



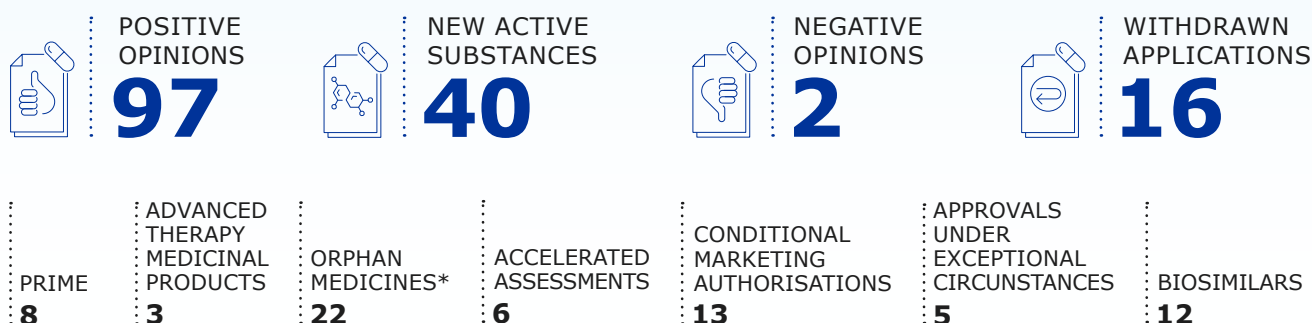
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



HUMAN MEDICINES HIGHLIGHTS 2020

AUTHORISATION OF NEW MEDICINES

Key figures on the European Medicines Agency's (EMA) recommendations for the authorisation of new medicines in 2020:



See more on the new recommendations from page 3.

KEEPING PATIENTS SAFE

Once a medicine has been put on the market, EMA and the European Union Member States continuously monitor its quality and benefit-risk balance. Important new safety advice issued in 2020 included:



Recommendation to restrict the use of **cyproterone acetate** due to the risk of meningioma (brain tumor). The risk of meningioma increases with increasing cumulative doses. The use of cyproterone acetate is contraindicated in patients with a meningioma or a history of meningioma.



Recommendation to update the safety information for **hormone replacement therapy (HRT)** used to treat symptoms of the menopause. The updates are based on evidence from a large study published in The Lancet in August 2019, which confirmed the known higher risk of breast cancer in women using HRT. The results showed that the risk may continue to be increased for ten years or more after stopping HRT, if it has been used for more than five years.



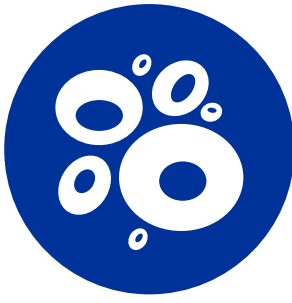
Recommendation to update the product information of **fluoroquinolone antibiotics** to reflect that systemic and inhaled fluoroquinolones may increase the risk of heart valve regurgitation/incompetence.

See more on monitoring of medicines from page 12.

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 2020. 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.

MEDICINES RECOMMENDED FOR APPROVAL



Cancer

Aybintio ●
Ayvakyt ● ●
Blenrep ● ● ● ●
 Cabazitaxel Accord
Daurismo ●
Enhertu ● ●
 Equidacent ●
 Lenalidomide Mylan
Nubeqa
 Nyvepria ●
 Onbevzi
 Phelinun
Phesgo
Piqray
Retsevmo ●
Rozlytrek ● ●
Sarclisa ●
 Sunitinib Accord
Tecartus ● ● ● ●
Tukysa
 Zercepac ●



Infections

Fetroja
Hepcludex ● ● ● ●
 Heklisav B
Obiltoxaximab SFL ● ●
Dovprela ● ●
 (previously Pretomanid FGK)
 Rekambys
Rukobia
 Tigecycline Accord
Vocabria
Xenleta
Xofluza



