



EUROPEAN MEDICINES AGENCY

SCIENCE MEDICINES HEALTH



Human medicines highlights 2019

Authorisation of new medicines in 2019



Keeping medicines safe

Once a medicine has been put on the market, EMA and the EU Member States continuously monitor its quality and benefit-risk balance. Important new safety advice issued in 2019 included:



Recommendation to add new measures to prevent serious and potentially fatal errors with the dosing of **methotrexate** for treating inflammatory diseases such as rheumatoid arthritis, psoriasis and Crohn's disease.



Recommendation to revoke the marketing authorisations for **fenspiride medicines** following a review that confirmed that these cough medicines could cause heart rhythm problems.



Recommendation to restrict the use of the multiple sclerosis medicine **Lemtrada (alemtuzumab)** due to reports of rare but serious side effects, including deaths.

Authorisation of new medicines in 2019

66 Positive opinions

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1 Advanced therapy medicinal product

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3 Accelerated assessments

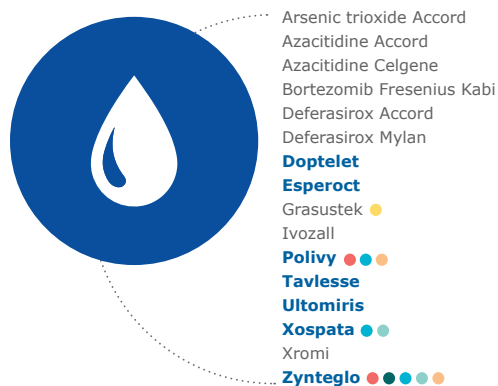
8 Conditional marketing authorisations

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Medicines recommended for approval

Haematology/ Haemostaseology



Infections



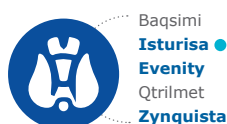
Cancer



Neurology



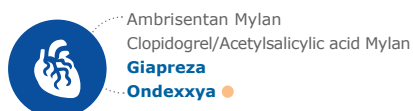
Endocrinology



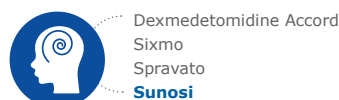
Immunology/ Rheumatology/ Transplantation



Cardiovascular



Psychiatry



Uro-nephrology



Dermatology



Metabolism



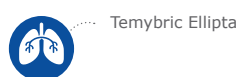
Ophthalmology



Hepatology/ Gastroenterology



Pneumology/ Allergology



Vaccines



● PRIME ● ATMP ● Orphan medicine ● Accelerated assessment ● Conditional marketing authorisation ● Approval under exceptional circumstances ● Biosimilar

Medicines that contain a new active substance are highlighted in blue

These figures reflect EMA's recommendations which are sent to the European Commission for the adoption of an EU-wide marketing authorisation.

* This figure refers to medicines that had their orphan designation confirmed by 31 December 2019. At time of approval, orphan designations are reviewed by EMA's Committee for Orphan Medicinal Products (COMP) to determine whether the information available allows maintaining the medicine's orphan status.

Important contributions to public health

Advances in medicines authorisations are essential to progressing public health as they bring new opportunities to treat certain diseases. Below is a selection of medicines approved in 2019 that represent significant progress in their therapeutic areas:



Cancer

Vitrakvi

the first 'histology-independent' treatment in the EU for solid tumours with a neurotrophic tyrosine receptor kinase (NTRK) gene fusion. NTRK gene fusions occur very frequently in a number of rare cancers.



Cardiovascular

Ondexxya

to be used as an antidote for adult patients taking the anticoagulant medicines apixaban or rivaroxaban, when reversal of their action is needed due to life-threatening or uncontrolled bleeding.



Endocrinology

Baqsimi

the first treatment for severe hypoglycaemia (low blood sugar level) that can be administered without an injection in patients with diabetes aged four years and older.

Zynquista

intended as an oral adjunct to insulin for certain patients with type 1 diabetes. Zynquista blocks the action of two proteins known as glucose transporters (SGLT1 and SGLT2) which are found in the intestine and the kidneys.



