

News from the EMA

SECTION EDITOR



Section Editor:

Anuradha Alahari

Anuradha.Alahari@parexel.com



EMA contact:

Monika Benstetter

press@ema.europa.eu

The articles included in this section are a selection from the European Medicines Agency (EMA)'s News and Press Releases archive. More information can be found on the Agency's website: www.ema.europa.eu



Ten recommendations to unlock the potential of big data for public health in the EU

January 20, 2020 – The joint Big Data Task Force of European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) proposes ten priority actions for the European medicines regulatory network to evolve its approach to data use and evidence generation, in order to make best use of big data to support innovation and public health, in a report published today.

Big data are extremely large, rapidly accumulating datasets captured across multiple settings and devices, for example through wearable devices, electronic health records, clinical trials, or spontaneous adverse reaction reports. 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 report makes several recommendations out of which ten are viewed as priorities. The most ambitious of these top ten recommendations is the establishment of an European Union (EU) platform to access and analyse healthcare data from across the EU (Data Analysis and Real World Interrogation Network, or DARWIN). This platform would create a European network of databases of verified quality and content with the highest levels of data security. It would be used to inform regulatory decision-making with robust evidence from healthcare practice.

Other recommendations are intended to enhance guidance and resources within the EU regulatory network for data quality and data discoverability (choice of key metadata) and to build up computing and analytical capacity. The joint task force advises to develop the skills to process and analyse big data within the network through training to enhance the capacity of regulators to assess applications for the authorisation of medicines that use big data sources as part of the evidence on benefits and risks. It proposes to

establish a learning initiative to track and review outcomes of these types of submissions.

The report also emphasises the need to ensure data are managed and analysed within a secure and ethical governance framework, and in active dialogue with key EU stakeholders including patients, healthcare professionals, industry, health technology assessment bodies (HTAs), payers, device regulators, and technology companies. All these activities should be done in collaboration with international initiatives on big data.

Established in 2017, the HMA – EMA Joint Big Data task force is composed of experienced medicines regulators and data experts appointed by national competent authorities, EMA, and the European Commission. The first phase of its work – published in early 2019 – reviewed the landscape of big data and identified opportunities for improvements in the operation of medicines regulation. Published today, the practical suggestions made in the second phase of its work aim to inform strategic decision-making and planning by the HMA and EMA and to contribute to the upcoming EU Network Strategy to 2025.

Key principles for the use of electronic product information (ePI) for EU medicines

January 29, 2020 – EMA, the HMA of EU Member States, and the European Commission (EC) have published today key principles outlining a harmonised approach to develop and use electronic product information (ePI) for human medicines across the EU.

The product information of a medicine includes the package leaflet for patients and the summary of product characteristics (SmPC) for healthcare professionals. These documents accompany every single medicine authorised in the EU and explain how it should be prescribed and used. The package leaflet is provided in the medicine's box and can also be found, often as a pdf document, on the websites of EU regulators. However, digital platforms open additional possibilities to disseminate the product information electronically. This can address some of the current limitations (e.g. the current PI is not interoperable with other



electronic health systems such as e-prescription and electronic health records) and better meet patients' and healthcare professionals' needs for accessible, trustworthy, and up-to-date information on medicines available at the right time.

The ePI initiative was launched to support the digital transformation of healthcare across the EU, and the commitment laid out by the EC to prioritise innovations that will empower citizens and build a healthier society. It is also in line with

EMA's current digitalisation efforts aiming to make best use of available resources and prepare for future challenges.

The key principles describe the benefits ePI can deliver for public health and the efficiencies it may introduce in regulatory procedures. They explain how ePI will comply with the existing legislative framework: it will be provided as open access information that complements the paper package leaflet.

They also outline a flexible, harmonised approach

to implementation across the EU, and describe how ePI will work in the EU's multilingual environment and will interact with other ongoing digital initiatives at EU and global level.

The key principles derive from extensive discussions and consultations carried out in 2018 and 2019 by EMA, HMA and the EC with representatives of all stakeholder groups concerned, from patients, healthcare professionals, and regulators to the pharmaceutical industry. In particular, during a public consultation that took place from January to July 2019, 71 contributions from all stakeholder groups were received, including over 500 comments which were considered for the final version. A summary of the main points raised in the consultation and the submissions were also published today.