Haematology/ Haemostaseology

Adakveo ● ●
 Arsenic trioxide medac
 Arsenic trioxide Mylan
 Azacitidine betapharm
 Azacitidine Mylan
Calquence
Elzonris ● ●
Inrebic ●
 Lenalidomide Krka
 Lenalidomide Krka d.d.
 Lenalidomide Krka d.d. Novo mesto
Lumoxiti ● ●
 Reblozyl ●
 Ruxience ●



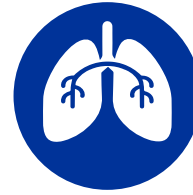
Endocrinology

Cinacalcet Accordpharma
Givlaari ● ● ● ●
 Insulin aspart Sanofi ●
 Kixelle ●
 Lyumjev
 Ogluo
 Rybelsus



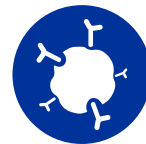
Neurology

Fampridine Accord
 Fingolimod Accord
 Fintepla ●
Libmeldy ● ●
 Zeposia
Zolgensma ● ● ● ●



Pneumology/ Allergology

Arikayce liposomal ●
 Ateectura Breezhaler
 Bemrist Breezhaler
 Budesonide/Formoterol Teva Pharma B.V.
 Enerzair breezhaler
 Gencebok
Kaftrio ●
 Palforzia
 Trepulmix ●
 Trixeo Aerosphere
 Zimbus Breezhaler



Immunology/ Rheumatology/ Transplantation

Idefirix ● ● ● ●
Jyseleca
 Livogiva ●
 Nepexto ●
 Qutavina ●
 Yuflyma ●



Vaccines

Fluad Tetra
 MenQuadfi
Mvabea ● ●
Supemtek
Vaxchora
Zabdeno ● ●

● 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



Cardiovascular

Apixaban Accord
Leqvio
Rivaroxaban Accord



Covid-19

Comirnaty ●
Veklury ●



Metabolism

Nilemdo
Nustendi



Pain

Zynrelef
Exparel



Uro-nephrology

Oxlumo ● ● ●
Sibnaya ●



Diagnostic agents

Methylthioninium chloride Cosmo



Dermatology

Staquis



Ophthalmology

Roclanda



Psychiatry

Paliperidone Janssen-Cilag International

OUTSTANDING CONTRIBUTIONS TO PUBLIC HEALTH

Authorisation of new medicines is essential to advancing public health as they bring new opportunities to treat certain diseases. Below is a selection of medicines approved in 2020 that represent significant progress in their therapeutic areas:



Cancer

Blenrep

to treat adult patients with relapsed and refractory multiple myeloma who no longer respond to treatment with an immunomodulatory agent, a proteasome inhibitor and a CD-38 monoclonal antibody.

Rozlytrek

for the treatment of patients whose solid tumours have a neurotrophic tyrosine receptor kinase gene fusion, or patients with ROS1-positive advanced non-small cell lung cancer.

Tecartus

for the treatment of adult patients with a rare cancer of white blood cells called mantle cell lymphoma (MCL) when the symptoms or the disease come back (relapse) or when they are not responding (refractory) after two or more lines of systemic therapy.



Endocrinology

Givlaari

the first treatment for acute hepatic porphyria in adults and adolescents aged 12 years and older.

Rybelsus

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.



Infections

Rekambys and Vocabria

to be used together for the treatment of patients with human immunodeficiency virus type 1 (HIV-1) infection. The two medicines are the first ARVs that come in a long-acting injectable formulation.



Immunology/Rheumatology/Transplantation

Idefirix

the first treatment for adult patients waiting for a kidney transplant, who are highly sensitised against tissue from the donor and who have a positive crossmatch test against an available kidney from a deceased donor.



Neurology

Libmeldy

to treat metachromatic leukodystrophy (MLD), a rare inherited metabolic disease that affects the nervous system.

Zolgensma

to treat babies and young children with spinal muscular atrophy, a rare and often fatal genetic disease that causes muscle weakness and progressive loss of movement.



Pneumology/Allergology

Enerzair breezhaler

the first asthma triple combination therapy that includes an optional electronic sensor to collect data on the use of the inhaler by the patient.