Haematology / Haemostaseology

Zynteglo

an advanced therapy medicinal product (ATMP) for beta-thalassaemia, a rare inherited blood condition that causes severe anaemia. Zynteglo is intended for adult and adolescent patients 12 years and older who need regular blood transfusions to manage their disease and have no matching donor for a stem cell transplant.



Neurology

Epidyolex

for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, two rare forms of epilepsy. Epidyolex contains an active substance derived from cannabis and is the first to receive a positive opinion in the EU centralised procedure.



Psychiatry

Sixmo

a substitution treatment for opioid dependence. Sixmo is an implant that releases low levels of buprenorphine into the patient's body for six months.

Ebola – A public health emergency

In October 2019, EMA's human medicines committee (CHMP) 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 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. Ervebo is a genetically engineered, replication-competent, attenuated live vaccine. Data from clinical trials and compassionate use programs have shown that Ervebo protects against Ebola virus disease in humans following a single dose administration.

EMA is working together with regulatory authorities around the world to support World Health Organization (WHO) and to advise on possible pathways for the development, evaluation and approval of medicines and vaccines to fight Ebola. Ervebo benefitted from support of the PRIME scheme and was assessed following an accelerated timetable.

Early access to medicines that address public health needs

Accelerated assessments

Three medicines received a recommendation for marketing authorisation following an accelerated assessment. This mechanism is reserved for medicines that are able to address unmet medical needs. It allows for faster assessment of eligible medicines by EMA's scientific committees (within a maximum of 150 days rather than 210 days).



Haematology/ Haemostaseology

Xospata

to treat adults with acute myeloid leukaemia, a cancer of white blood cells.

Zynteglo

to treat a blood disorder known as beta thalassaemia in patients 12 years and older who require regular blood transfusions.



Vaccines

Ervebo

for prophylaxis against Zaire Ebola virus disease.

Conditional marketing authorisation

Eight medicines received a recommendation for a conditional marketing authorisation, one of the possibilities in the EU to give patients early access to new medicines. As these medicines address unmet medical needs the conditional authorisation allows for early approval on the basis of less complete clinical data than normally required (products for use in emergency situations may have less complete pharmaceutical or non-clinical data). These authorisations are subject to specific post-authorisation obligations to generate complete data on the medicines.



Cancer

Libtayo

to treat adults with a type of skin cancer called cutaneous squamous cell carcinoma when the cancer is locally advanced (has spread nearby) or metastatic (has spread to other parts of the body).

Post-authorisation obligations:

The company will provide data from an ongoing study on the effectiveness and safety of the medicine for cutaneous squamous cell carcinoma. It will also investigate whether the medicine works differently depending on the levels of PD-L1 produced by the cancer cells.

Lorviqua

to treat adults with non-small cell lung cancer (NSCLC), when the disease is advanced and 'ALK-positive', which means that the cancer cells have certain changes affecting the gene responsible for a protein called ALK (anaplastic lymphoma kinase).

Post-authorisation obligations:

The company will conduct a study with the medicine in patients whose disease has worsened after treatment with alectinib or ceritinib. In addition, it will provide the results of an ongoing study comparing Lorviqua with crizotinib in patients with ALK-positive NSCLC who have not been treated before.



Cancer

Vitrakvi

for treating solid tumours with NTRK gene fusion. NTRK gene fusion is a rare genetic abnormality that can occur in tumours from different parts of the body such as the lungs, thyroid gland and intestines.

Post-authorisation obligations:

The company will provide data from the three ongoing studies which aim to confirm the benefits and safety of Vitrakvi and its longer term effect in children.



Cardiovascular

Ondexxya

used for stopping life-threatening or uncontrolled bleeding in adults taking the anticoagulant medicines apixaban or rivaroxaban.

Post-authorisation obligations:

The company will provide evidence from studies in patients with major bleeding to reliably link antifactor X activity with the ability to stop bleeding and to clarify the risk of thromboembolism. It will also carry out studies to gain more information on the effects and blood levels of Ondexxya and to confirm the dosage recommendations.



