

News from the EMA

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EMA implements new measures to minimise animal testing during medicines development

September 29, 2021

EMA is putting in place special support to developers to replace, reduce and refine animal use for the development, manufacturing and testing of human and veterinary medicines. The Agency is promoting these three principles – replace, reduce and refine; commonly referred to as 3Rs – through EMA's Innovation Task Force (ITF). This action will facilitate the development

and implementation of New Approach Methodologies (NAMs) that are in line with the European Union legislation on the protection of animals used for scientific purposes.

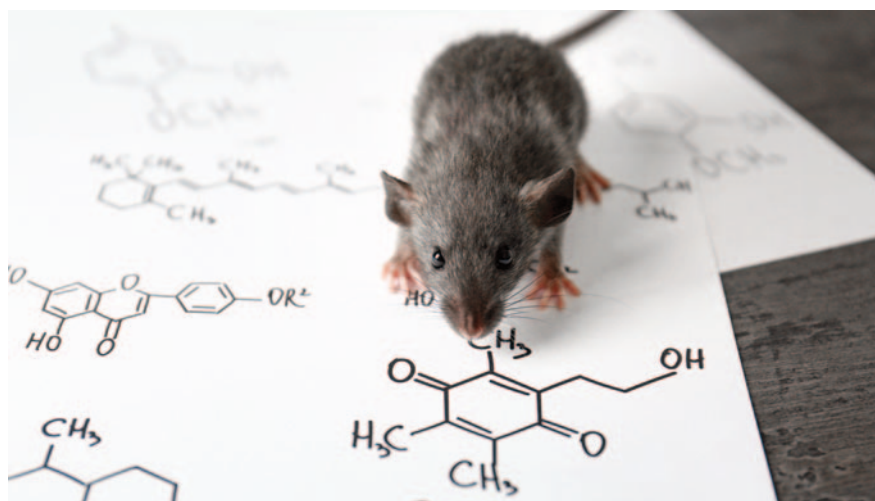
ITF is a dedicated forum for early dialogue between regulators and developers of medicines to discuss innovative aspects such as emerging therapies, methods and technologies. Set up to

ensure coordination across the Agency, the ITF is a multidisciplinary group that includes scientific, regulatory and legal competences. It will provide an opportunity to discuss 3R-compliant methods and facilitate their integration into the development and evaluation of medicinal products.

The ITF's service is free of charge and any NAMs adhering to the 3Rs principles that can be used to fulfil testing requirements are eligible for consideration.

Alternative approaches to animal models, such as improved tests based on human and animal cells, organoids, organ-on-chips, and in silico modelling, provide opportunities to develop better and more predictive scientific tools to protect human and animal health as well as the environment.

Opening the ITF platform to discussions of 3Rs-compliant methodologies is expected to encourage prioritising and speeding up the integration of alternative methods into the regulatory framework. This action supports the reduction of animal use and is in line with EMA's Regulatory Science Strategy to 2025 aiming to build a more adaptive regulatory system that will encourage innovation in human and veterinary medicine.



First-in-class medicine to treat aggressive form of breast cancer

October 15, 2021

EMA has recommended granting a marketing authorisation in the European Union (EU) for Trodelvy (from Gilead Sciences Ireland UC), a first-in-class medicine to treat adult patients with unresectable (cannot be removed by surgery) or metastatic triple-negative breast cancer who have received two or more prior systemic therapies, at least one of them for advanced disease.

Triple-negative breast cancer is an

aggressive type of breast cancer that does not have the usual receptors (targets) which other targeted cancer medicines act on.

Currently, chemotherapy remains the standard treatment for patients with metastatic triple-negative breast cancer. However, it is estimated that only 10 to 15% of patients with this type of cancer respond to this treatment and the time without their disease worsening is only 2 to 3 months. Therefore, there is a high unmet

medical need for new treatments that improve the outlook for patients.

Trodelvy's active ingredient is sacituzumab govitecan. It combines a humanised antibody (a type of protein) designed to recognise and attach to the Trop-2 receptor with a type of an antineoplastic agent called topoisomerase I inhibitor. This is intended to inhibit the cancer to grow, divide, and spread.