Kaftrio

the first triple combination therapy for the treatment of cystic fibrosis in patients aged 12 years and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or heterozygous for *F508del* in the CFTR gene with a minimal function (MF) mutation.



Uro-nephrology

Oxlumo

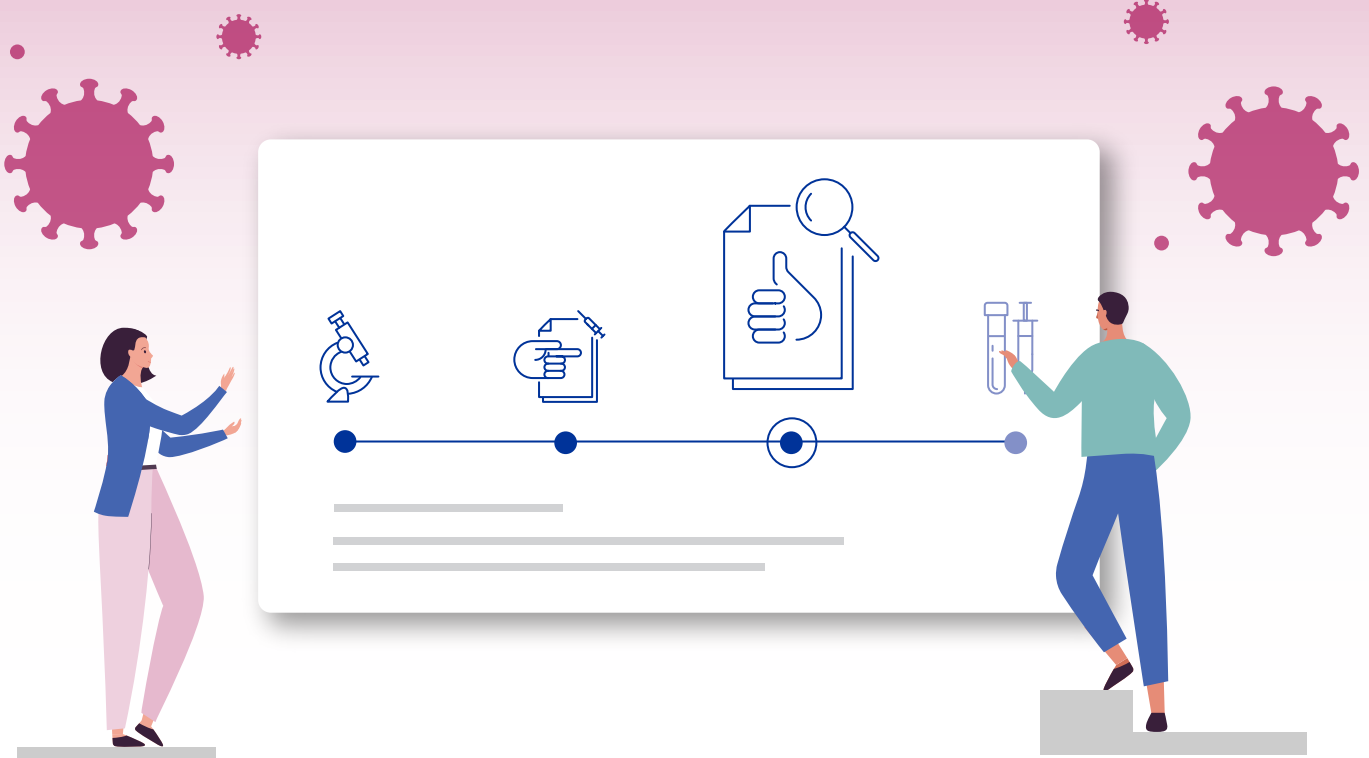
for the treatment of the rare inherited disorder primary hyperoxaluria type 1.



Vaccines

Zabdeno and Mvabea

the two components of a new vaccine that provides active immunisation to prevent Ebola virus disease in individuals aged one year and older.



