EURORDIS RARE DISEASES EUROPE

# EURORDIS THERAPEUTIC REPORT

June 2024

ISSUE 6

UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

# GENERAL NEWS

## Multi-stakeholder workshop on pharmacogenomics

The European Commission, the Heads of Medicines Agencies and the European Medicines Agency are organising a **multi-stakeholder hybrid workshop on pharmacogenomics** on **24 September from 09:00 to 17:00 CET at EMA** in Amsterdam.

The **outcome** of the workshop **will inform a roadmap towards the clinical implementation of pharmacogenomics in Europe**.

Find *here* the draft agenda and register to attend online *here*.

## Two new advice pilots to improve clinical trials in Europe

The Accelerating Clinical Trials in the EU (ACT EU) initiative is **launching two advice pilots aimed at improving the quality of applications for clinical trials**, the foundation for the development of safe and effective medicines in Europe.

**Developers of medicinal products who wish to receive advice** on the requirements for **marketing authorisation applications** (MAA) or **clinical trial applications** (CTA) **may apply to these pilots**. All this information will inform a **possible change** of scope **on how to optimise clinical trial support** in the future.

Read more *here*!

## In this issue



## Joint HMA/EMA multi-stakeholder workshop on Artificial Intelligence

An hybrid **joint HMA/EMA multi-stakeholder workshop on Artificial Intelligence** (AI) will be held on **5 November 2024**.

The workshop aims at providing an **update on the state-of-the-art of AI developments** in regard to policy and legislative environment, HMA/EMA activities on AI, and to discuss with stakeholders the progress of the multi-annual AI workplan.

The event will be broadcast live and a video recording will be available.

Find more information *here*.

It's nomination time again! Nominate your ***EURORDIS Black Pearl Awards 2025*** *here!*

EURORDIS Black Pearl AWARDS

# In the spotlight: EURORDIS Open Academy

## EURORDIS Open Academy

The objective of the *EURORDIS Open Academy* is to **build the capacity** of rare disease patient advocates at large, as well as a select number of researchers and clinicians, so that they can go on **to advocate for rare diseases** at both local or international levels. **By providing training, EURORDIS empowers patients and ensures they have the confidence and knowledge needed** to bring their expertise to discussions on health care, research and medicines development with policy makers, industry and scientists.

The Open Academy also offers **free online training** where online modules are available for anyone to use. For more information, please visit the *EURORDIS Open Academy website*.

## EURORDIS Open Academy Schools

Since its launch in 2008, the EURORDIS *School on Medicines Research & Development (MRD)* has taken place every year in Barcelona except from the editions during the COVID-19 pandemic, that it took place online. This year the School was held from 3rd to 7th June in Barcelona. Its **programme** is targeted to patient advocates and researchers to be trained in **different aspects of medicines development, from clinical trial methodology and EU regulatory processes to health technology assessment.**

In 2018 the EURORDIS *School on Scientific Innovation and Translational Research (SITR)* was launched. This School aims at deepening patient representatives' understanding of **how pre-clinical research translates into real benefits for rare disease patients**. It equips participants with knowledge and skills, so they are empowered to effectively participate in discussions with the researchers, policymakers, and companies responsible for research or research infrastructures. The School took place at the same time as the MRD during the week of the 3rd to the 7th of June in Barcelona.

A total **of 69 attendees from 25 countries attended EURORDIS Open Academy Schools this year.**

**Congratulations to all alumni!**

# Pharmacovigilance Risk Assessment Committee (PRAC) June 2024

Minutes May 2024
Agenda June 2024
Meeting Highlights June 2024

## CAR T-cell medicines: risk of secondary malignancies of T-cell origin

The PRAC has concluded that **secondary malignancies of T-cell origin** (a new cancer, different from the previous one, that begins in a type of white blood cells of the immune system called T-cells) **may occur after treatment with chimeric antigen receptor (CAR) T-cell medicines**.