EMA's human medicines committee (CHMP) reviewed the application for marketing authorisation under an accelerated timetable to

Generating high-quality evidence from registry-based studies

October 26, 2021



EMA has published guidance to provide key methods and good regulatory practices to pharmaceutical organisations on the planning and conduct of registry-based studies.

A patient registry is an organised system that collects uniform data over time on patients who are diagnosed with a particular disease or condition, or who receive particular medicines. A registry-based study is a clinical trial or a non-interventional study that investigates a research

question using the data collection infrastructure or the patient population of one or several patient registries.

Medicine regulators may sometimes suggest that pharmaceutical companies use the data collection infrastructure or population of a patient registry to exploit information from clinical use and to monitor the safety and effectiveness of authorised medicines when used in the real-world setting.

enable faster patient access to this medicine.

The CHMP based its recommendation on data from a Phase 3, multicentre, open-label, randomised clinical trial. The study investigated the safety and efficacy of Trodelvy in 529 patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC). All patients enrolled had relapsed after at least two prior chemotherapies for breast cancer. Participants were randomised (1:1) to receive sacituzumab govitecan 10 mg/kg as an intravenous infusion on days 1 and 8 of a 21-day cycle or treatment of physician's choice (eribulin,

vinorelbine, gemcitabine, or capecitabine).

The medicine prolonged the overall survival (i.e. how long patients live) by approximately 5 months (11.8 months for sacituzumab govitecan compared to 6.9 months for treatment of physician's choice) and the progression-free survival (i.e. how long patients live without their disease getting worse) by about 3 months (4.8 months for sacituzumab govitecan compared to 1.7 months for treatment of physician's choice).

The most common side effects with Trodelvy in clinical trials included diarrhoea, nausea, neutropenia, fatigue, alopecia, anaemia, vomiting,

There can be significant differences in requirements for types, structures, and processing of data across existing registries. These often present challenges in the assessment of the suitability of existing registries to be used in clinical studies.

This guideline aims to help those involved in registry-based studies to better define study populations and design study protocols; it provides further guidance on data collection, data quality management, and data analysis to achieve higher quality evidence. This in turn will facilitate EU regulators' assessment of the safety and effectiveness of medicines, for the benefit of public health.

As patient registries are key to conducting registry-based studies, the guidance includes an annex with good practices in the establishment and management of patient registries and their use for other regulatory purposes.

This guideline will facilitate a more data-driven, robust regulation of medicines, as foreseen in the Big Data Steering Group Workplan that implements the Network Strategy to 2025. It is based on a discussion paper on methodological and operational aspects for use in patient registries for regulatory purposes, which was available for public consultation and generated almost 1,000 comments from 68 stakeholder organisations. Experience gained from EMA's human medicines committee (CHMP) qualification opinions for two networks of registries, and input collected during five workshops on specific patient registries organised by the Agency also fed into the final guidance.

constipation, decreased appetite, cough, and abdominal pain.

The opinion adopted by the CHMP is an intermediary step on Trodelvy'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/use of this medicine in the context of the national health system of that country.



Repurposing of authorised medicines: pilot to support not-for-profit organisations and academia

October 28, 2021

EMA and the Heads of Medicines Agencies (HMA) are launching a pilot project to support the repurposing of medicines as a follow-up to the European Commission's Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) discussions on a proposal for a medicines repurposing framework.

The aim of this initiative is to support not-for-profit organisations and academia to gather or generate sufficient evidence on the use of an established medicine in a new indication with the view to have this new use formally authorised by a regulatory authority. This is a way of making new treatment options available to patients.

As part of the pilot, EMA and the national medicines agencies will provide regulatory support, primarily scientific advice, to help these stakeholders generate a data package robust enough to support a future application by a pharmaceutical company.

Conditions for which no or few medicines are currently authorised, or which are associated with high morbidity and/or mortality despite available medicines, will be the focus of the pilot. Candidate medicines for the pilot should fulfil the following criteria:

- contain a well-established active substance;
- be an authorised medicine (containing the concerned active substance) out of data exclusivity and market protection periods and out of basic patent/supplementary protection certificate (SPC) protection;
- target an indication in a condition distinct from the currently authorised indication(s);
- target an indication in an area where important public health benefits are likely to be achieved.