Highlights on COVID-19

EMA is contributing to tackling the **COVID-19 pandemic** by expediting the development and approval of safe and effective treatments and vaccines while maintaining its high standards of quality, safety and efficacy. This includes the reduction of timelines for evaluation and the use of rolling reviews. The Agency also provides reliable information to patients and healthcare professionals.

In December 2020, EMA's human medicines committee (CHMP) recommended granting a conditional marketing authorisation for the vaccine Comirnaty, developed by BioNTech and Pfizer, to prevent coronavirus disease 2019 (COVID-19) in people from 16 years of age.

By the end of the year, one vaccine (Moderna's mRNA-1273 COVID-19 vaccine) was under evaluation by the Committee and rolling reviews of two additional vaccines were also ongoing – one for the vaccine being developed by AstraZeneca with the University of Oxford and one for the vaccine from Janssen Cilag.

In June 2020, the CHMP recommended granting a conditional marketing authorisation to Veklury (remdesivir) for the treatment of COVID-19 in adults and adolescents from 12 years of age with

pneumonia who require supplemental oxygen. In December, the Committee recommended a change to the product information for Veklury to provide clearer instructions in which COVID-19 patients requiring supplementary oxygen it should be used.

In September 2020, the Committee completed its review of results from the RECOVERY study arm that involved the use of the corticosteroid medicine dexamethasone in the treatment of patients with COVID-19 admitted to hospital, and concluded that dexamethasone can be considered a treatment option for patients who require oxygen therapy (from supplemental oxygen to mechanical ventilation).

Throughout the year, EMA issued reminders to healthcare professionals to closely monitor patients with COVID-19 who received chloroquine or hydroxychloroquine, given the serious side effects that can result from treatment with these medicines. Both chloroquine and hydroxychloroquine, which are authorised for malaria and certain autoimmune diseases, have been used to treat patients with COVID-19 but their beneficial effects in this patient population are not established.

11th medicine recommended for use outside the European Union

In July 2020, EMA's human medicines committee (CHMP) adopted a positive opinion for Dapivirine Vaginal Ring (dapivirine) used to reduce the risk of infection with the human immunodeficiency virus type 1 (HIV-1), in combination with safer sex practices when oral pre-exposure prophylaxis (PrEP) is not used, cannot be used or is not available. Placed in the vagina, the ring slowly releases the antiretroviral medicine dapivirine over a period of 28 days.

This is the eleventh medicine recommended by EMA under [EU Medicines for all \(EU-M4All\)](#), a mechanism that allows the CHMP to assess and give opinions on medicines that are intended for use in countries outside the EU under Article 58 of Regulation (EC) No 726/2004.



EARLY ACCESS TO MEDICINES THAT ADDRESS PUBLIC HEALTH NEEDS

Accelerated assessments

Six* 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).



Cancer

Blenrep

to treat relapsed and refractory multiple myeloma.

Enhertu

for the treatment of metastatic HER2-positive breast cancer.



Endocrinology

Givlaari

for treating acute hepatic porphyria in patients aged 12 years or over.



Uro-nephrology

Oxlumo

for treating primary hyperoxaluria type 1, an inherited disease in which a substance called oxalate builds up in the body, causing damage to the kidneys and other organs.



Vaccines

Mvabea and Zabdeno

the two components of a vaccine to protect adults and children aged one year and older against Ebola virus disease caused by *Zaire ebolavirus*.

*Veklury and Comirnaty are not included in this figure as they followed a specific accelerated timetable for COVID-19 related medicines.

Conditional marketing authorisations

Thirteen 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

Ayvakyt

to treat gastrointestinal stromal tumour, a cancer of the stomach and bowel, that cannot be removed by surgery and has spread to other parts of the body. Ayvakyt is used when the cancer cells have a D842V mutation, a change in the gene for the platelet-derived growth factor receptor alpha.

Post-authorisation obligations:

the company will provide additional results on the safety and effectiveness of the medicine from two ongoing studies, and will also carry out a study of the medicine as it is used by patients in the real-life setting.

Blenrep

to treat relapsed and refractory multiple myeloma.