The committee **evaluated data on 38 cases of secondary malignancy of T-cell origin**, including T-cell lymphoma and leukaemia, reported among approximately 42,500 patients who have been treated with CAR T-cell medicines. These medicines are used to treat blood cancers in patients whose cancer has come back (relapsed) or has stopped responding to previous treatment (refractory). **CAR T-cell medicines belong to a type of personalised cancer immunotherapies** where one type of a patient's white blood cells (T-cells) are reprogrammed and reinjected to attack the cancer.

**Since approval, the product information has advised** that patients treated with **these products may develop secondary malignancies**. The product information and the risk management plans will be updated to include the new information concerning secondary malignancy of T-cell origin.

More information is available *here*.


### Medicines safety resources

- List of medicines under additional monitoring
- EudraVigilance
- Shortages catalogue
- Recommendations on medication errors
- Good Pharmacovigilance Practices
- Patient registries
- Rules of procedure on the organisation and conduct of public hearings at the


Click on the image to get the latest issue of *QPP Update*, an EMA newsletter with the latest news on EU Pharmacovigilance

# Orphan medicines key figures

## Since 2000

**2944** Orphan designations

**294** Orphan designations included in authorised indication

**261** Authorised OMPs

**102** To be used in children

**6** Removed from the market

**94** Marketed, but no longer "orphans"

## To date

**161**

**Products with a marketing authorisation and an orphan status in the European Union**

25 July 2024

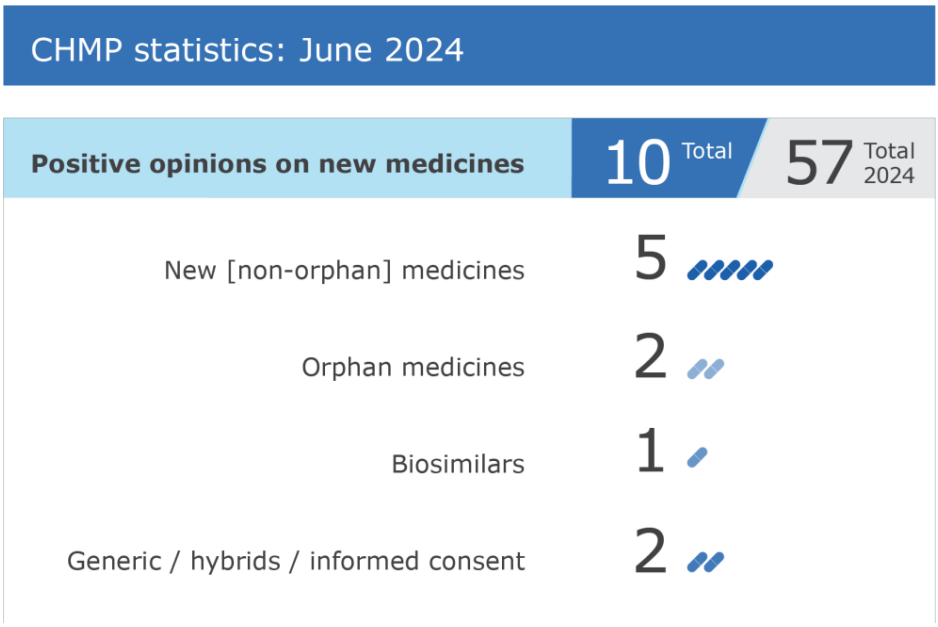
# CHMP Meeting Highlights June 2024

Minutes April 2024
Agenda June 2024
Meeting Highlights June 2024

In June, the CHMP recommended **10 new medicines for approval, two of them orphan medicines**:

- *Ordspono* (odronextamab), for the treatment of follicular lymphoma and diffuse large B-cell lymphoma, two types of blood cancer that affect the immune system.
- *Winrevair* (*sotatercept*), to treat adult patients with pulmonary arterial hypertension, a rare, long-term, debilitating and life-threatening condition in which patients have abnormally high blood pressure in the arteries in the lungs.
- *Balversa* (*erdafitinib*), for the treatment of adult patients with unresectable or metastatic urothelial carcinoma, a cancer of the bladder and urinary system.
- *Eurneffy* (*epinephrine*), the first emergency treatment against allergic reactions that is administered as a nasal spray, not as an injection.
- *mResvia* (*Respiratory Syncytial Virus (RSV) mRNA vaccine*), for prevention in adults 60 years of age and older of lower respiratory tract disease and acute respiratory disease caused by respiratory syncytial virus.
- *Piasky* (crovalimab), for the treatment of paroxysmal nocturnal haemoglobinuria, a rare genetic disorder that causes the premature breakdown of red blood cells by the immune system and is potentially life-threatening.
- *Tauvid* (*flortaucipir (18F)*), for positron emission tomography (PET) imaging of the brain in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease.
- *Steqeyma* (*ustekinumab*), a biosimilar medicine for the treatment of adult patients with moderately-to severely-active Crohn's disease, plaque psoriasis, paediatric plaque psoriasis and psoriatic arthritis.
- *Enzalutamide Viatris* (*enzalutamide*) for the treatment of prostate cancer.
- *Nilotinib Accord* (*nilotinib*) for the treatment of Philadelphia chromosome positive chronic myelogenous leukaemia.

For further details, read the full *CHMP meeting highlights*.





Click on the image to get the latest issue of ***Human Medicines Highlights***, a newsletter published by EMA address to organisations representing patients, consumers and healthcare professionals summarising key information on medicines for human use.

**COMP will no longer publish meeting reports, all the information now in the minutes**

# COMP

**The Committee for Orphan Medicinal Products (COMP) is the European Medicines Agency's (EMA) committee responsible for recommending orphan designation of medicines for rare diseases.**

The COMP was established in 2000, in line with *Regulation (EC) No 141/2000* and is responsible for evaluating applications for *orphan designation and reviewing it at time of marketing authorisation*. This designation is for medicines to be developed for the diagnosis, prevention or treatment of **rare diseases** that are life-threatening or very serious. In the European Union (EU), a disease is defined as rare if it affects fewer than 5 in 10,000 people across the EU. The European Commission decides whether to grant an orphan designation for the medicine based on the COMP's opinion.

An orphan designation allows a pharmaceutical company to benefit from incentives from the EU, such as reduced fees and protection from competition once the medicine is placed on the market.

The COMP also advises and assists the European Commission on matters related to orphan medicines, including:

- developing and establishing an EU-wide policy;
- drawing up detailed guidelines;
- liaising internationally.

COMP activities for the year 2024 include (non-exhaustive list):

- Defining the requirements for major contribution to patient care (MCPC) at orphan designation as well as at marketing authorisation stage.
- Work on the flexibility in the definition of orphan conditions to be more in line with innovative scientific development.
- Continue the pilot of RWE studies to support COMP decision-making including identification of use cases.
- Mapping the orphan designations for very rare conditions.
- Establishing the use of patient experience data for orphan medicines in regulatory purposes through a patient-validated methodology.

For more information read the full work plan *here.*

COMP members celebrating rare diseases day 2024!

