic kidney disease (CKD) stages 4–5 or with CKD on dialysis. Patients with severe kidney disease cannot eliminate phosphate from their bodies. This leads to hyperphosphataemia (high blood phosphate levels), which, in the long term, can cause complications such as heart and bone disease.

The active substance in Velphoro, sucroferric oxyhydroxide, a mixture of iron (III)-oxyhydroxide, sucrose, and starches, is a phosphate binder. When taken with meals, the iron contained in Velphoro attaches to phosphate from food within the gut, preventing it from being absorbed into the body and helping to keep down the phosphate levels in the blood. Velphoro should be used with other treatments such as calcium or vitamin-D supplements, which help to control bone disease linked to kidney failure and high phosphate levels.

Velphoro in the new therapeutic indication brings a significant clinical benefit compared to existing treatments. There are currently no

New treatment for children with chronic kidney disease



existing therapies of phosphate binders indicated for the control of serum phosphorus levels in children between 2 and 6 years old with CKD stages 4–5 who are not on dialysis. In addition, the medicine has been re-formulated into 125 mg powder for oral suspension, which is easier to be administered to small children.

EMA's human medicines committee (CHMP) based its recommendation for Velphoro on the assessment of an open-label, randomised phase 3 clinical study, which included 85 children from 2 years of age with CKD and hyperphosphatemia. The results showed normal phosphorus range after treatment in a large proportion of

patients, comparable to what was observed for adults. The adverse reactions most frequently reported with this treatment were gastrointestinal disorders, including diarrhoea, vomiting, gastritis and discoloured faeces.

The marketing authorisation (valid throughout the European Union since August 26, 2014) holder is Vifor Fresenius Medical Care Renal Pharma France. Currently, Velphoro is approved as 500 mg chewable tablets for use in adults only. Following the CHMP recommendation, the summary of product characteristics, the package leaflet, and the labelling for Velphoro will be updated accordingly.

EMA endorses use of dexamethasone in COVID-19 patients on oxygen or mechanical ventilation

September 18, 2020 – EMA's human medicines committee (CHMP) has completed its review of results from the RECOVERY study arm that involved the use of the corticosteroid medicine dexamethasone in the treatment of patients with COVID-19 admitted to hospital, and has concluded that dexamethasone can be considered a treatment option for patients who require oxygen therapy (from supplemental oxygen to mechanical ventilation).

Based on the review of available data, EMA is endorsing the use of dexamethasone in adults and adolescents (from 12 years of age and weighing at least 40 kg) who require supplemental oxygen therapy. Dexamethasone can be taken by mouth or given as an injection or infusion (drip) into a vein. In all cases, the recommended dose in adults and adolescents is 6 milligrams once a day for up to 10 days.

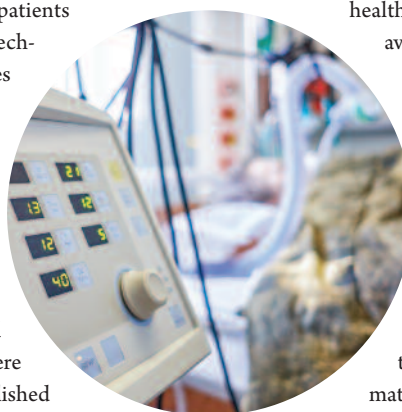
Published data from the RECOVERY study show that in patients on invasive mechanical ventilation, 29% of those treated with dexamethasone died within 28 days of starting dexamethasone treatment compared with 41% of

patients receiving usual care, with a relative reduction of about 35%. In patients receiving oxygen without mechanical ventilation, the figures were 23% with dexamethasone and 26% with usual care, with a relative reduction of about 20%. No reduction in the risk of death occurred in patients who were not receiving oxygen therapy or mechanical ventilation. These results were supported by additional published data, including a meta-analysis conducted by the World Health Organization, which looked at data from seven clinical studies investigating the use of corticosteroids for the treatment of patients with COVID-19.

Companies that market dexamethasone medicines can request this new use to be added to their product's licence by submitting an application to national medicines agencies or to EMA. The proposed changes to the dexametha-

some product information for patients and healthcare professionals are available.

Dexamethasone is a corticosteroid medicine that has been authorised in the EU by national medicines authorities and has been available for several decades. It can be used by mouth and by injection for treating a range of inflammatory conditions and for reducing the body's immune response in the treatment of allergies and autoimmune diseases. It is also used with cancer medicines to treat certain cancers and to prevent vomiting. Dexamethasone was first considered a potential treatment for COVID-19 because of its ability to reduce inflammation, which plays an important role in the disease process in some patients who have been admitted to hospital with COVID-19.



How incidents with medicines are managed in the EU – a 10-year analysis

September 23, 2020 – The EU medicines network is supported by a robust regulatory framework with defined processes and clear responsibilities in place to handle public health incidents, according to a 10-year analysis of the European Union incident management plan (EU-IMP) published in the journal *Pharmacoepidemiology and Drug Safety*.