Post-authorisation obligations:

the company will provide the final results of the main study, still ongoing at the time of authorisation, and the results of another study comparing Blenrep with pomalidomide plus low-dose dexamethasone, which is an approved treatment option for patients with multiple myeloma that has come back.

Enhertu

for the treatment of metastatic HER2-positive breast cancer.

Post-authorisation obligations:

the company will provide interim results from a study comparing Enhertu with treatment of investigator's choice in patients with metastatic breast cancer or breast cancer that cannot be surgically removed.



Cancer

Retsevmo

for the treatment of cancers that display a rearranged during transfection (RET) gene fusion: RET-fusion positive non-small cell lung cancer, RET-fusion positive thyroid cancer and RET-mutant medullary-thyroid cancer.

Post-authorisation obligations:

the company will provide results of studies set up to confirm its efficacy and safety, particularly in comparison with other medicines that are used for the cancers for which Retsevmo has been authorised.

Rozlytrek

for the treatment of patients whose solid tumours have a neurotrophic tyrosine receptor kinase gene fusion, or patients with ROS1-positive advanced non-small cell lung cancer.

Post-authorisation obligations:

the company that markets Rozlytrek will provide further data from ongoing studies on the effectiveness and safety of Rozlytrek in adults and children who have solid tumours with neurotrophic tyrosine receptor kinase (NTRK) gene fusion.

Tecartus

for the treatment of relapsed or refractory mantle cell lymphoma.

Post-authorisation obligations:

the company will submit long-term follow-up data from the main study. The company will also collect data on the long-term efficacy and safety of the medicine in specific subgroups (elderly, females, patients with severe disease) through a registry-based study.



COVID-19

Comirnaty

to prevent COVID-19 in people from 16 years of age.

Post-authorisation obligations:

the company will continue to provide results from the ongoing clinical trial. This trial and additional studies will provide information on how long protection lasts, how well the vaccine prevents severe COVID-19, how well it protects immunocompromised people, children and pregnant women, and if it prevents asymptomatic cases.

In addition, independent studies coordinated by EU authorities will also give more information on the vaccine's long-term safety and benefit.

The company will also carry out studies to provide additional assurance on the pharmaceutical quality of the vaccine as the manufacturing continues to be scaled up.

Veklury

an antiviral medicine used to treat COVID-19. It is used in adults and adolescents (from 12 years of age and weighing at least 40 kilograms) with pneumonia requiring supplemental oxygen.

Post-authorisation obligations:

the company provided EMA with more data on the quality, effectiveness and safety of the medicine and the final reports of studies with Veklury before the end of 2020. Following the submission of the final day 28 mortality data of Study NIAID-ACTT1, the CHMP recommended a change to the product information for Veklury to provide clearer instructions in which COVID-19 patients requiring supplementary oxygen it should be used. The rest of the provided data are already under evaluation.



Haematology/ Haemostaseology

Adakveo

for the prevention of recurrent vaso-occlusive crises (when blood vessels are blocked by abnormal red blood cells, restricting the flow of blood to an organ) in patients with sickle cell disease.

Post-authorisation obligations:

the company will provide further data on the safety and effectiveness of the medicine from two additional studies.



Infections

Hepcludex

for the treatment of chronic hepatitis delta virus infection in adult patients with compensated liver disease.

Post-authorisation obligations:

the company will collect data on the use of the medicine in a patient registry and will provide the final results from two ongoing studies.

Dovprela (previously Pretomanid FGK)

for treating adults with drug-resistant tuberculosis.

Post-authorisation obligations:

the company will provide the final results of ongoing studies looking at the safety and effectiveness of various doses and treatment durations.



Immunology / Rheumatology/ Transplantation

Idefirix

for adult patients waiting for a kidney transplant who are highly sensitised against tissue from the donor and who have a positive crossmatch test against an available kidney from a deceased donor.

Post-authorisation obligations:

the company will provide additional data from an ongoing study into the long-term graft functioning and survival in patients who have undergone kidney transplantation after Idefirix treatment. The company will also provide data from a new study to confirm the long-term effectiveness and safety of Idefirix.