| Medicinal Product | Marketing Authorisation Holder | Therapeutic Indication | Date of Marketing Authorisation |
|---|---|---|---|
| ***Spexotras®*** *(Trametinib dimethyl sulfoxidetinib)* | Novartis Europharm Limited | Glioma | 05/01/2024 |
| ***Rystiggo®*** *(Rozanolixizumab)* | UCB Pharma | Myasthenia Gravis | 05/01/2024 |
| ***Omjjara®*** *(Momelotinib)* | GlaxoSmithKline Trading Services Limited | Splenomegaly | 25/01/2024 |
| ***Skyclarys®*** *(Omaveloxolone)* | Reata Ireland Limited | Friedreich's ataxia | 09/02/2024 |
| ***Casgevy®*** *(Exagamglogene autotemcel)* | Vertex Pharmaceuticals (Ireland) Limited | Beta- Tahalassemia, Anemia, Sickle Cell | 09/02/2024 |
| ***Voydeya®*** *(Danicopan)* | Alexion Europe SAS | Paroxysmal nocturnal haemoglobinuria (PNH) | 19/04/2024 |
| ***Zynyz®*** *(Retifanlimab)* | Incyte Biosciences Distribution B.V. | Merkel cell carcinoma (MCC) | 19/04/2024 |
| ***Filspari®*** *(Sparsentan)* | Vifor France | Primary immunoglobulin A nephropathy | 19/04/2024 |
| ***Fabhalta®*** *(Iptacopan)* | Novartis Europharm Limited | Paroxysmal nocturnal haemoglobinuria (PNH) | 17/05/2024 |
| ***Qalsody®*** *(Tofersen)* | Biogen Netherlands B.V. | Amyotrophic lateral sclerosis (ALS) | 29/05/2024 |
| ***Altuvoct®*** *(Efanesoctocog alfa)* | Swedish Orphan Biovitrum AB (publ) | Hemophilia A | 17/06/2024 |

**Please click also on the following links to see:**

*Orphan medicinal products authorised during 2024*

*Orphan medicinal products authorised since 2000*

PDCO no longer publishes meeting reports. All the information now can be found in the minutes!

Minutes May 2024
Agenda June 2024

# PDCO

**The *Paediatric Committee* (*PDCO*) is the European Medicines Agency's (EMA) scientific committee responsible for activities on medicines for children and to support the development of such medicines in the European Union by providing scientific expertise and defining paediatric needs.**

The *PDCO* was established in line with the *Paediatric Regulation*, which came into effect in 2007, to improve the health of children in Europe by facilitating the development and **availability of medicines for children** aged 0 to 17 years.

The *PDCO*'s main role is to assess the content of *paediatric investigation plans* (PIPs), which determine the studies that companies must carry out in children when developing a medicine. This includes assessing applications for a full or partial **waiver** and for **deferrals**.

The PDCO is not responsible for *marketing authorisation applications* for medicines for use in children, which is in the remit of the CHMP.

PDCO activities for the year 2024 include (non-exhaustive list):

- Continue the pilot on RWE studies including through DARWIN EU to support PDCO decision-making including identification of use cases where the evidence from real word data can support the scientific assessment. Provide expert input to a review of the experience gained with real-world data (RWD) studies conducted (as part of the pilot) across the regulatory network to support regulatory decision making.
- Define a framework for use of RWD/RWE in support of extrapolation of efficacy data to the paediatric population.
- To contribute to the elaboration of a reflection paper to provide advice on the best EU approach to generate, collect and analyse patient experience data.
- To explore ways on when, how and to what extent Young Persons Advisory Groups (YPAGs) could be involved in PIP procedures.

Read *here* the full work plan for more information.

