

# News from the EMA

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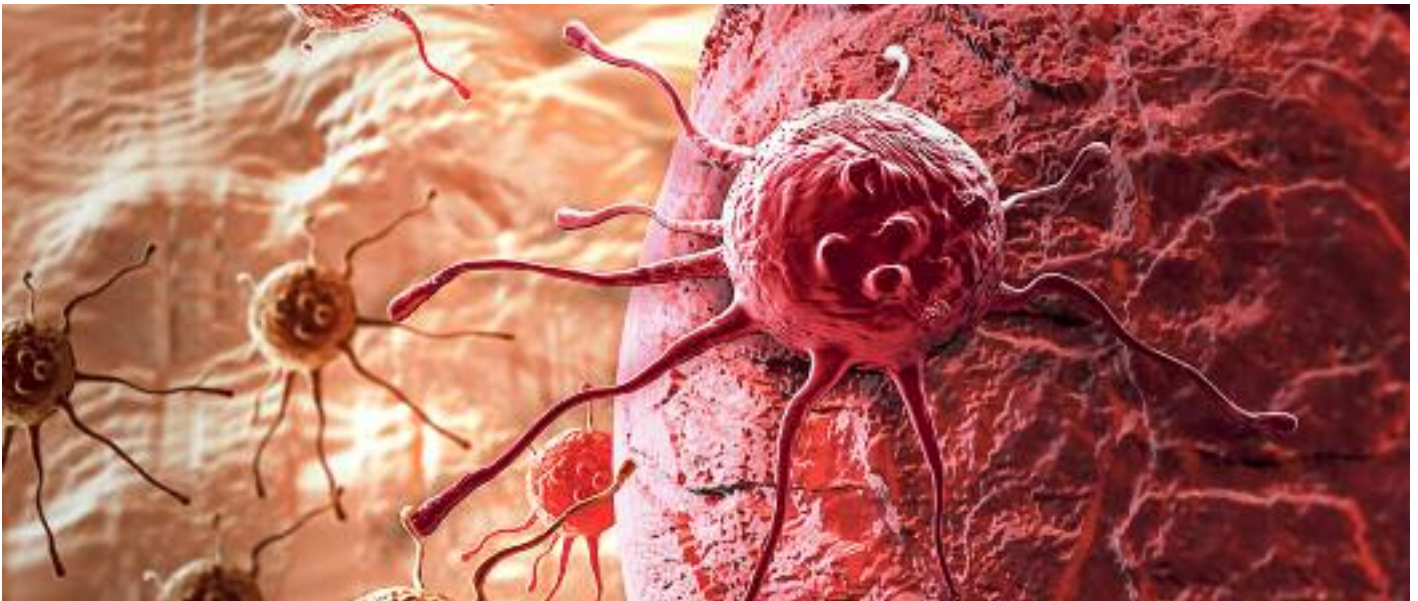


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The articles included in this section are a selection from the European Medicines Agency (EMA)'s News and Press Releases archive from July 2019 to September 2019. More information can be found on the Agency's website: [www.ema.europa.eu](http://www.ema.europa.eu).



## First “histology-independent” treatment for solid tumours with a specific gene mutation

**July 26, 2019** – European Medicines Agency (EMA)'s human medicines committee (CHMP) has recommended granting a marketing authorisation in the European Union (EU) for Vitrakvi (larotrectinib) for the treatment of adult and paediatric patients with solid tumours that display a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion. Treatment with Vitrakvi is recommended for patients whose disease has spread or cannot be surgically removed, and who have no other satisfactory treatment options.

Vitrakvi is the first so-called “histology-independent” cancer treatment recommended for approval in the EU. This means that it can be used to treat non-haematological (i.e., that do not begin in the blood or bone marrow) tumours with this specific mutation, regardless of where in the body the tumour originated. Before patients can be started on the medicine, the presence of the mutation in the tumour should be confirmed by a validated test.