Neurology

Zolgensma

a gene therapy medicine for treating spinal muscular atrophy (SMA), a serious condition of the nerves that causes muscle wasting and weakness.

Post-authorisation obligations:

the company will provide additional data on its benefits and risks. These include data from two studies in patients younger than six months with SMA type I and one study in patients younger than six weeks who do not have symptoms but for whom the diagnosis of SMA is confirmed based on genetic testing.

Approval under exceptional circumstances

Five medicines were 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.



Haematology/ Haemostaseology

Elzonris

for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN).

Post-authorisation obligations:

to further characterise the effectiveness and safety of Elzonris, the company will submit the results of a study based on a registry of patients with BPCDN.

Lumoxiti

for the treatment of relapsed or refractory hairy cell leukaemia, a cancer of a type of white blood cell called B-lymphocytes.

Post-authorisation obligations:

the company will carry out a study based on data from a disease registry of patients with hairy cell leukaemia to provide further information on the safety and effectiveness of the medicine.



Infections

Obiltoximab SFL

to treat inhalational anthrax, a serious disease caused by the bacteria *Bacillus anthracis*.

Post-authorisation obligations:

the company will provide further data on methods for measuring how the medicine is absorbed, modified and removed from the body in laboratory studies. In addition, data on the effectiveness and safety of the medicine during a potential outbreak of anthrax should be submitted.



Vaccines

Mvabea and Zabdeno

the two components of a vaccine to protect adults and children aged one year and older against Ebola virus disease caused by *Zaire ebolavirus*.

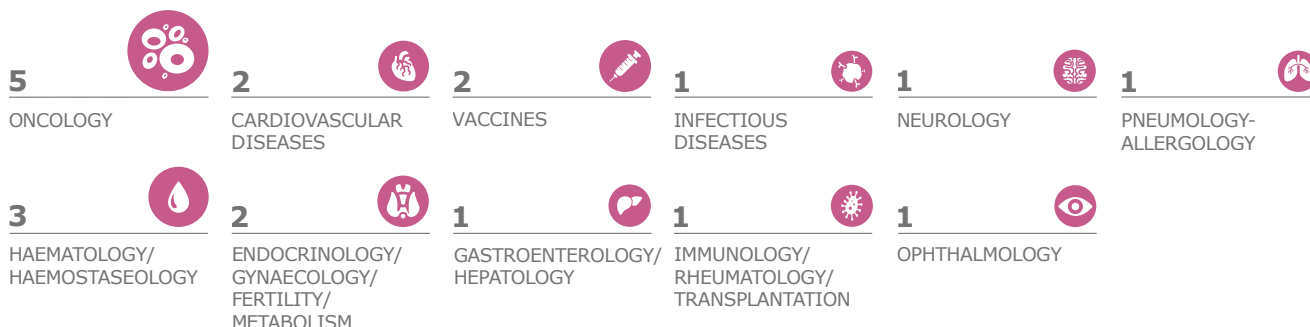
Post-authorisation obligations:

the company will provide an update on the collection of data on the effectiveness of the vaccine regimen in the intended population on a yearly basis.

Priority medicines (PRIME)

The enhanced development support provided by PRIME aims at helping patients to benefit as early as possible from promising medicines that target an unmet medical need, by optimising the generation of robust data and enabling accelerated assessment. This year, 8 PRIME-designated medicines were recommended for approval (Blenrep, Rozlytrek, Tecartus, Givlaari, Hepcludex, Zolgensma, Idefirix and Oxlummo).

20 medicines under development were included in the scheme in 2020:



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 to date allows maintaining the medicine's orphan status and granting the medicine ten years of market exclusivity. Among the 97 medicines recommended for marketing authorisation in 2020, 22 had their orphan designation confirmed by the end of the year.

New orphan medicines with the potential to significantly benefit patients for which there are no other approved products included:



Haematology/ Haemostaseology

Elzonris

for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN).