CAT updates are now quarterly- will be updated when EMA publishes

Minutes April 2024
Agenda June 2024
Meeting February 2024-April 2024

# CAT highlights February 2024– April 2024 meeting update

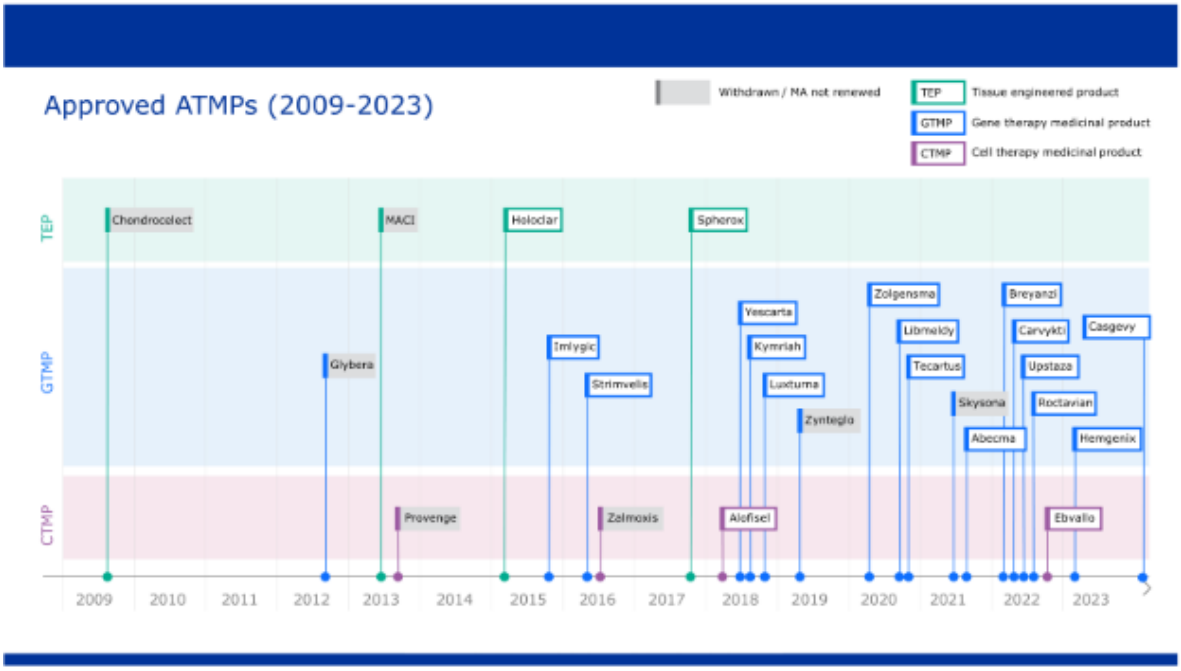
This report provides information on ATMP approvals and extension of indications of authorised ATMPs, as well as statistical data on product-related activities.

The outcome of these assessments can be found here: *Summaries of scientific recommendations on classification of ATMPs*.

There are **no approvals** of **Advanced therapy medicinal products** in the period covered by this report.

The CAT adopted an **extension of indication for Carvykti** to include the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least one prior therapies.

For more information, see also the *EMA meeting report*.



# EMA's Management Board

Minutes March 2023
Agenda June 2024

## What is the EMA Management Board?

**The Management Board is the European Medicines Agency's integral governance body. It has a supervisory role with general responsibility for budgetary and planning matters, the appointment of the Executive Director and the monitoring of the Agency's performance.**

## EMA's Management Board role

The Management Board role is to **set the Agency's budget**, approve the **annual work programme** and is responsible for **ensuring that the Agency works effectively** and **co-operates successfully** with partner organisations across the EU and beyond.

The **operational tasks** of the management board range from adopting legally binding implementing rules, to setting strategic directions for scientific networks, to reporting on the use of European Union (EU) contributions for the Agency's activities.

The Board generally meets four times a year. Check out the minutes of the last meeting (October 2023) *here*.

## EMA's Management Board composition

The Management Board consists of **36 members**, appointed to act in the public interest, who do not represent any government, organisation or sector. The members of the Management Board are appointed on the basis of their expertise in management and, if appropriate, experience in the field of human or veterinary medicines. They are selected to guarantee the highest levels of specialist qualifications, a broad spectrum of relevant expertise and the broadest possible geographical spread within the EU. Find out more about the members *here*.

The Management Board is made up of **members and observers**. **Virginie Hivert**, Therapeutic Development Director at the European Organisation For Rare Diseases EURORDIS, is one of the two **representatives of patients' organisations** in the board.

# PATIENTS' AND CONSUMERS' WORKING PARTY

The Patients' and Consumers' Working Party (PCWP), established in 2006, serves as a platform for exchange of information and discussion of issues of common interest between EMA and patients and consumers. It provides recommendations to EMA and its human scientific committees on all matters of interest in relation to medicines.