The key principles were endorsed at the end of 2019 by EMA's Management Board and by the HMA. They are now expected to be followed by all parties involved in the process of developing and implementing ePI for medicines across the EU.

First oral GLP-1 treatment for type 2 diabetes

January 31, 2020 – The EMA's human medicines committee (CHMP) has recommended granting a marketing authorisation in the EU for Rybelsus (semaglutide) for the treatment of adults with insufficiently controlled type 2 diabetes to improve glycaemic control as an adjunct to diet and exercise. It is the first glucagon-like peptide (GLP-1) receptor agonist treatment – a class of non-insulin medicines for people with type 2 diabetes – developed for oral use, providing patients with another option to treat the disease without injections.

Type 2 diabetes is a disease in which the pancreas does not make enough insulin to control the level of glucose in the blood or when the body is unable to use insulin effectively. Most people with diabetes have this form of diabetes. Possible complications of diabetes include heart attack, stroke, kidney failure, leg amputation, vision loss, and nerve damage.

The active substance in Rybelsus, semaglutide, acts in the same way as the incretin hormone GLP1: it reduces blood glucose by stimulating pancreatic secretion of insulin and lowering the secretion of glucagon (a hormone

that works to raise blood sugar concentration) when blood sugar is high.

The safety and efficacy of Rybelsus were studied in eight clinical trials that included patients at various stages of the disease. In three of these studies, Rybelsus was compared to a placebo. In the development programme, it was either used on its own, added to the standard treatment or compared to an injection treatment of its same class (GLP-1 receptor agonist).

The most common side effects observed during the clinical trials were gastrointestinal side effects, such as nausea and diarrhoea. Hypoglycaemia may occur when used in combination with insulin or sulphonylurea.

The opinion adopted by the CHMP is an intermediary step on Rybelsus's path to patient access. The CHMP 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/use of this medicine in the context of the national health system of that country.



First treatment for acute hepatic porphyria: Use of small interfering RNA

January 31, 2020 – EMA's CHMP has recommended granting a marketing authorisation in the EU for Givlaari (givosiran), the first treatment for acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older.

Acute hepatic porphyria is a rare genetic condition in which patients lack certain enzymes needed to produce haem, a basic structure of haemoglobin that binds to oxygen and is characterised by an accumulation of porphyrins in the body to toxic amounts. This can cause attacks of severe abdominal pain, vomiting, and nervous system disorders, such as seizures, depression, and anxiety. AHP is life-threatening due to the possibility of paralysis and respiratory arrest during attacks.

The new active substance givosiran is made of a short, synthetic strand of genetic material called 'small interfering RNA' that has been designed to interfere with the production of an enzyme involved in an early step in making haem. By blocking this early step of haem production in patients with AHP, the medicine is expected to prevent the next steps which produce substances that accumulate in the body and cause the



symptoms of the disease.

There are no approved treatments that directly ameliorate or prevent chronic symptoms experienced by many AHP patients and no approved treatments to reduce the risk of attacks. Intravenous hemin, a human blood-derived haem formulation, is the only therapy currently approved for the treatment of acute attacks. However, it is not approved as a chronic treatment to prevent attacks. Additional treatments include painkillers and antiemetics (to treat nausea and vomiting), chemically-induced menopause with hormonal suppression therapy, and liver transplantation.

The benefits and safety of Givlaari were demonstrated in a phase III clinical study which

enrolled 94 patients with AHP who experienced at least two attacks in the past six months. Data from the study showed that the treatment resulted in a significant decrease of annual attacks, less pain, and an improved quality of life.

At the time of designation, AHP affected approximately 0.1 in 10,000 people in the EU and Norway, Iceland, and Liechtenstein, which makes it a rare disease. This product was designated as an orphan medicine during its development. At the time of approval, orphan designations are reviewed by EMA's Committee for Orphan Medicinal Products (COMP) to determine whether the information available to date allows maintaining the medicine's orphan status and granting the medicine ten years of market exclusivity.

Since Givlaari addresses an unmet medical need, it benefited from PRIME, EMA's platform for early and enhanced dialogue with developers of promising new medicines. This interaction led to a more robust application package to demonstrate the medicine's benefits and risks, which allowed the accelerated assessment of Givlaari in 150 days.