Neurology

Libmeldy

to treat metachromatic leukodystrophy (MLD), a rare inherited metabolic disease that affects the nervous system.



Infections

Hepcludex

for the treatment of chronic hepatitis delta virus infection in adult patients with compensated liver disease.



Uro-nephrology

Oxlumo

for the treatment of the rare inherited disorder primary hyperoxaluria type 1.

NEW USES FOR EXISTING MEDICINES

83 extensions of indication were recommended in 2020. 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

Orfadin

to include the treatment of alkaptonuria in adult patients.



Uro-nephrology

Velphoro

to include control of serum phosphorus levels in children aged 2 years or older with chronic kidney disease (CKD) stages 4-5 or with CKD on dialysis.



Dermatology

Olumiant

to include the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy.

NEGATIVE OPINIONS

The Committee for Medical Products for Human Use (CHMP) adopted a negative opinion for two* medicines in 2020:

- Gamifant
- Turalio

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 for this opinion. Applicants have the right to request a re-examination of the negative opinion within 15 days of receipt of the notification. More information is available on our [website](#).

KEEPING PATIENTS 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, safety 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 2020 included:

Cyproterone acetate

Restrictions in the use of **cyproterone acetate** due to risk of meningioma (brain tumor). The risk of meningioma increases with increasing cumulative doses. The use of cyproterone acetate is contraindicated in patients with a meningioma or a history of meningioma.

Hormone replacement therapy (HRT)

Recommendation to update the safety information for **hormone replacement therapy (HRT)** used to treat symptoms of the menopause. As already indicated in the product information of HRT medicines, women should only take hormone replacement therapy for the treatment of symptoms of menopause at the lowest dose and for the shortest possible time that works for them. The updates are based on evidence from a large study published in The Lancet in August 2019, which confirmed the known higher risk of breast cancer in women using HRT. The results showed that the risk may continue to be increased for ten years or more after stopping HRT, if it has been used for more than five years.

Fluoroquinolone antibiotics

The product information of **fluoroquinolone antibiotics** was updated to reflect that systemic and inhaled fluoroquinolones may increase the risk of heart valve regurgitation/incompetence.

Ulipristal acetate 5 mg

Recommendation to restrict the use of medicines containing **ulipristal acetate 5 mg** (Esmya and generic medicines) as a result of cases of serious liver injury. The medicines can now only be used to treat uterine fibroids in premenopausal women for whom surgical procedures are not appropriate or have not worked. The medicines must not be used for controlling symptoms of uterine fibroids while awaiting surgical treatment.

* This figure does not include the initial negative opinion adopted by the CHMP on Elzonris (tagraxofusp) in July 2020. The applicant for this medicine 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 Elzonris in November 2020.