For more information, see also the *PCWP mandate, objectives and rules of procedure.*

## EMA PCWP & HCPWP meeting working parties joint meeting

Last 27th and 28th February 2024 took place *the Patients and Consumers' (PCWP) and 'Healthcare Professionals' (HCPWP) Working Parties meeting* at the EMA.

Topics discussed during the two day meeting included an update on the progress with patient experience data, an update on the network training centre, EMA's policy on competing interests, pharmacovigilance related-topics and shortages.

## EMA Glossaries

The EMA just published a *medical terms simplifier* that gives plain-language descriptions of medical terms commonly used in information about medicines.

A *glossary of regulatory terms* that gives definitions for the main terms used on the EMA website and in their documents has also been published.

For more information, please check the *glossaries here.*

# GLOSSARY

**Accelerated assessment**
Rapid assessment of medicines in the centralised procedure aimed at facilitating patient access to new medicines that address an unmet medical need. Accelerated assessment usually takes 150 evaluation days, rather than 210.

**Advanced therapies or advanced-therapy medicinal products (ATMPs)**
ATMPs are new medical products based on genes, cells and tissues, which offer new treatment opportunities for many diseases and injuries. There are four main groups:

- **Gene-therapy medicines**
  They are medicines that contain genes leading to a therapeutic effect. They work by inserting 'recombinant' genes into cells, usually to treat a variety of diseases, including genetic disorders, cancer or long-term diseases. A recombinant gene is a stretch of DNA that is created in the laboratory, bringing together DNA from different sources.
- **Somatic-cell therapy medicines**
  These contain cells or tissues that have been manipulated to change their biological characteristics. They can be used to cure, diagnose or prevent diseases;
- **Tissue-engineered medicines**
  These contain cells or tissues that have been modified so they can be used to repair, regenerate or replace tissue.
- **Combined advanced-therapy medicines**
  These are medicines that contain one or more medical devices as an integral part of the medicine. An example of this is cells embedded in a biodegradable matrix or scaffold.

**Authorisation under exceptional circumstances**
It 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, 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.

**Compliance check**
It is performed to verify that all the measures agreed in a *Paediatric Investigation Plan* (PIP) and reflected in the Agency's decision have been conducted in accordance with the decision, including the agreed timelines. Full compliance with all studies/measured contained in the PIP is one of several prerequisites for obtaining the rewards and incentives provided for in Articles 36 to 38 of the Paediatric Regulation.

**Conditional marketing authorisation**
It is granted to a medicine that addresses unmet medical needs of patients on the basis of less comprehensive data than normally required. The available data must indicate that the medicine's benefits outweigh its risks and the applicant should be in a position to provide the comprehensive clinical data in the future.

**Designation, orphan medicinal product**
A status assigned to a medicine intended for use against a rare condition. The medicine must fulfil certain criteria for designation as an orphan medicine so that it can benefit from incentives such as protection from competition once on the market.

**European Public Assessment Report (EPAR)**
It is a lay-language document, which provides a summary of the grounds on which the EMA/CHMP based its recommendation for the medicine to receive a marketing authorisation. This happens when a manufacturer develops a generic medicine based on a reference medicine, but with a different strength or given by a different route.

**Hybrid application for marketing authorisation**
Hybrid applications rely partly on the results of tests on the reference medicine and partly on new data from clinical trials.

**Informed consent application for marketing authorisation**
An informed consent application makes use of data from the dossier of a previously authorised medicine, with the marketing authorisation holder of that medicine giving consent for the use of their data in the application.

**Orphan Legislation**
*Regulation (EC) No 141/2000* on orphan medicinal products

**Paediatric Investigation Plan (PIP)**
It sets out a programme for the development of a medicine in the paediatric population. It aims to generate the necessary quality, safety and efficacy data through studies to support the authorisation of the medicine for use in children of all ages. These data have to be submitted to the EMA, or national competent authorities, as part of an application for a marketing authorisation for a new medicine, or for one covered by a patent.