While marketing authorisation holders may develop medicines for uses in other indications, sometimes they lack the incentives or the commercial interest to pursue the necessary research and development and complete the regulatory process needed for the authorisation of a new indication for old medicines which are no longer protected by a patent or data exclusivity. This could be a wasted opportunity for public health. At the same time, academic institutions and/or patient organisations may be interested in carrying out this development for the benefit of public health. However, they may not have the necessary regulatory experience and have no intention of becoming a marketing authorisation holder themselves.

The pilot will run until the completion of

scientific advice for the selected repurposing candidate projects and optimally until the filing of an application by a pharmaceutical company for the new indication. A report will be published after the pilot.

The medicines repurposing framework proposal was developed by the European Commission's STAMP Expert Group composed of representatives of EU Member States together with EMA and stakeholders from not-for-profit organisations, patients, healthcare professionals, industry, health technology assessment bodies, and payers.

EMA proposes to support the development and implementation of a repurposing framework in its Regulatory Science Strategy to 2025, which is its plan for advancing engagement with regulatory science over the next five to ten years.

Repurposing of medicines for COVID-19 falls outside the scope of this pilot project. The development and authorisation of treatments for COVID-19 is coordinated by the COVID-19 EMA pandemic Task Force (COVID-ETF) and should follow the steps outlined in the following document: [PDF icon EMA initiatives for acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines](#). Repurposing programmes for medicines intended for COVID-19 will therefore not be considered for this pilot.

2011-2020: More than 40% decrease in sales of antimicrobials for use in animals

November 23, 2021

The annual report on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) published by EMA shows that European countries have substantially reduced the use of antimicrobials in animals. According to data from the 25 countries that provided input for the full 2011–2020 period, overall sales of veterinary antimicrobials in European countries were 43% lower in 2020 than in 2011. While an increase of 6% in overall sales for the 25 countries in 2020 compared to 2019 was registered, data for the next years are necessary to better understand this observation. These data show that “EU policy initiatives combined with guidance and national campaigns promoting prudent use of antimicrobials in animals are having a positive effect,” said Ivo Claassen, Head of EMA’s Veterinary Medicines Division.

Sales of those antimicrobials that are considered critically important in human medicine, decreased noticeably between 2011 and 2020 and accounted for only 6% of total sales in 2020. In particular, sales of third- and fourth-generation cephalosporins dropped by 33%,

polymyxins by 76%, fluoroquinolones by 13% and sales of other quinolones dropped by 85%. These classes include antimicrobials used to treat serious infections in humans that are caused by bacteria resistant to most other antimicrobial treatments. In animals, they should be used with restrictions in order to preserve their effectiveness and mitigate the risk to public health, as indicated in the Antimicrobial Advice Ad Hoc Expert Group (AMEG) categorisation.

The eleventh ESVAC report presents data from 30 EU/EEA countries (including the UK as an EU Member State during the calendar years covered in the report) and Switzerland. All participating countries voluntarily provided information on sales of veterinary antimicrobial medicinal products. In order to present more recent data, and in preparation for the timelines for the reporting of sales and use data for antimicrobials in animals as required by Regulation (EU) 2019/6, data for both 2019 and 2020 were collected and presented in this ESVAC report.

For each of the participating countries there is a separate section presenting sales trends by

antimicrobial class. Some countries have described their main activities to combat antimicrobial resistance and how these activities have contributed to the observed changes in sales in their country. These measures include national action plans, national campaigns for prudent use of antimicrobials in animals, restrictions on use of certain antimicrobials in food-producing animals, or measures to control prescription of antimicrobials in animals.

The ESVAC project was launched by EMA in September 2009 following a request from the European Commission. Since then, the Agency has coordinated and supported European countries in establishing the standardised and harmonised reporting on the volume of sales of veterinary antimicrobial medicinal products. The ESVAC report is published annually and is used as a reference source of information for scientists, veterinarians and other health professionals, risk assessors, and policy makers in the EU Member States on the topic of antimicrobial resistance. Under Regulation (EU) 2019/6, reporting of sales and use data for antimicrobials in animals will become a legal obligation for EU Member States and the Agency. The new requirements will apply to data from 2023 onwards.



