News from the EMA

The articles included in this section are an edited selection from the European Medicines Agency (EMA)'s News and Press Releases archive from October 2019 to December 2019. More information can be found on the Agency's website: www.ema.europa.eu

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First vaccine to protect against Ebola

October 10, 2019 – EMA's human medicines committee (CHMP) has recommended granting a conditional marketing authorisation in the EU for Ervebo (rVSVΔG-ZEBOV-GP), the first vaccine for active immunisation of individuals aged 18 years and older at risk of infection with the Ebola virus.

Ebola virus disease is a rare but severe illness caused by the Ebola virus. Death rates in patients who have contracted the disease have varied from 25% to 90% in past outbreaks. The largest outbreak to date occurred in West Africa in 2014-2016 with more than 11,000 deaths. The 2019 outbreak in the Democratic Republic of Congo (DRC), which was caused by Ebola Zaire, had shown case fatality rates of approximately 67%. More than 3,000 people were infected with the Ebola virus during the outbreak, which was declared a public health emergency of international concern by the World Health Organization (WHO) in July 2019.

Ervebo is a genetically engineered, replication-competent, attenuated live vaccine. Data from clinical trials and compassionate use programmes have shown that Ervebo protects against Ebola virus disease in humans following a single dose administration.

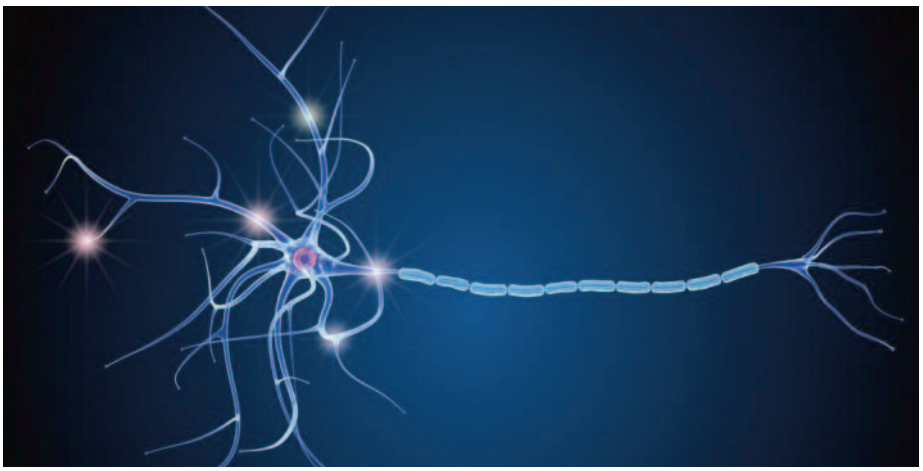
The clinical development of Ervebo was initiated in response to the 2014–2016 Ebola outbreak in cooperation with public health stakeholders, including national institutes of health, ministries of health in countries such as Guinea and DRC, WHO, the US Centers for Disease Control and Prevention, the Public Health Agency of Canada, Médecins Sans Frontières, and others. In the 2019 Ebola outbreak in DRC, the vaccine was used under an Expanded Access Protocol or 'compassionate use' to protect people at highest risk of infection such as healthcare workers, or people who have come into contact with infected patients or contacts of contacts according to a ring vaccination strategy.

Ervebo has been tested in approximately 16,000 individuals involved in several clinical studies in Africa, Europe, and the United States where it has been proven to be safe, immunogenic (i.e., able to make the immune system respond to the virus) and effective against the Zaire Ebola virus that circulated in West Africa in 2014–2016. Preliminary data suggest that it is effective in the current outbreak in DRC. Additional efficacy and safety data are being collected through the Expanded Access Protocol and should be included in post-marketing safety reports, which are continuously reviewed by EMA.

Currently, there are no therapies approved for Ebola. Ervebo 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. Ervebo was granted eligibility to PRIME in June 2016 for active immunisation against Ebola.

Ervebo received a positive opinion for a conditional marketing authorisation from the CHMP. The opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation.

Measures to minimise risk of serious side effects of multiple sclerosis medicine Lemtrada



November 15, 2019 – EMA is recommending restriction of the use of the multiple sclerosis medicine Lemtrada (alemtuzumab) due to reports of rare but serious side effects, including deaths. New measures to identify and manage the serious side effects are also recommended. The side effects include cardiovascular disorders (affecting the heart, circulation and bleeding as well as stroke) and immune-related disorders (caused by the body's defence system not working properly).

Lemtrada should now only be used to treat relapsing-remitting multiple sclerosis if the disease is highly active despite treatment with at least one disease-modifying therapy or if the disease is worsening rapidly. Lemtrada must also no longer be used in patients with certain heart, circulation, or bleeding disorders or in patients who have autoimmune disorders other than multiple sclerosis. The medicine should only be given in a hospital with ready access to intensive care facilities and specialists who can manage serious adverse reactions.

EMA has also recommended updating the physician's guide and the patient information pack with advice on minimising the risk of serious cardiovascular disorders, which may occur shortly after a Lemtrada infusion (drip), and immune-related conditions, which may occur many months and possibly years after the last treatment.

Lemtrada was authorised in the EU in 2013. It is used to treat adults with relapsing-remitting multiple sclerosis, a disease of the nerves in which the body's immune system acts incorrectly to destroy the protective sheath surrounding the nerve cells. Relapsing-remitting means that the patient has attacks (relapses) in between periods with few or no symptoms (remissions).