Haematology / Haemostaseology

Polivy

for the treatment of relapsed/refractory diffuse large B-cell lymphoma, a rare type of cancer of the white blood cells.

Post-authorisation obligations:

The company will provide further data on its effects to confirm Polivy's safety and effectiveness when used in combination with other cancer medicines in patients with diffuse large B-cell lymphoma.

Zynteglo

to treat a blood disorder known as beta thalassaemia in patients 12 years and older who require regular blood transfusions.

Post-authorisation obligations:

The company will provide data from a registry of patients treated with Zynteglo to study its long-term safety and effectiveness, as well as further data on the tests used in the manufacturing of the medicine to ensure its quality.



Metabolism

Waylivra

to treat familial chylomicronaemia syndrome (FCS), a genetic condition that gives rise to high levels of fats called triglycerides in the blood.

Post-authorisation obligations:

The company will provide results of a study based on a registry of patients to investigate how blood checks and adjustments to frequency of injections are carried out in practice and how well they work to prevent thrombocytopenia and bleeding.



Vaccines

Ervebo

for prophylaxis against Zaire Ebola virus disease.

Post-authorisation obligations:

The company will provide additional details on certain aspects of the production of the vaccine, including further data on the manufacturing process and completion of specific impurity, viral safety and reagent tests.

Approval under exceptional circumstances

One medicine was authorised under exceptional circumstances, a route that allows patients access to medicines that cannot be approved under a standard authorisation as comprehensive data cannot be obtained, either because there are only very few patients with the disease, or the collection of complete information on the efficacy and safety of the medicine would be unethical, or there are gaps in the scientific knowledge. These medicines are subject to specific post-authorisation obligations and monitoring.



Infections

Dectova

to treat complicated and potentially life-threatening influenza (flu) caused by either the influenza A or B virus in adults and children from 6 months of age.

Post-authorisation obligations:

The company will conduct two observational studies in patients with complicated influenza to obtain further data on the effectiveness of Dectova.

Medicines for rare diseases

The EU framework for orphan medicines aims to encourage the development and marketing of medicines for patients with rare diseases by providing incentives for developers. Orphan designations are reviewed by EMA's Committee for Orphan Medicinal Products (COMP) at the time of approval to determine whether the information available allows maintaining the medicine's orphan status and granting the medicine ten years of market exclusivity. Among the medicines recommended for marketing authorisation in 2019, seven had their orphan designation confirmed by the end of the year.

New orphan medicines with the potential to significantly benefit patients included:



Endocrinology

Isturisa

for the treatment of Cushing's syndrome, a rare disorder that occurs when the body produces too much corticosteroid hormone.



Metabolism

Palynziq

for patients aged 16 and older with phenylketonuria, a rare but serious inherited metabolic disease.

Waylivra

the first medicine for the treatment of familial chylomicronaemia syndrome, a rare genetic disease that prevents the body from breaking down fats.



Haematology / Haemostaseology

Zynteglo

to treat a blood disorder known as beta thalassaemia in patients 12 years and older who require regular blood transfusions.

Xospata

for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation. AML is a rare type of cancer of the white blood cells (cells that fight infections).

Polivy

for the treatment of relapsed/refractory diffuse large B-cell lymphoma, a rare type of cancer of the white blood cells.



Neurology

Epidyolex

for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, two forms of epilepsy.

New uses for existing medicines

Sixty extensions of indication were recommended in 2019. The extension of the use of a medicine that is already authorised for marketing in the EU can also offer new treatment opportunities for patients. Extensions of indication included:



Endocrinology

Forxiga and its duplicate Edistride

as an oral adjunct treatment with insulin for certain patients with type 1 diabetes.

Victoza

to include the treatment of children and adolescents aged ten years or older with type 2 diabetes.



Pneumology / Allergology

Dupixent

as an add-on maintenance treatment for patients 12 years and older with certain forms of severe asthma.

Negative opinions

The Committee for Medical Products for Human Use (CHMP) adopted a negative opinion for four** medicines in 2019. When the Committee cannot reach an agreement on a positive benefit-risk, it issues a negative opinion on the marketing authorisation application and elaborates on the grounds. Applicants have the right to request a re-examination of the negative opinion within 15 days of receipt of the notification.