The active substance in Vitrakvi – larotrectinib – targets a very specific genomic alteration of a patient's tumour. This occurs when NTRK genes that encode specific proteins are abnor-

mally fused to a gene. This mutation, called NTRK gene fusion, leads to the development of proteins that can cause cancer cells to grow. Vitrakvi blocks the action of these proteins and in doing so inhibits the growth of the cancer. NTRK gene fusions can be observed very frequently in a certain number of rare cancer types that affect both adults and children. In addition, this gene fusion occurs rarely in some of the most common cancer types.

The efficacy and safety of Vitrakvi were studied in three single-arm trials (i.e., studies with no control group) that included a total of 102 adults and children with cancer that were evaluated. These patients had either already received standard therapy, or would have had to undergo disfiguring surgery, or were unlikely to respond to available therapies.

The share of patients who responded to treatment with Vitrakvi was 67%. Of those, the response lasted six months or longer in 88% and 12 months or longer in 75%. Tumour responses were seen both in rare tumour types such as infantile fibrosarcoma and salivary gland tumours, as well as in common diseases such as

lung and colon cancer. The most common side effects were tiredness, increased levels of liver enzymes, dizziness, constipation, nausea, anaemia (low red blood cell count), and vomiting.

The CHMP recommended a conditional approval for this medicine. This is one of the EU's regulatory mechanisms to facilitate early access to medicines that fulfil an unmet medical need. This approval type allows the Agency to recommend a medicine for marketing authorisation with less complete data than normally expected, where 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.

The opinion adopted by the CHMP is an intermediary step on Vitrakvi'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 the 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.

## Names of liposomal medicines to be changed to avoid medication errors

**July 30, 2019, and September 26, 2019** – In July 2019, all marketing authorisation holders of medicines containing liposomal drug delivery systems were requested to submit to EU regulators a variation to change the names of these medicines as soon as possible before the end of September 2019. In September 2019, a clarification was added to indicate that the name variation should be done only if there is a high risk of medication errors which would raise concerns regarding the safe use of the medicinal product.

The initial recommendation was made jointly by EMA's CHMP and the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) at their July meetings and the clarification was adopted in the September meetings. The recommendation aims to make a clearer distinction between liposomal and non-liposomal formulations of the same active substance to avoid medication errors. Since the two formulations may have different biodistribution and release properties, medication errors can pose serious risks to the health of patients.

So far, there was no agreed approach to the naming of medicines containing liposomal or pegylated liposomal formulations. This recommendation is made to enable healthcare professionals and patients to better distinguish

them from conventional non-liposomal medicines. This is a particular concern when electronic prescribing and dispensing tools are used, as in the absence of a more descriptive term for the liposomal medicines, they can be mixed up with non-liposomal medicines.

Following a number of reports of serious medication errors, some leading to death, and after consultation with EMA's safety committee (PRAC), the CHMP and CMDh agreed on the following actions to reduce the risk of mix-up between these medicines:

- In section 1 of the summary of product characteristics (SmPC), the qualifier “liposomal” or “pegylated liposomal” should be added after the invented name and before the strength. This is in line with the standard practice for qualifiers.
- In those cases where a name change is considered necessary, applicants are requested to update the name throughout the product information, including all annexes.
- In those cases where a medicine is approved with an “international non-proprietary name (INN)+company or trademark” name, the qualifier “liposomal” or “pegylated liposomal” will be placed between the INN and the company name or trademark in section 1 of the SmPC.
- The currently existing European Directorate



for the Quality of Medicines standard term “dispersion”, which includes liposomes in its definition, should be used consistently throughout the product information.

- The CHMP and the CMDh have now clarified that for medicines administered topically or by other routes of administration, the qualifier “liposomal” or “pegylated liposomal” should only be added to the invented name in those cases when a clear risk of medication errors has been identified. Elements such as route of administration, medication error reporting, or long established use should be taken into consideration when assessing the need for the qualifier.