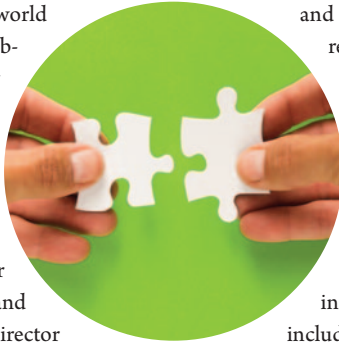
A vision for use of real-world evidence in EU medicines regulation

November 24, 2021

Enabling the use of real-world evidence (RWE) and establishing its value for regulatory decision-making on the development, authorisation, and supervision of medicines in Europe by 2025: this is the vision of European regulators as outlined in an article from Peter Arlett, Head of Data Analytics and Methods at EMA, Jesper Kjær, Director of Data Analytics Centre at the Danish Medicines Agency, Karl Broich, President of the Federal Institute for Drugs and Medical Devices (BfArM), and Emer Cooke, EMA's Executive Director, published in *Clinical Pharmacology & Therapeutics*.

The authors emphasise that delivering this vision, anchored in the Network Strategy to 2025, will support the development and use of better medicines for patients.

The creation of the Data Analytics and Real-World Interrogation Network (DARWIN EU) will be key to delivering this vision. This EU-wide network will allow to access and analyse healthcare data from across the EU. It will be launched in early 2022 with the establishment of a coordination centre to on-board data partners



and to drive the conduct of studies requested by medicines regulators and, at a later stage, also requested by other stakeholders.

The article explains plans to establish methods and standards for high-quality collection and use of RWE, in cooperation with stakeholders including patients, healthcare professionals, industry, regulatory and public health agencies, health technology assessment bodies, payers, and academia.

According to the authors, it will be important to advance the debate on the value of RWE compared to randomised clinical trials (RCTs), the gold standard to demonstrate efficacy of a medicine. The vision is that RWE and RCTs should be seen as complementary, each having strengths and weaknesses, with their relative importance depending on the regulatory question. A rigorous and systematic approach to learning from doing will help to identify and establish the use-cases in regulatory decision-making for which RWE will add most value.

In this context, EMA has also contributed to an article that examines when and how RWE was

used to support marketing authorisation applications for new products and extensions of indications, submitted to the Agency in 2018 and 2019. The retrospective analysis shows that 40% of initial marketing authorisation applications and 18% of applications for extension of indication for products currently on the market contained RWE. The article describes the characteristics of RWE included in these applications and identifies areas where further research is required.

Both articles aim to support transformation to data-driven regulatory decision-making and to advance patient-centred access to better medicines. They are available through open access:

1. Arlett, P., Kjær, J., Broich, K. and Cooke, E. Real-World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value. *Clin. Pharmacol. Ther.* 2022; 111:21-23.
2. Flynn, R., Plueschke, K., Quinten, C., Strassmann, V., Duijnhoven, R.G., Gordillo-Marañon, et al. Marketing Authorization Applications Made to the European Medicines Agency in 2018–2019: What was the Contribution of Real-World Evidence?. *Clin. Pharmacol. Ther.*, 2022; 111:90-97.

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New treatment for sickle cell disease

December 17, 2021

EMA has recommended granting a marketing authorisation in the EU for Oxbryta (from Global Blood Therapeutics Netherlands B.V.) for the treatment of haemolytic anaemia (excessive breakdown of red blood cells) due to sickle cell disease in patients 12 years of age and older. Oxbryta is to be used on its own or in combination with hydroxycarbamide (also known as hydroxyurea).

Sickle cell disease is a genetic condition in which the red blood cells become rigid and sticky and change from being disc-shaped to being crescent-shaped (like a sickle). The change in shape is caused by the presence of an abnormal form of haemoglobin (the protein in red blood cells that carries oxygen around the body).

In patients with sickle cell anaemia, the abnormal sickle shaped red blood cells block the blood vessels, restricting the flow of blood to organs, such as the heart, lungs and spleen. This situation causes episodes of acute pain called vaso-occlusive crisis (VOC). Furthermore, these abnormal red blood cells are destroyed at a faster rate than normal, leading to a condition called haemolytic anaemia. Vaso-occlusive crisis and haemolytic anaemia are the most common complications of sickle cell disease and are frequent causes of visits to emergency departments and hospitalisation.