EMA, in collaboration with the HMA and the European Commission, established the EU-IMP in 2009 to enable rapid and effective actions across the EU in case of an event or new information on medicines authorised in the EU with a potential serious impact on public health. Such incidents can affect the safety, quality, efficacy, or availability of a medicinal product and causes may include the product's safety profile, manufacturing compliance, or supply chain issues.

When an incident is suspected, a group of experts from EMA and its scientific committees, the European Commission, and the national

competent authorities, called the Incident Review Network (IRN), convenes within the shortest possible time to assess the potential public health impact and recommend the appropriate regulatory pathway and the most appropriate communications.

During the first ten years of operation of the EU-IMP, a total of 78 incidents were managed through the IRN. Of these, 70% were triggered by information that came to EMA from national competent authorities, followed by information from marketing authorisation holders (17%). During the observation period, more than half of the issues addressed concerned the safety of medicines, while quality and non-compliance with good manufacturing practices accounted for over one third of issues.

Regarding the final outcomes of the incidents managed through the IRN, almost half resulted in a variation to the marketing authorisation and/or risk minimisation measures of the

concerned medicine. 22% led to no change to the marketing authorisation, 10% led to the suspension and 9% to the revocation of a medicine's marketing authorisation.

The analysis also highlights that the implementation of the revised pharmacovigilance legislation in 2012 has offered robust regulatory instruments and has established clear roles and responsibilities to directly manage most safety issues without the need to go through the IRN mechanism.

The published article can be accessed free of restrictions: Santoro A, Caplanusi I, Sweeney F, Cappelli B, Nolan L, Straus S, Arlett P. Navigating stormy waters: 10 years of operation of the European Union Regulatory Network Incident Management Plan for Medicines for Human Use. *Pharmacoepidemiol Drug Saf.* 2020 Sep 21. doi: 10.1002/pds.5133. PMID: 32954565.





EMA recommends first COVID-19 vaccine for authorisation in the EU

December 21, 2020 – EMA has recommended granting a conditional marketing authorisation for the vaccine Comirnaty, developed by BioNTech and Pfizer, to prevent coronavirus disease 2019 (COVID-19) in people from 16 years of age. EMA's scientific opinion paves the way for the first marketing authorisation of a COVID-19 vaccine in the EU by the European Commission, with all the safeguards, controls, and obligations this entails.

EMA's human medicines committee (CHMP) has completed its rigorous evaluation of Comirnaty, concluding by consensus that sufficiently robust data on the quality, safety, and efficacy of the vaccine are now available to recommend a formal conditional marketing authorisation. This will provide a controlled and robust framework to underpin EU-wide vaccination campaigns and protect EU citizens.

"Today's positive news is an important step forward in our fight against this pandemic, which has caused suffering and hardship for so many", said Emer Cooke, Executive Director of EMA. "We have achieved this milestone thanks to the dedication of scientists, doctors, developers and trial volunteers as well as many experts from all EU Member States.

"Our thorough evaluation means that we can confidently assure EU citizens of the safety and efficacy of this vaccine and that it meets necessary quality standards. However, our work

does not stop here. We will continue to collect and analyse data on the safety and effectiveness of this vaccine to protect people taking the vaccine in the EU."

A very large clinical trial showed that Comirnaty was effective at preventing COVID-19 in people from 16 years of age.

The trial involved around 44,000 people in total. Half received the vaccine and half were given a dummy injection. People did not know whether they received the vaccine or the dummy injection.

Efficacy was calculated in over 36,000 people from 16 years of age (including people over 75 years of age) who had no sign of previous infection. The study showed a 95% reduction in the number of symptomatic COVID-19 cases in the people who received the vaccine (8 cases out of 18,198 got COVID-19 symptoms) compared with people who received a dummy injection (162 cases out of 18,325 got COVID-19 symptoms). This means that the vaccine demonstrated a 95% efficacy in the clinical trial.

The trial also showed around 95% efficacy in the participants at risk of severe COVID-19, including those with asthma, chronic lung disease, diabetes, high blood pressure or a body mass index ≥ 30 kg/m². The high efficacy was maintained across genders, racial and ethnic groups.

Comirnaty is given as two injections into the

arm, at least 21 days apart. The most common side effects with Comirnaty were usually mild or moderate and got better within a few days after vaccination. They included pain and swelling at the injection site, tiredness, headache, muscle and joint pain, chills and fever. The safety and effectiveness of the vaccine will continue to be monitored as it is used across the member states, through the EU pharmacovigilance system and additional studies by the company and by European authorities.

Where to find more information

The product information approved by the CHMP for Comirnaty contains prescribing information for healthcare professionals, a package leaflet for members of the public and details of conditions of the vaccine's authorisation.

An assessment report, with details of EMA's evaluation of Comirnaty, and the full risk management plan will be published within days. Clinical trial data submitted by the company in the application for marketing authorisation will be published on the agency's clinical data website in due course.

More information is available in an overview of the vaccine in lay language, including a description of the vaccine's benefits and risks and why EMA recommended its authorisation in the EU.