EURORDIS
THERAPEUTIC REPORT
December 2023
ISSUE 11
UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

# GENERAL NEWS

## EMA interactive webinar on Rare Disease Day

EMA's Orphan Medicines Office is hosting an **interactive webinar on Rare Disease Day on 29 February 2024,** to answer questions that developers of products for rare diseases or researchers in this field might have **on orphan designations and rare disease development**.

The event is directed towards **healthcare professionals, academia, industry representatives and patients**.

Please find more information on the event *here* and check out the agenda *here*!

Registration will close on 23 February 2024.

## IN THIS ISSUE



## 12th Edition of ECRD

Don't miss the opportunity to attend the **next European Conference on Rare Diseases and Orphan Products (ECRD)** taking place on **15 and 16 May 2024**.
Check out *what's on the programme* and register *here*!

**Poster abstracts** submissions for the conference are now open until **23rd February 2024**.
**Patient groups, academics, health care professionals** and all other interested parties having conducted research or studies on rare diseases or public health projects are encouraged to **submit a poster abstract** *here*!

## EURORDIS Black Pearl Awards

The **13th EURORDIS Black Pearl Awards** is taking place on the evening of **20 February 2024** in **Brussels and online!**

Registration for the **online ceremony is free** of charge, and fees for the in person attendance can be checked *here*.

*Register now* for the **next edition of the EURORDIS Black Pearl Awards** and **join us** in recognising the major achievements and outstanding commitment of the **people who strive to make a difference for the rare disease community**!

**Get involved in *rare disease day!***

RAREDISEASEDAY.ORG

# In the spotlight: Drug Repurposing

## What is Drug Repurposing?

According to the European expert group *Safe and Timely Access to Medicinal Product (STAMP)*, drug repurposing is the process of **identifying a new use for an existing drug in an indication outside the scope of the original indication**.

It offers an **innovative opportunity** on the drug development field for many conditions and especially for rare diseases **to address unmet medical patient needs**. In comparison to the development of an entire new drug, repurposing might have fewer risks, might be less costly and has the potential to speed up research and development for the benefit of the patients. This makes it particularly attractive for rare and neglected conditions where no effective treatments are available.

We are seeing a **growing interest** in policy, regulation, funding and research in the drug repurposing field, and there are several drug repurposing European initiatives going on such as *REMEDi4ALL* (EURORDIS is part of the Consortium), *RePo4EU* and *SIMPATHIC*.

## IRDiRC Taskforce- Drug Repurposing Guidebook

The *International Rare Diseases Research Consortium (IRDiRC)* creates Task Forces to tackle specific topics within rare diseases research. Each Task Force reviews current barriers to efficient and effective rare disease research, and proposes solutions through policy recommendations and/or technical applications.

The *Drug Repurposing Guidebook Task Force* aimed at helping developers navigating the rare disease landscape and identifying specific tools and practices of relevance for repurposing projects.

This Task Force has recently published a second paper- *Drug repurposing for rare: progress and opportunities for the rare disease community* focusing on **lessons learned from drug repurposing case studies** and **upcoming trends** that will help progress the field of drug repurposing. The article is open access and has been published in Frontiers in Medicine.
Read the full article *here*.

## International Drug Repurposing Conference 2024 (#iDR24): Bridging Boundaries for Innovative Drug Repurposing

The **first International Drug Repurposing conference** will take **place 6-7 March 2024,** at Sant Pau Art Nouveau World Heritage Site, Barcelona, uniting key players in drug repurposing. Co-organised by REMEDi4ALL Consortium, Beacon for Rare Diseases, and MeRIT, the conference showcases **how patient communities, researchers, industry, and health authorities can benefit from cutting-edge drug repurposing**.

The agenda of the event follows 3 topical paths in parallel:

- Cancer path
- Rare diseases path
- Methodologies path

Explore cutting-edge insights, discuss challenges, and engage with experts.
Find out more about the speakers, location, and ticket prices *here*!