Currently, most patients with sickle cell disease are treated with hydroxyurea and crizanlizumab, medicines for preventing VOC. However, there is a high unmet need for medicines to treat haemolytic anaemia, which is experienced to various degrees by all patients. Available treatment options are limited to blood transfusions and allogenic haematopoietic stem cell transplantation (a procedure where the

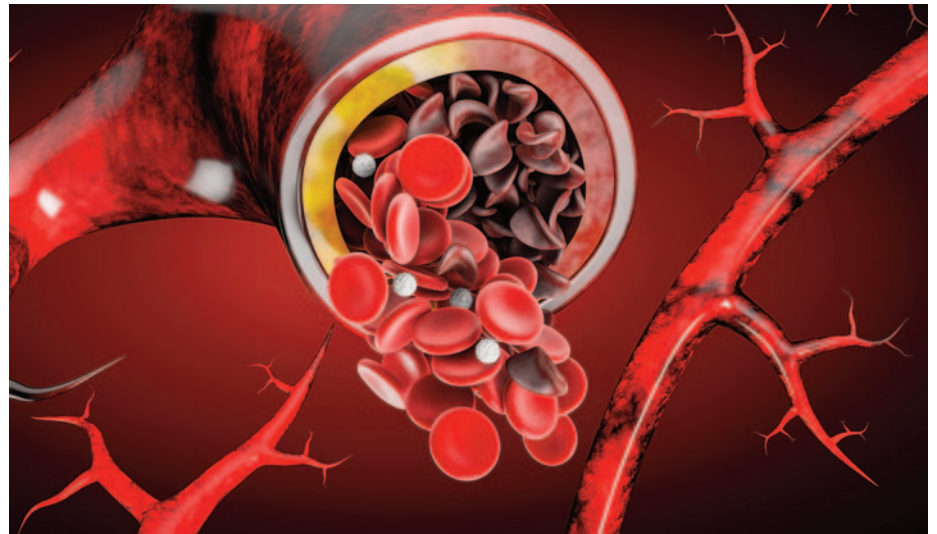
patient receives stem cells to help the bone marrow produce healthy blood cells). Therefore, new medicines for this manifestation of the disease are needed.

The active substance of Oxbryta is voxelotor, a small molecule which attaches to and stabilises haemoglobin, preventing haemoglobin polymerisation (i.e. formation of abnormal haemoglobin) that causes the red blood cells to become sickle shaped.

The main study that EMA's recommendation is based on was a Phase 3, randomised, double blind, placebo-controlled, multicentre study. The study investigated the safety and efficacy of voxelotor in 274 patients with sickle cell disease aged 12 to 65 years. Patients enrolled in the clinical trial had a baseline haemoglobin level between 5.5 and 10.5 g/dL. Ninety patients received 1500 mg of voxelotor, 92 patients received 900 mg of voxelotor and 92 patients

received a placebo. After 24 weeks of treatment, 51.1% of patients treated with 1500 mg of voxelotor had a greater than 1 g/dl increase in their haemoglobin levels compared to 6.5% of those receiving placebo. These results were observed when Oxbryta was used on its own or in combination with hydroxyurea, which is the standard treatment for patients with sickle cell disease. The most common side effects reported in clinical trials for Oxbryta included headache, diarrhoe, and abdominal pain.

Oxbryta was supported through EMA's Priority Medicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support for promising medicines with a potential to address unmet medical needs. Representatives of patient organisations were also consulted during the assessment of benefits and risks of Oxbryta to share their unique real-life perspectives and ensure that patients' needs are taken into account in the regulatory decision-making process.



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This is called the hash, pound, or number character. A hashtag is a keyword or set of keywords that is preceded by the # character. It is used in social media to create a thread of conversations around a specific theme or topic conveyed in short texts or microblogs. It is commonly used in Twitter, Instagram, YouTube, Pinterest, etc.

A dictionary of most common hashtags can be found at <https://www.hashtags.org/definition/~h/>.

For your info, EMWA is compiling a list of standardised hashtags for our social media use.

@

This is called the "at" sign or symbol. The @ sign is part of email addresses and social media user names ("handles"). Our EMWA handles are as follows: @Official_EMWA (Twitter), @EMWA (LinkedIn), and @europeanmedicalwritersassociation (Facebook)

The two most important keys on your keyboard