## EMA/FDA analysis shows high degree of alignment in marketing application decisions between EU and US

**August 16, 2019** – EMA and the US Food and Drug Administration (FDA) are aligned in more than 90% of marketing authorisation decisions for new medicines.

This is one of the findings of a joint EMA/FDA analysis comparing decisions on 107 new medicine applications at the two agencies between 2014 and 2016. The study also looked at applications for which the agencies had differing outcomes in terms of type of approval and indication. The most common reason for diverging decisions at the two agencies was differences in conclusions about efficacy. Differences in clinical data submitted in support of an application were the second most common root of divergent FDA and EMA decisions.

This is the first analysis by EMA and the FDA that compares the agencies' decisions related to

marketing authorisations.

Some differences were observed in the clinical data due to the difference in timing of submissions (more applications were submitted to the FDA before they were submitted to EMA). Compared to the FDA, EMA often reviewed applications including additional clinical trials or, particularly for oncology medicines, more mature data from the same clinical trial. In those instances, EMA was more likely than the FDA to grant standard approval, a broader indication, or use of a medicine as first-line therapy.

Over the past decade, EMA and the FDA have established joint working groups and several forums for information sharing and collaboration around many aspects of medicine development and regulation, including “clusters” on special topics and therapeutic areas, as well as parallel scientific advice and protocol assistance. These

groups bring together experts for example on plans for manufacturing or clinical site inspections, development of medicines for children, oncology products, biostatistics, rare diseases, and vaccines. While these groups are not forums for shared decision-making, the strong alignment in decisions on marketing authorisations suggests that they may be contributing to alignment on regulatory science.

Most of the information used for the study was sourced from EMA's publicly available European Public Assessment Reports and FDA reviews, which contain the agencies' rationale for their decisions on applications.

The article, entitled “A comparison of EMA and FDA decisions for new drug marketing applications 2014–2016: concordance, discordance and why”, is available through open access in *Clinical Pharmacology and Therapeutics*.

## EMA's work on new veterinary regulation advances



**September 23, 2019** – EMA has launched a new webpage that shows the progress made by the Agency in the implementation of the new Veterinary Medicines Regulation (Regulation (EU) 2019/6), which becomes applicable on January 28, 2022. On this webpage, stakeholders can find all relevant information regarding EMA's scientific and technical recommendations to the European Commission that will feed into delegated and implementing acts as part of the implementation of the legislation, as well as updates on other activities

such as the preparation for implementation progresses.

The new regulation contains new measures for increasing the availability of veterinary medicines and enhances EU action against antimicrobial resistance, a high priority for the Agency and the European medicines regulatory network. It also aims to reduce administrative burden and encourage medicine innovation and development.

As part of the implementation of the veterinary regulation, the Commission is now

preparing legislative acts, for which EMA provides scientific and technical recommendations when requested. Some of the topics covered by the Agency's recommendations are new requirements for the collection of data on the sales and use of antimicrobials in animals, which will complement the work already carried out by European Economic Area states and Switzerland to gather data on sales of antibiotics, or the development of a Union Product Database on veterinary medicines, which will provide information on all veterinary medicines that have been approved, and their availability in EU Member States.

Preparations are being carried out by experts from EMA and the EU Member States, in consultation with other EU bodies; where necessary. EMA's Committee for Medicinal Products for Veterinary Use (CVMP) adopts the Agency's scientific recommendations before EMA provides them to the European Commission. A number of recommendations were sent already to the Commission in August. The relevant documents on the progress of the work on this legislation will be published on the Agency's website as they become available.

Regulation (EU) 2019/6 repeals Directive 2001/82/EC and amends the provisions of Regulation (EU) 726/2004 relating to the authorisation and supervision of veterinary medicines, which currently governs the centralised marketing authorisation procedure for both human and veterinary medicines. The European Parliament and the European Council adopted Regulation (EU) 2019/6 in December 2018.

**Save the date: EMWA Conference in the Czech Republic**

# PRAGUE

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