Guidance to sponsors on how to manage clinical trials during the COVID-19 pandemic

March 20, 2020 – The EC, the EMA and national HMAs have published new recommendations for sponsors on how to manage the conduct of clinical trials in the context of the coronavirus disease (COVID-19) pandemic. The impact of the pandemic on European health systems and more broadly

on society, will make it necessary for sponsors to adjust how they manage clinical trials and the people who participate in these trials.

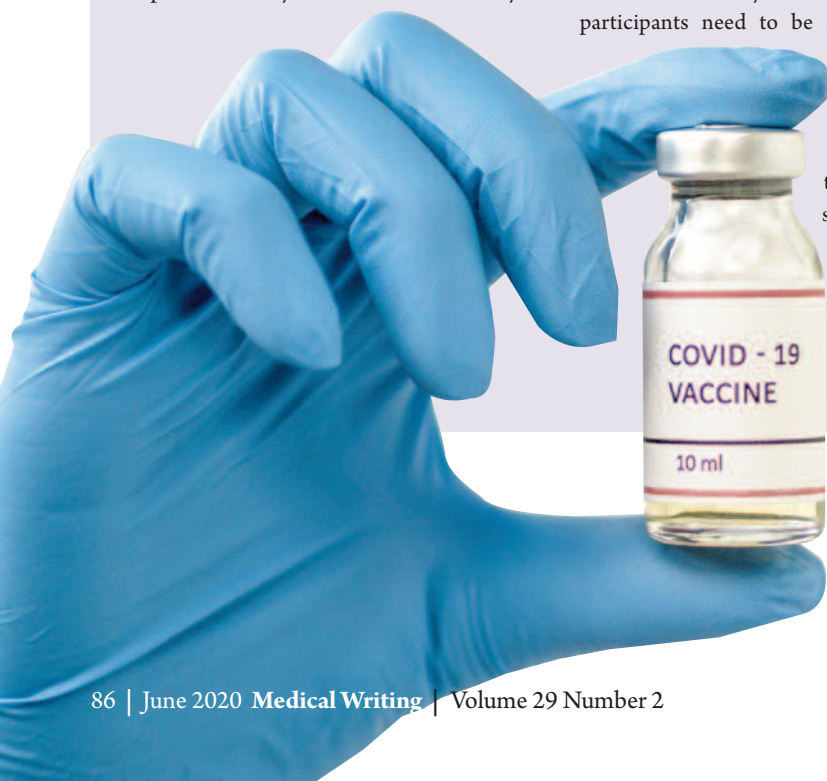
The guidance provides concrete information on changes and protocol deviations which may be needed in the conduct of clinical trials to deal with extraordinary situations, e.g. if trial participants need to be in self-isolation or quarantine, access to public places (including hospitals) is limited due to the risk of spreading infections, and healthcare professionals are being reallocated.

This guidance includes a harm-

onised set of recommendations, to ensure the utmost safety of trial participants across the EU while preserving the quality of the data generated by the trials. It also advises how these changes should be communicated to authorities.

There is specific advice on the initiation of new clinical trials for treatments of COVID-19, and in particular on the need for large, multinational trial protocols. This is in line with the call issued by EMA's CHMP for robust trial methodology in clinical trials for potential COVID-19 treatments or vaccines.

In the EU, clinical trials are authorised and supervised at national level. Sponsors are advised to also check whether there might be specific national legislation and guidance in place to complement or in some cases to take priority over this new guidance.



COVID-19: How EMA fast-tracks development support and approval of medicines and vaccines

May 4, 2020 – As researchers race to develop vaccines and therapeutics against COVID-19, EMA has published an overview of how the Agency will accelerate its regulatory procedures so that marketing authorisations of safe, effective and high-quality COVID-19 related medicines can be granted as soon as possible. The rapid procedures described in the inventory can accelerate every step of a medicine's regulatory pathway and the Agency is fully mobilised to deliver these fast-track assessments in the shortest possible timeframes while ensuring robust scientific opinions are reached.