The active substance in Lemtrada, alemtuzumab, is a monoclonal antibody that has been designed to recognise and attach to CD52 found on white blood cells. By attaching to CD52, alemtuzumab causes the white blood cells to die and be replaced, thereby reducing damaging activity of the immune system.

The review of Lemtrada was initiated on April 10, 2019, at the request of European Commission (EC) and was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC). While the review was ongoing, the PRAC had issued temporary recommendations restricting the use of the medicine. The PRAC issued its final recommendations on October 31 to the CHMP. The CHMP opinion will now be forwarded to the EC, which will issue a final legally binding decision applicable in all EU Member States in due course.

EMA update on metformin diabetes medicines

December 6, 2019 – trace amounts of an impurity, N-nitrosodimethylamine (NDMA), have been found in a small number of metformin diabetes medicines outside the EU. The levels of NDMA in the affected non-EU metformin medicines are very low and appear to be within or even below the range that people can be exposed to from other sources, including certain foods and water. At this point, there are no data indicating that EU metformin medicines are affected.

Authorities in the EU are in the process of working with companies to test EU medicines and will provide further updates as more information becomes available. Patients in the EU should continue taking their metformin medicines as normal. The risk from not having adequate diabetes treatment far outweighs possible effects of the low levels of NDMA seen in tests. Healthcare professionals should remind patients of the importance of keeping their diabetes under control.

Metformin is widely used alone or in combination with other medicines to treat type 2 diabetes. It is usually the first-line treatment, and it works by reducing the production of glucose in the body and reducing its absorption from the gut.

NDMA is classified as a probable human carcinogen (a substance that could cause cancer) on the basis of animal studies. It is present in some foods and in water supplies, but it is not expected to cause harm when ingested in very low levels. Last year, NDMA and other impurities of the same class (nitrosamines) were found in some blood pressure medicines known as sartans. Subsequently, EMA started a review of ranitidine medicines and launched a procedure to request companies to take specific measures to avoid the presence of nitrosamines in human medicines, including metformin. The expedited testing of metformin medicines in the EU is part of this procedure.

Launch of international pilot programme on inspection of manufacturers of sterile medicines

December 17, 2019 – EMA and its European and international partners are launching a pilot programme to increase their cooperation in the inspection of manufacturers of sterile medicines for human use. This new initiative is built on the success of and experience gained from a similar collaboration, the international active pharmaceutical ingredients (APIs) inspection programme.

This collaboration will allow EMA, EU national authorities (France and the United Kingdom), the United States Food and Drug Administration, Australia's Therapeutic Goods Administration, Health Canada, the Japanese Pharmaceuticals and Medical Devices Agency, and the WHO to share information on good manufacturing practice inspections of manufacturers of sterile medicines who are located outside the participating countries, and to organise joint inspections for manufacturing sites of common interest.

International collaboration in inspections has demonstrated its benefits in improving oversight of manufacturers and making best use of inspection resources worldwide, through mutual reliance between participating regulatory bodies, the reduction of duplication of inspections and the increase in the coverage of sites inspected worldwide. The objectives, scope, and general principles of this new collaboration are laid out in the of reference for the programme.

The products in scope are sterile medicinal products for human use of chemical origin and certain therapeutic biotechnology-derived products (such as monoclonal antibodies and recombinant proteins). Products currently out of scope of this pilot are vaccines, cell and gene therapies, and plasma-derived pharmaceuticals.

The pilot will last for a minimum of 2 years after which the participating authorities will assess the programme and determine the next steps in the collaboration.

Four-year overview of pharmacovigilance activities in the EU shows robust and effective medicines safety system

December 17, 2019 – A report on the activities ensuring the safety of medicines carried out by EMA and the national competent authorities of the EU Member States, Norway, and Iceland from 2015 to 2018 shows that the EU pharmacovigilance system is strong and adaptable and has had a positive impact on public health.

The report measures the longer-term impact of the pharmacovigilance legislation, which came into effect in July 2012, in terms of simplification of pharmacovigilance processes, improved transparency and stakeholder engagement, and protection of patient health. The measurement of impact is based on a strategy and action plan for measuring the impact of pharmacovigilance activities, adopted by EMA's safety committee (PRAC) in 2017.

Some key outcomes 2015–2018:

- More than 500 new or updated risk management plans were assessed by the PRAC each year, ensuring the safety monitoring and risk minimisation is proportionate and planned. In addition, nearly 7,000 risk management plans were assessed by the Member States for nationally authorised medicines during the reporting period.
- Enhanced EudraVigilance database of suspected side effects, resulting in improved reporting and greater analytical power;
- Evaluation of nearly 9,000 potential signals (information about new or changing safety issues potentially caused by a medicine) by EMA's signal management team over the period covered by the report, and a similar number of potential signals assessed by Member States;
- Radical simplification and improvement of the way periodic safety update reports are handled, by establishing a common repository with a single portal for access;
- Development of criteria to determine when a public hearing on issues of medicines' safety would be of value, and the successful holding of the first such hearings, for valproate-containing medicines in 2017 and for quinolone and fluoroquinolone antibiotics in 2018;
- Continued development of the "Article 57 database", which now contains information on more than 800,000 medicinal products authorised through central, decentralised, mutual recognition and national procedures across the European Economic Area.

The report on the impact of pharmacovigilance measures was prepared by EMA in collaboration with the national competent authorities and aims to meet the European Commission's ongoing obligation to publish information on pharmacovigilance activities carried out by the Agency and the competent authorities of the EU Member States, Norway, and Iceland. It includes quantitative data covering the period 01/01/2015 to 31/12/2018 and shows that the European regulatory network for medicines is held accountable for the implementation of the pharmacovigilance legislation.