EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HUMAN MEDICINES HIGHLIGHTS 2023

An agency of the European Union

AUTHORISATION OF NEW MEDICINES

Key figures[1] on the European Medicines Agency's (EMA) recommendations for the authorisation of new medicines in 2023:

77

POSITIVE OPINIONS

3

NEGATIVE OPINIONS

19

WITHDRAWN APPLICATIONS[4]

Among these:

39 New active substances

3 PRIME

17 Orphan medicines[2,3]

1 Advanced therapy medicinal product (ATMP)

8 Biosimilars

14 Generics

3 Accelerated assessments

8 Conditional marketing authorisations

1 Approval under exceptional circumstances

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

[2] This figure refers to medicines that had their orphan designation confirmed by 31 December 2023. 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.

[3] The orphan status of one medicine was removed after authorisation at the request of the marketing authorisation holder.

[4] Detailed information is available on EMA's website.

MEDICINES RECOMMENDED FOR APPROVAL[4]

THERAPEUTIC AREA/ PRODUCT NAME	New active substance	PRIME	Orphan	ATMP	Biosimilar	Generic	Accelerated assesment	Conditional approval	Exceptional circumstances
Cancer									
Akeega									
Azacitidine Kabi						●			
Columvi	●		●					●	
Degarelix Accord						●			
Elrexfio	●	●						●	
Enrylaze									
Finlee			●						
Herwenda					●				
Inaqovi	●								
Jaypirca	●							●	
Krazati	●							●	
Lytgobi	●							●	
Mevlyq						●			
Naveruclif						●			
Omjjara	●		●						
Orserdu	●								
Pedmarqsi									
Pomalidomide Viatris						●			
Spexotras			●						
Talvey	●	●	●				●	●	
Tepkinly	●		●					●	
Tevimbra[5]	●		●						
Tibsovo	●		●						
Tidhesco[6]									
Vanflyta	●								

[4] Some medicines might fall into more than one therapeutic area but have been reflected only in one.

[5] The orphan status was removed after authorisation at the request of the marketing authorisation holder.

[6] Duplicate of Tibsovo. The marketing authorisation application was withdrawn after the positive CHMP opinion.

THERAPEUTIC AREA/ PRODUCT NAME	New active substance	PRIME	Orphan	ATMP	Biosimilar	Generic	Accelerated assesment	Conditional approval	Exceptional circumstances
Cardiovascular									
Aqumeldi									
Camzyos	●								
Dabigatran Etexilate Accord						●			
Dabigatran Etexilate Leon Farma						●			
Ibuprofen Gen.Orph						●			
Qaialdo									
Dermatology									
Ebglyss	●								
Hyftor			●						
Opzelura									
Litfulo	●								
Sotyktu	●								
Diagnostic agents									
Elucirem	●								
Pylclari	●								
Vueway[7]									
Endocrinology									
Dapagliflozin Viatris						●			
Sitagliptin/Metformin hydrochloride Sun						●			
Tolvaptan Accord						●			
Yorvipath	●		●						
Veoza	●								
Gastroenterology/ Hepatology									
Omvoh	●								
Velsipity	●								
Haematology/ Haemostaseology									
Bekemv					●				
Casgevy	●	●	●	●				●	
Epysqli					●				
Jesduvroq	●								
Vafseo	●								

[7] Duplicate of Elucirem

THERAPEUTIC AREA/ PRODUCT NAME	New active substance	PRIME	Orphan	ATMP	Biosimilar	Generic	Accelerated assesment	Conditional approval	Exceptional circumstances
Immunology/ Rheumatology/ Transplantation									
Tyenne					●				
Uzpruvo					●				
Infections									
Apretude									
Rezzayo	●		●						
Metabolism									
Elfabrio									
Loargys	●		●						●
Opfolda									
Neurology									
Agamree	●		●						
Aquipta	●								
Briumvi	●								
Lacosamide Adroiq						●			
Rystiggo	●		●						
Skyclarys	●		●						
Sugammadex Adroiq						●			
Sugammadex Piramal						●			
Tyruko					●				
Zilbrysq	●								
Ztalmy	●		●						
Ophthalmology									
Catiolanze									
Rimmyrah					●				
Yesafili					●				
Pneumology/Allergology									
Lyfnua	●								
Vaccines									
Abrysvo	●						●		
Arexvy	●						●		
Bimervax	●								
Zoonotic Influenza Vaccine Seqirus									