Fosfomycin	Recommendation to use fosfomycin medicines given by infusion (drip) into a vein only to treat serious infections when other antibiotic treatments are not suitable. Fosfomycin medicines given by mouth can continue to be used to treat uncomplicated bladder infections in women and adolescent girls. They can also be used to prevent infection in men undergoing a procedure whereby a tissue sample is taken from their prostate (biopsy). Fosfomycin medicines given by mouth to children (under 12 years of age) and intramuscular formulations (fosfomycin medicines for injection into a muscle) should no longer be used as there are insufficient data available to confirm their benefits to patients.
Fluorouracil	Recommendation to test patients for the lack of the enzyme dihydropyrimidine dehydrogenase (DPD) before starting cancer treatment with fluorouracil given by injection or infusion (drip) and related medicines containing capecitabine and tegafur. Patients who completely lack DPD must not be given these fluorouracil medicines because of high fluorouracil toxicity which can have fatal outcome.
Creams containing 100 micrograms/gram (0.01%) of estradiol	Recommendation to limit the use of high-strength creams containing 100 micrograms/gram (0.01%) of estradiol to a single treatment period of up to 4 weeks. Data on these creams showed that in postmenopausal women who use them, the levels of estradiol in the blood were higher than normal postmenopausal levels. The absorption of estradiol into the bloodstream is of concern and could result in side effects such as venous thromboembolism (formation of blood clots in the veins), stroke, endometrial cancer (cancer of the lining of the womb) and breast cancer.
Dimethyl fumarate	Updated recommendations for dimethyl fumarate to help minimise the risk of progressive multifocal leukoencephalopathy (a rare brain infection) in patients treated with this medicine. Dimethyl fumarate is authorised in the EU for the treatment of adults with relapsing-remitting multiple sclerosis.
Leuprorelin	Recommendation on measures to avoid handling errors in preparation and administration of leuprorelin depot medicines, which are used to treat prostate cancer, breast cancer, certain conditions that affect the female reproductive system and early puberty. Handling errors resulted in some patients receiving insufficient amounts of their medicine.
Dolutegravir	The data from the <i>Tsepamo</i> study confirmed that there is no indication for an overall increased risk of major birth defects in children exposed to dolutegravir (anti-HIV treatment) during pregnancy. Furthermore, the signal for a potentially increased risk of neural tube defects has weakened when the number of exposed patients has increased. The Product information was updated accordingly.
Brivudine and fluoropyrimidines	Update of product information, introduction of a patient card and prescriber checklist to minimize the risk of fatal outcomes as a result of interaction between brivudine and fluoropyrimidines (e.g. fluorouracil, capecitabine, tegafur, flucytosine). At least 4 weeks must be awaited after the end of brivudine treatment before starting treatment with a fluoropyrimidine.
Pirfenidone	Recommendation to perform a liver function test before starting a treatment with pirfenidone , and subsequently every month for the first 6 months and then every 3 months for the duration of the treatment, to prevent drug induced liver injury. Pirfenidone is an anti-fibrotic and anti-inflammatory medicine indicated for the treatment of idiopathic pulmonary fibrosis.
Ranitidine	Recommendation to suspend all ranitidine medicines in the EU due to the presence of low levels of an impurity called <i>N</i> -nitrosodimethylamine (NDMA). Ranitidine medicines are used for reducing levels of stomach acid mainly in patients with conditions such as heartburn and stomach ulcers. NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on animal studies. More information is available in the next section.

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 2020, EMA has undertaken several reviews to provide recommendations to marketing authorisation holders to avoid the presence of **nitrosamine impurities** in medicines.


In April 2020, EMA recommended to suspend all ranitidine medicines in the EU due to the presence of low levels of an impurity called N-nitrosodimethylamine (NDMA). Available safety data did not show that ranitidine increased the risk of cancer, and any possible risk was likely to be very low. However, NDMA had been found in several ranitidine medicines above levels considered acceptable, and there were unresolved questions about the source of this impurity and potential increase of NDMA over the shelf life. Companies were asked to provide reassuring data on degradation of ranitidine and endogenous formation of NDMA to support a positive benefit-risk balance and lift the suspended marketing authorisations.

In June 2020, EMA finalised its review of nitrosamine impurities in human medicines and recommended companies to review their manufacturing processes and, where necessary, take measures to limit the presence of nitrosamines in human medicines. These measures are meant to ensure that nitrosamines are either not present or are present below levels identified to protect public health.

In November 2020, the Agency adopted an opinion on the impact of the above review on the outcome of the review for sartans with a tetrazole ring that finalised in January 2019. This led to an amendment of the previous conclusions requiring companies now to carry out risk assessments, establish control strategies and carry out testing for nitrosamines at the level of the finished product.

In 2020, EMA recommended to suspend the marketing authorisations of generic medicines tested by **Panexcell Clinical Laboratories Priv. Ltd** at its site in Mumbai, India. This was due to irregularities found by Inspectors in how the company carried out bioequivalence studies, which are used to show that a generic medicine delivers the same amount of active substance in the body as the reference medicine.

Three centralised marketing authorisation and one type II variation applications were withdrawn as a result of **good clinical practice (GCP) non-compliance**. The CHMP adopted one negative opinion (refusing the granting of the marketing authorisation) for a medicine for which there were GCP-related non-compliance issues in the clinical study submitted by the applicant.



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Human medicines highlights 2020

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