- Cabazitaxel Teva
- Doxolipad
- Hopveus
- Vanflyta

** This figure does not include the initial negative opinions adopted by the CHMP on Xyndari (glutamine) in May and Evenity (romosozumab) in June 2019. The applicant for Xyndari withdrew its application for a marketing authorisation in September 2019. The initial negative opinion for Xyndari was under re-examination at the company's request at the time of withdrawal. The applicant for Evenity requested re-examination of the Committee's negative opinion and, after considering the grounds for this request, the CHMP recommended granting a marketing authorisation for this medicine in October 2019.

Keeping medicines safe

Monitoring in real-life – optimising safe and effective use

Once a medicine has been authorised, EMA and the EU Member States continuously monitor the quality and the benefit-risk balance of the medicine used in real-life on the market. This is to optimise how the medicine is used by patients to achieve its full benefit and to protect patients from avoidable side effects. Regulatory measures range from a change to the product information to the suspension or withdrawal of a medicine or recall of a limited number of batches.

Important new safety advice issued in 2019 included:

Methotrexate	Recommendation to add new measures to prevent serious and potentially fatal errors with the dosing of methotrexate for treating inflammatory diseases such as rheumatoid arthritis, psoriasis and Crohn's disease.
Fenspiride medicines	Recommendation to revoke the marketing authorisations for fenspiride medicines following a review that confirmed that these cough medicines could cause heart rhythm problems.
Lemtrada	Recommendation to restrict the use of the multiple sclerosis medicine Lemtrada (alemtuzumab) due to reports of rare but serious side effects, including deaths.
Xeljanz	Recommendation of new risk minimisation measures for Xeljanz (tofacitinib) to protect patients at high risk of blood clots. The review concluded that the medicine could increase the risk of blood clots in the lungs and in deep veins in patients who are already at high risk.
Gilenya	Recommendation to restrict the use of the multiple sclerosis medicine Gilenya (fingolimod) in pregnant women and in women able to have children who are not using effective contraception. The review confirmed that the medicine can harm the unborn child.
Light-exposed intravenous nutrition products	Warning to healthcare professionals that light-exposed intravenous nutrition products containing amino acids and/or lipids may lead to severe adverse effects in premature newborn babies. These products (containers and administration sets) should be protected from light.
Eliquis/ Pradaxa/ Lixiana/ Roteas and Xarelto	Direct acting oral anticoagulants Eliquis (apixaban) , Pradaxa (dabigatran etexilate) , Lixiana (edoxaban) , Roteas (edoxaban) and Xarelto (rivaroxaban) should not be used in patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome, a disorder that causes an increased risk of blood clots.
Xarelto	Recommendation not to use Xarelto (rivaroxaban) to prevent thrombosis (formation of blood clots in the blood vessels) in patients that have recently undergone transcatheter aortic valve replacement.

Ensuring integrity of clinical trial conduct and the manufacture and supply of medicines

Medicine development and manufacturing is global. It is important for regulators to ensure that EU standards are adhered to no matter where clinical trials or manufacturing takes place.

In 2019 one centralised marketing authorisation application was withdrawn as a result of good clinical practice (GCP) non-compliance.

The CHMP concluded its review of sartan medicines which set strict new manufacturing requirements for these medicines. The review was initiated due to the presence of nitrosamine impurities, including N-nitrosodimethylamine (NDMA), in a number of these blood pressure medicines. Subsequently, a nitrosamine impurity has also been detected in batches of ranitidine, and the CHMP has started a review.

In September 2019 EMA initiated a review to provide guidance to marketing authorisation holders on how to avoid the presence of nitrosamine impurities in human medicines. As part of this review, the CHMP has requested marketing authorisation holders for human medicines containing chemically synthesised active substances to review their medicines for the possible presence of nitrosamines and test all products at risk.

EMA and national competent authorities continue to monitor the presence of nitrosamine impurities in medicines, in co-operation with regulators from outside the EU.

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