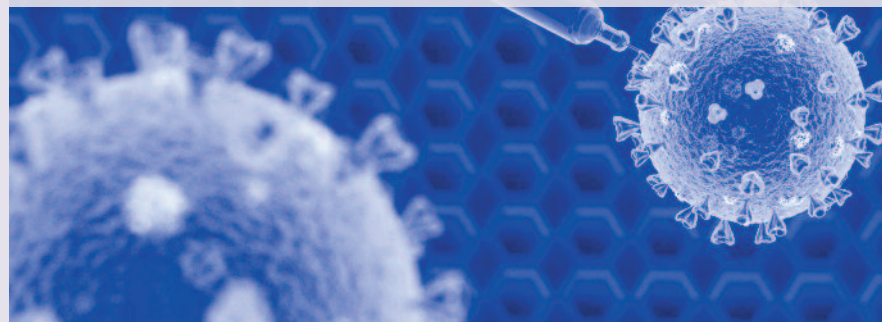
“Supporting the development and marketing authorisation of safe, effective and high-quality therapeutics and vaccines as soon as possible is one of EMA's top priorities in the COVID-19 public health emergency. Together with our scientific committees and working parties, we have adapted our procedures in order to significantly shorten our own regulatory timelines for the review of new medicines and vaccines against COVID-19,” said Executive Director Guido Rasi. “However, the rapid approval of therapeutics and vaccines will only be possible if applications are supported by robust and sound scientific evidence that allows EMA to conclude on a positive benefit-risk balance for these products.”

These “rapid” procedures stem from EMA's emerging health threats plan. The flexible and fast review of medicines is supported by **EMA's pandemic Task Force (COVID-ETF)**, which brings together in one group the best scientific experts from the EU regulatory network. It will work closely with EMA's human medicines committee (CHMP) for optimal and fast coordination of activities related to the development, authorisation and safety monitoring of medicines and vaccines against COVID-19.

Accelerated support during research and development

For products under development, in early stages and/or before the submission of a marketing authorisation application, mechanisms put in place by EMA include:

- **Rapid scientific advice**, through which developers can receive prompt guidance and direction on the best methods and study designs to generate robust data on how well a medicine or vaccine works, how safe it is, as well as on the manufacturing and control process to establish its quality.



In the context of COVID-19, fees for scientific advice are waived and the procedure is reduced to a maximum of **20 days**, compared to normally 40–70 days.

- **Rapid agreement of paediatric investigation plans (PIPs) and rapid compliance check.** The total review time for a PIP for COVID-19 products will be reduced to **20 days**, compared to normally up to 120 days active review time. In case needed, EMA also carries out a check to ensure companies comply with the agreed measures listed in each PIP before a marketing authorisation can be submitted, which will now also be reduced to 4 days.

All these accelerated mechanisms will require developers to submit well-prepared dossiers to EMA. The Agency therefore continues to encourage developers of vaccines or therapeutics against COVID-19 to make contact as soon as possible, to discuss their strategy for evidence-generation, by emailing 2019-ncov@ema.europa.eu. Depending on the maturity of the development, initial discussions on the various mechanisms to fast-track development and approval will take place, with priority given to the most relevant proposals.

Accelerated evaluation in authorisation and post-authorisation procedures

According to the EU pharmaceutical legislation, the standard timeline for the evaluation of a medicine is a maximum of 210 active days. However applications for marketing authorisation for COVID-19 products will be treated in an expedited manner:

- **Rolling review.** This procedure, used in a public health emergency, allows EMA to assess data for a promising medicine as they become available on a rolling basis. Under normal circumstances, all data supporting a

marketing authorisation application must be submitted at the start of the evaluation procedure. In the case of a rolling review, CHMP rapporteurs are appointed whilst development is still ongoing and the Agency reviews data as they become available. Several rolling review cycles can be carried out during the evaluation of one product as data continue to emerge, with each cycle requiring around **two weeks**, depending on the amount of data to be assessed. Once the data package is considered complete, a developer submits a formal marketing authorisation application to EMA which is then processed under a shortened timetable.

- **Accelerated assessment.** This procedure can reduce the review time of products of major interest for public health from 210 days to less than 150 days. In practice, where there is an urgent public health need, assessment timelines will be reduced to the absolute minimum.
- EMA is ready to apply **further flexibility**, where it is established that shortening of any other procedural step could have an important public health impact in dealing with the COVID-19 pandemic.

The various rapid procedures are also available in the context of extensions of indications for already approved medicines, which are being repurposed in the fight against COVID-19.

The inventory also describes the support EMA can provide in the context of **compassionate use** programmes. Such programmes are set up at the level of individual EU Member States, to give patients access to treatments that are still under development and that have not yet received a marketing authorisation. EMA can provide scientific recommendations as to how these medicines should be used in this context, to support a harmonised EU-wide approach.