IMPORTANT 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 recommended for approval in 2023 that represent significant progress in their therapeutic areas:

CANCER

Columvi (*glofitamab*) and **Tepkinly** (*epcoritamab*)
for the treatment of diffuse large B-cell lymphoma, an aggressive type of non-Hodgkin lymphoma, a cancer of the lymphatic system that can arise in lymph nodes or outside of the lymphatic system.

Elrexfio (*elranatamab*)
for the treatment of adult patients with relapsed or refractory multiple myeloma, a rare cancer of the bone marrow that affects plasma cells, a type of white blood cell that produces antibodies.

Finlee (*dabrafenib*)
in combination with Spexotras (*trametinib*) for the treatment of paediatric patients aged one year and older with glioma, a type of brain tumour that begins in glial cells, the cells that surround and support nerve cells.

Jaypirca (*pirtobrutinib*)
for the treatment of relapsed or refractory mantle cell lymphoma which develops when B-cells, a type of white blood cell that makes antibodies, become abnormal.

Krazati (*adagrasib*)
for the treatment of adults with advanced non-small cell lung cancer with a G12C mutation in the KRAS gene whose disease has worsened after at least one systemic treatment.

Lytgobi (*futibatinib*)
for the treatment of cholangiocarcinoma or bile duct cancer, a type of cancer that forms in the slender tubes that carry the digestive fluid.

Omjjara (*momelotinib*)
the first treatment for myelofibrosis, a rare blood cancer that affects the bone marrow, in patients with moderate-to-severe anaemia.

Pedmarqsi (*sodium thiosulfate*)
for the prevention of ototoxicity induced by cisplatin chemotherapy in children from one month up to 18 years of age with localised, non-metastatic, solid tumours. Ototoxicity is the development of hearing or balance problems due to a medicine.

Talvey (*talquetamab*)
for the treatment of adult patients with relapsed and refractory multiple myeloma, a rare cancer of the bone marrow that affects plasma cells, a type of white blood cell that produces antibodies.

CARDIOVASCULAR

Aqumeldi (*enalapril maleate*)
for the treatment of heart failure in children from birth to less than 18 years.

Camzyos (*mavacamten*)
for the treatment of symptomatic obstructive hypertrophic cardiomyopathy, a disease in which the heart muscle becomes thickened and can make it harder for the heart to pump blood.

HAEMATOLOGY

Casgevy (*exagamglogene autotemcel*)
for the treatment of transfusion-dependent beta-thalassemia and severe sickle cell disease, two inherited rare diseases caused by genetic mutations that affect the production or function of haemoglobin, the protein found in red blood cells that carries oxygen around the body. This is the first medicine using CRISPR/Cas9, a novel gene-editing technology.

METABOLISM

Loargys (*pegzilarginase*)
for the treatment of hyperargininaemia, a rare disease with neurological clinical signs including spasticity, ataxia, hyperreflexia, incoordination, and seizures.

NEUROLOGY

Skyclarys (*omaveloxolone*)
for the treatment of Friedreich's ataxia, an inherited disease causing a range of symptoms that worsen over time, including difficulty walking, inability to co-ordinate movements, muscle weakness, speech problems, damage to the heart muscle and diabetes.

VACCINES

Abrysvo (*bivalent, recombinant*)
a vaccine to protect small infants, via immunisation of the mother during pregnancy, and adults from the age of 60 against lower respiratory tract disease caused by respiratory syncytial virus (RSV).RSV is a common respiratory virus that usually causes mild, cold-like symptoms that can be serious in vulnerable people, including older adults and those with lung or heart disease and diabetes.