**Paediatric Use Marketing Authorisation (PUMA)**
It is a dedicated marketing authorisation for medicinal products indicated exclusively for use in the paediatric population, or subsets thereof, with, if necessary, an age-appropriate formulation. It has been designed to promote paediatric development of already authorised products which are no longer covered by a patent. Benefits are 8 years of data protection and 10 years market protection

**Patient-reported outcomes (PROs)**
Measurements based on data provided directly by patients regarding their health condition without interpretation of the patient's response by a clinician or anyone else.

**Patient-reported outcome measures (PROMs)**
They are instruments, scales, or single-item measures that have been developed to measure PROs, for example a self-completed questionnaire to assess pain.

**Periodic Safety Update Reports (PSURs)**
Periodic reports that the evaluate the benefit-risk balance of a medicine as evidence is gathered in clinical use. They are submitted by marketing authorisation holders at defined time points after the authorisation.

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**Post-authorisation efficacy studies (PAES)**
PAES are studies relating to authorised medicinal products conducted within the therapeutic indication with the aim of addressing well-reasoned scientific uncertainties on aspects of the evidence of benefits of a medicine that could not be resolved before authorisation or were identified afterwards.

**Post-authorisation safety studies (PASS)**
A PASS is carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC is responsible for assessing the protocols of imposed PASSs and for assessing their results.

**Prevalence**
In the context of the Orphan Legislation, the prevalence refers to the number of persons with the condition at the time the application is made, divided by the population of the European Union (EU) at that time. It requires demonstration through authoritative references that the disease or condition for which the medicinal product is intended affects not more than 5 in 10,000 persons in the EU, when the application is made.

**Public summaries of PDCO evaluations of PIPs**
They describe the applicant's proposal for the development of their medicine in children, the PDCO's conclusion on the potential use of the medicine in the paediatric population, the plan agreed between the committee and the applicant at the completion of the procedure (including any partial waivers or deferrals) and the next steps.

**Referral procedures for safety reasons**
A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or a class of medicines on behalf of the European Commission or a Member State.

**Risk Management Plans (RMPs)**
RMPs are regulatory documents submitted by medicine developers when they apply for marketing authorisation and include information on the medicine's safety profile; how its risks will be prevented or minimised in patients; plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine; risk factors for developing adverse reactions; measuring the effectiveness of risk-minimisation measures.

**Scientific advice/protocol assistance**
Through scientific advice, companies can ask the EMA for advice on whether they are conducting the appropriate tests and studies during the clinical development of a given product. In the case of orphan medicines for the treatment of rare diseases, it also includes advice on1) the demonstration of significant benefit for the designated orphan indication and on 2) similarity or clinical superiority over other medicines; which are criteria for the authorisation of an orphan medicine.

**Significant benefit**
Demonstrating a significant benefit, this is demonstrating a "clinically relevant advantage or a major contribution to patients" is one of the criteria that medicines for the treatment of rare diseases must fulfil to benefit from 10 years of market exclusivity once they have been authorised. For further information, read the *workshop report: Demonstrating significant benefit of orphan medicines*, held at the EMA in December 2015.

**Safety signal**
A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature, but their presence does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of a safety signal is required to establish whether or not there is a causal relationship between the medicine and the adverse event.

**Similar active substance**
It means an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of them) and which acts via the same mechanism.

**Scientific Advisory Group (SAG)**
SAGs have been established to provide an independent recommendation on scientific/technical matters related to products under evaluation through centralised regulatory procedures and referrals by the CHMP or any other scientific issue relevant to the work of the Committee.

**Waiver**
A waiver can be issued if there is evidence that the medicine concerned is likely to be ineffective or unsafe in the paediatric population, or that the disease or condition targeted occurs only in adult populations, or that the medicine, or the performance of trials, does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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