# Pharmacovigilance Risk Assessment Committee (PRAC) December 2023

Minutes October 2023
Agenda January 2024
Meeting Highlights January 2024

## Start of safety review of CAR T-cell medicines

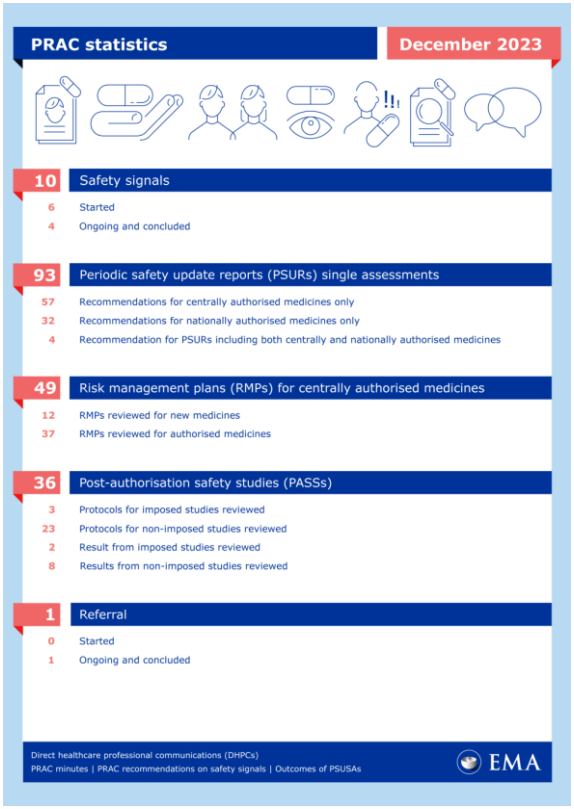
The PRAC started a signal procedure to **review data on secondary malignancies related to T-cells** (cancers that begin in a type of white blood cells called T-cells) **for the six approved chimeric antigen receptor (CAR) T-cell medicines**.

**CAR T-cell based gene therapy** products belong to a type of personalised cancer immunotherapies where patients' white blood cells (T-cells) are reprogrammed and reinjected to attack the cancer. There are **six CAR T-cell products approved** in the European Union (EU). These medicines are **used to treat blood cancers** in patients whose cancer has come back (relapsed) or has stopped responding to previous treatment (refractory).

A **secondary malignancy** is when a patient who has cancer develops a second cancer different from the first cancer. For all six **CAR T-cell products, secondary malignancies were considered as an important potential risk** at the time of their authorisation.

The PRAC is now reviewing all available evidence and will decide on the need for any regulatory action.