Arexvy (*recombinant, adjuvanted*)
first vaccine for active immunisation to protect adults aged 60 years and older against lower respiratory tract disease caused by respiratory syncytial virus (RSV).

COVID-19 vaccines

One new vaccine, **Bimervax**, was recommended as a booster in people aged 16 years and older who have previously been vaccinated with a mRNA COVID-19 vaccine. Bimervax was evaluated as part of 'OPEN', an initiative started in December 2020 to increase international collaboration in the EU review of COVID-19 medicines.

Three approved vaccines (**Comirnaty, Spikevax and Nuvaxovid**) were adapted to the Omicron XBB.1.5 variant.

MEDICINES RECOMMENDED FOR USE OUTSIDE THE EUROPEAN UNION

In December 2023, the CHMP adopted a positive opinion for **Arpraziquantel** (*arpraziquantel*), a new treatment option for the estimated 50 million young children with schistosomiasis, a neglected tropical disease caused by parasitic blood flukes (trematode worms) that can in the long term cause damage to organs such as the bladder, the kidneys, and the liver.

The CHMP also adopted a positive opinion for **Fexinidazole Winthrop** (*fexinidazole*), a medicine used to treat human African trypanosomiasis, also known as sleeping sickness. In 2018, the medicine had received a positive opinion for sleeping sickness caused by the parasite trypanosoma brucei gambiense. The CHMP's opinion extends the use of this medicine to also include treatment of the more acute and lethal form of the disease caused by trypanosoma rhodesiense. Both of these parasites are transmitted by the tsetse fly.

These two medicines were assessed under a regulatory procedure known as EU-Medicines for all (EU-M4All) that enables EMA, in cooperation with the World Health Organization, to support global regulatory capacity building and contribute to the protection and promotion of public health beyond the EU.

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).

Cancer

Talvey (*talquetamab)*

Vaccines

Abrysvo (*bivalent, recombinant)*

Arexvy (*recombinant, adjuvanted)*

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, **three PRIME-designated medicines** were recommended for approval:

Cancer

Elrexfio (*elranatamab)*

Talvey (*talquetamab)*

Haematology

Casgevy (*exagamglogene autotemcel)*

Eighteen medicines under development were included in the scheme in 2023:

- Endocrinology - Gynaecology - Fertility - Metabolism (**4**)
- Cardiovascular diseases (**3**)
- Oncology (**3**)
- Ophthalmology (**3**)
- Vaccines for infectious diseases (**2**)
- Gastroenterology - Hepatology (**1**)
- Neurology (**1**)
- Other, Congenital, familial and genetic disorders (**1**)

CONDITIONAL APPROVAL

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

Columvi (*glofitamab)*

Elrexfio (*elranatamab)*

Jaypirca (*pirtobrutinib)*

Krazati (*adagrasib)*

Lytgobi (*futibatinib)*

Talvey (*talquetamab)*

Tepkinly (*epcoritamab)*

Haematology

Casgevy (*exagamglogene autotemcel)*

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.

Metabolism

Loargys (*pegzilarginase)*

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.

In 2023, **17 medicines** had their orphan designation confirmed by the end of the year:

Cancer

Columvi (*glofitamab)*

Finlee (*dabrafenib)*

Omjjara (*momelotinib)*

Spexotras (*trametinib)*

Talvey (*talquetamab)*

Tepkinly (*epcoritamab)*

Tevimbra[8] (*tislelizumab)*

Tibsovo (*ivosidenib)*

Dermatology

Hyftor (*sirolimus)*

Endocrinology

Yorvipath (*palopegteriparatide)*

Haematology

Casgevy (*exagamglogene autotemcel)*

Infections

Rezzayo (*rezafungin)*

Metabolism

Loargys (*pegzilarginase)*

Neurology

Agamree (*vamorolone)*

Rystiggo (*rozanolixizumab)*

Skyclarys (*omaveloxolone)*

Ztalmy (*ganaxolone)*

[8] The orphan status was removed after authorisation at the request of the marketing authorisation holder.

NEGATIVE OPINIONS

The Committee for Medical Products for Human Use (CHMP) adopted a negative opinion for **three medicines** in 2023. When the Committee cannot reach an agreement on a positive benefit-risk balance, 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.

Albrioza (*sodium phenylbutyrate/ursodoxicoltaurine*), for the treatment of amyotrophic lateral sclerosis, a rare neurological disease affecting nerve cells in the brain and spinal cord that control voluntary muscle movement.

Lagevrio (*molnupiravir*), for the treatment of COVID-19 in adults.

Sohonos (*palovarotene*), to treat fibrodysplasia ossificans progressiva, a rare genetic disease that causes extra bone to form in places outside the skeleton, such as in joints, muscles, tendons and ligaments, leading to progressively decreasing mobility and other severe impairments.

NEW USES FOR EXISTING MEDICINES

77 extensions of indication were recommended in 2023, including 38 for paediatric use[9]. 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.

[9] Most paediatric extensions of indication are based on the results of clinical studies agreed in the medicine's paediatric investigation plan (PIP).

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 clinical practice. 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 advice issued in 2023 included:

Adakveo (*crizanlizumab*)
Recommendation to no longer use Adakveo to prevent painful crises in patients aged 16 years and older with sickle cell disease, 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 recommendation followed a review by the CHMP of the results of the STAND study which showed that Adakveo did not reduce the number of painful crises leading to a healthcare visit when compared to placebo (a dummy treatment).

Fluoroquinolone antibiotics
Reminder of measures to reduce the risk of long-lasting, disabling and potentially irreversible side effects. These restrictions were introduced in 2019 following an EU-wide review of these very rare, but serious side effects. An EMA-funded study (EUPAS37856) has shown that although the use of fluoroquinolone antibiotics has decreased over time, these medicines are still prescribed outside of their recommended uses.

Gavreto (*pralsetinib*)
Recommendation to evaluate patients for active and inactive ('latent') tuberculosis before starting treatment and to initiate standard antimycobacterial therapy in patients with active or latent tuberculosis before treatment with Gavreto. Also, to avoid co-administration of pralsetinib with strong CYP3A4 inducers, or increase the dose of pralsetinib if co-administration cannot be avoided.

Olumiant (*baricitinib*)
Recommendation to use a lower dose in patients at higher risk of blood clots, cardiovascular conditions, and cancer in line with the dosing recommendations for other JAK inhibitors used to treat several chronic inflammatory disorders.

Omega-3-acid ethyl esters
Recommendation to update the product information to add atrial fibrillation as a common side effect, to inform healthcare professionals and patients of the risk of atrial fibrillation, and to permanently discontinue treatment if atrial fibrillation develops.

Pseudoephedrine-containing medicines
Recommendation to not use pseudoephedrine in patients with severe or uncontrolled high blood pressure, or with severe acute or chronic kidney disease or failure, to minimise the risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS). In addition, healthcare professionals should advise patients to stop using these medicines immediately and seek treatment if they develop symptoms of PRES or RCVS, such as severe headache with a sudden onset, feeling sick, vomiting, confusion, seizures, and visual disturbances.

Topiramate-containing medicines
Recommendation to not use topiramate for the treatment of epilepsy during pregnancy unless there is no other suitable treatment available, and to reassess at least annually the need for topiramate treatment in line with a new pregnancy prevention programme.

Zolgensma (*onasemnogene abeparvovec*)
Updated recommendations on monitoring liver function, assessing suspected liver injury after infusion and further advice regarding tapering the corticosteroid treatment, following fatal cases of acute liver failure.

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 December, EMA recommended the suspension of marketing authorisations of more than 350 generic medicines tested by Synapse Labs Pvt. Ltd., a contract research organisation (CRO) located in Pune, India. The recommendation followed a good clinical practice (GCP) inspection which showed that supporting data were lacking or insufficient to show bioequivalence. The list of the medicines concerned is available on the EMA website.

European Medicines Agency

Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Telephone +31 (0)88 781 6000
Send a question: www.ema.europa.eu/contact

www.ema.europa.eu

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