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

**2806** Orphan designations

**283** Orphan designations included in authorised indication

**250** Authorised OMPs

**100** To be used in children

**6** Removed from the market

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

## To date

**158**

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

25 January 2024

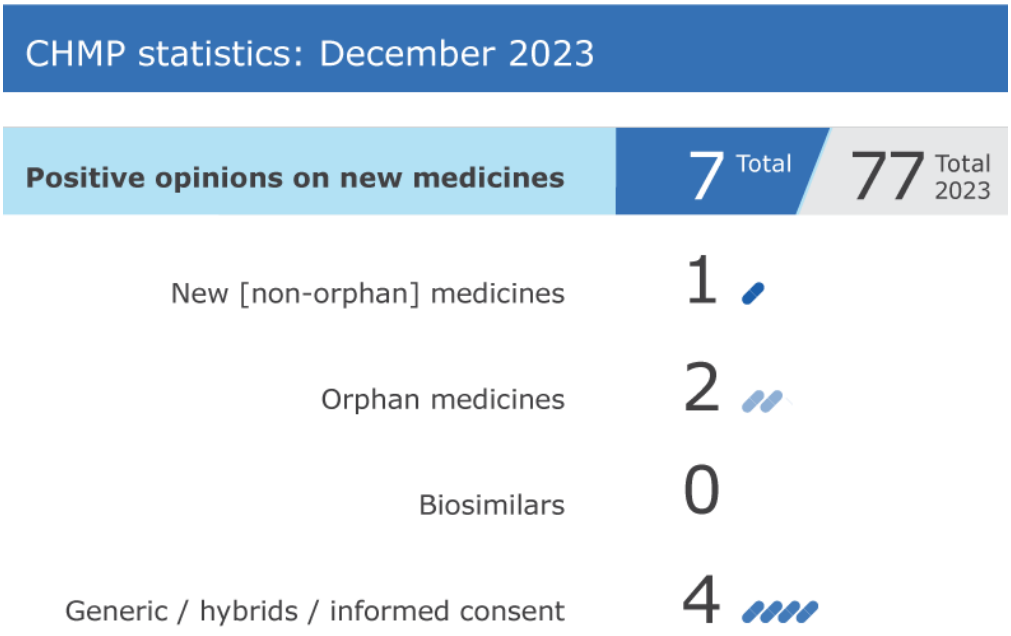
# CHMP Meeting Highlights December 2023

Minutes November 2023
Agenda December 2023
Meeting Highlights December 2023

In December, the CHMP recommended **7 new medicines for approval, 2 of them orphan medicines**:

- *Casgevy* (*exagamglogene autotemcel)*, an advanced therapy medicinal product (ATMP) for the treatment of transfusion dependent beta-thalassemia and severe sickle cell disease, two inherited rare diseases caused by genetic mutations..
- *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.
- *Velsipity* (*etrasimod*), for the treatment of patients with moderate to severe ulcerative colitis, an inflammation of the large intestine causing ulceration and bleeding.
- *Dabigatran etexilate Leon Farma* (*dabigatran etexilate*), for prevention and treatment of venous thromboembolic events, prevention of stroke and systemic embolism, and prevention and treatment of deep vein thrombosis and pulmonary embolism.
- *Ibuprofen Gen.Orph* (*ibuprofen*), for the treatment of a haemodynamically significant patentductus arteriosus in preterm newborn babies less than 34 weeks of gestational age.
- *Mevlyq* (*eribulin*), for the treatment of breast cancer and liposarcoma, a rare cancer that develops in fat tissue.
- *Pomalidomide Viatris* (*pomalidomide*), for the treatment of adult patients with relapsed and refractory multiple myeloma, a cancer of the bone marrow.

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.

Minutes November 2023
Agenda December 2023

**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 members celebrating rare diseases day 2023!

| Medicinal Product | Marketing Authorisation Holder | Therapeutic Indication | Date of Marketing Authorisation |
|---|---|---|---|
| ***Hemgenix®*** *(etranacogene dezaparvovec)* | CSL Behring Gmbh | Haemophilia B | 20/02/2023 |
| ***Tibsovo®*** *(ivosidenib)* | Les Laboratoires Servier | Acute Myeloid Leukaemia and cholangiocarcinoma | 12/05/2023 |
| ***Hyftor®*** *(sirolimus)* | Plusultra pharma GmbH | Facial angiofibroma | 15/05/2023 |
| ***Columvi®*** *(glofitamab)* | Roche Registration GmbH | Diffuse large B cell lymphoma (DLBCL) | 07/07/2023 |
| ***Ztalmy®*** *(ganaxolone)* | Marinus Pharmaceuticals Emerald Limited | Epileptic seizures in children with CDKL5 | 26/07/23 |
| ***Talvey®*** (*talquetamab*) | Janssen-Cilag International N.V. | Multiple Myeloma | 21/08/2023 |
| ***Tepkinly®*** *(epcoritamab)* | AbbVie Deutschland GmbH & Co. KG | Diffuse large B-cell lymphoma (DLBCL) | 22/09/2023 |
| ***Finlee®*** *(dabrafenib mesylate)* | Novartis Europharm Limited | Glioma | 15/11/2023 |
| ***Yorvipath®*** *(palopegteriparatide)* | Ascendis Pharma Bone Diseases A/S | Chronic hypoparathyroidism | 17/11/2023 |
| ***Agamree®*** *(vamorolone)* | Santhera Pharmaceuticals (Deutschland) GmbH | Duchenne muscular dystrophy | 14/12/2023 |
| ***Loargys®*** *(pegzilarginase)* | Immedica Pharma AB | Hyperargininemia | 15/12/2023 |
| ***Rezzayo®*** *(rezafungin)* | Mundipharma GmbH | Invasive candidiasis | 22/12/2023 |

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

*Orphan medicinal products authorised during 2023*

*Orphan medicinal products authorised since 2000*

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

Minutes November 2023
Agenda December 2023

# 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:

- 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 October 2023
Agenda December 2023
Meeting August 2023-October 2023

# CAT highlights August– October meeting update

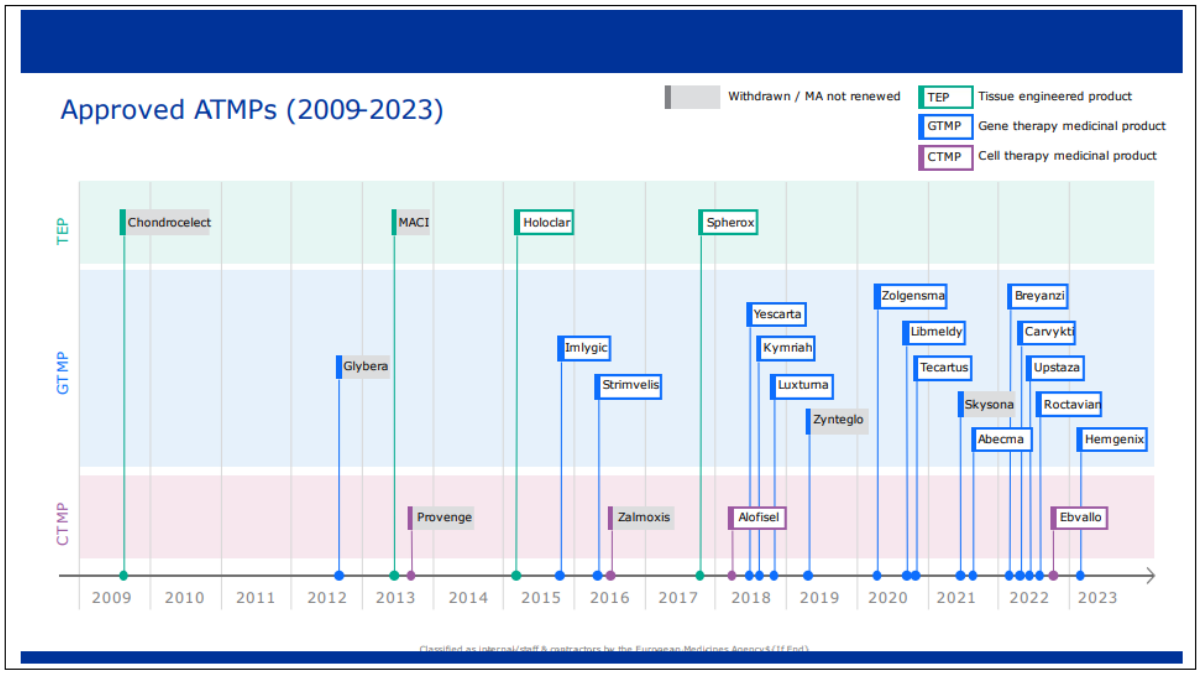
This report provides information on ATMP approvals and extension of indications of authorised ATMPs, as well as statistical data on product-related activities.

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.

There are **no extension of indication of authorised ATMPs.**

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



# EMA's Management Board

Minutes October 2023
Agenda December 2023

**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.**

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 Board's operational tasks 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 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 Board generally meets four times a year. Check out the minutes of the October meeting *here*.

# 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 14th and 15th November 2023 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 the availability and accessibility of medicines, EMA data related initiatives and digitalisation, regulatory science and innovation, and EMA communications.

For more information, please see the agenda and presentations of the meeting *here*.

## 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.

Co-funded by the European Union

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