EURORDIS
THERAPEUTIC REPORT
April 2023
ISSUE 4
UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

IHI call for patients experts

The Innovative Health Initiative (IHI) is calling on patients and caregivers to apply to be part of the new IHI Patient Pool. Members of the pool may be invited to participate in project meetings, scientific events, webinars, or trainings organised by IHI. All applicants who meet the requirements and want to be part of the IHI Patient Pool will be accepted.

Deadline for applications: 8 June 2023 at 17:00 CEST! For details of how to apply, and the link to the *online application form here*.

For more information visit the IHI Patient Pool page of the IHI website*!*

IN THIS ISSUE

EJP RD training summer school

The **International Summer School on Rare Disease Registries and FAIRification of data** is a part of a series of training activities proposed by the ***European Joint Programme on Rare Diseases (EJP-RD)***.

In these five days of face-to-face training taking place from **25-29 September at Rome**, you will learn about rare disease registries and FAIRification of data at the source.

Registration is open *here* until July 5th.

For more information on the training, read *here*.

New survey on training needs!

The EURORDIS Open Academy want to continue to improve the relevance and quality of our patient empowerment work! For this reason, a survey open to patient advocates and researchers has been launched to know their **main reasons for engaging in training**, their **main topics of interest, and the main roadblocks** that would prevent them from attending a training event.

Join the movement, share your voice, and shape the future of patient empowerment. Take the *survey* today and **spread the word before 31st May!**

It's nomination time again!
Nominate your ***EURORDIS Black Pearl Awards 2024*** *here!*

EURORDIS Black Pearl AWARDS

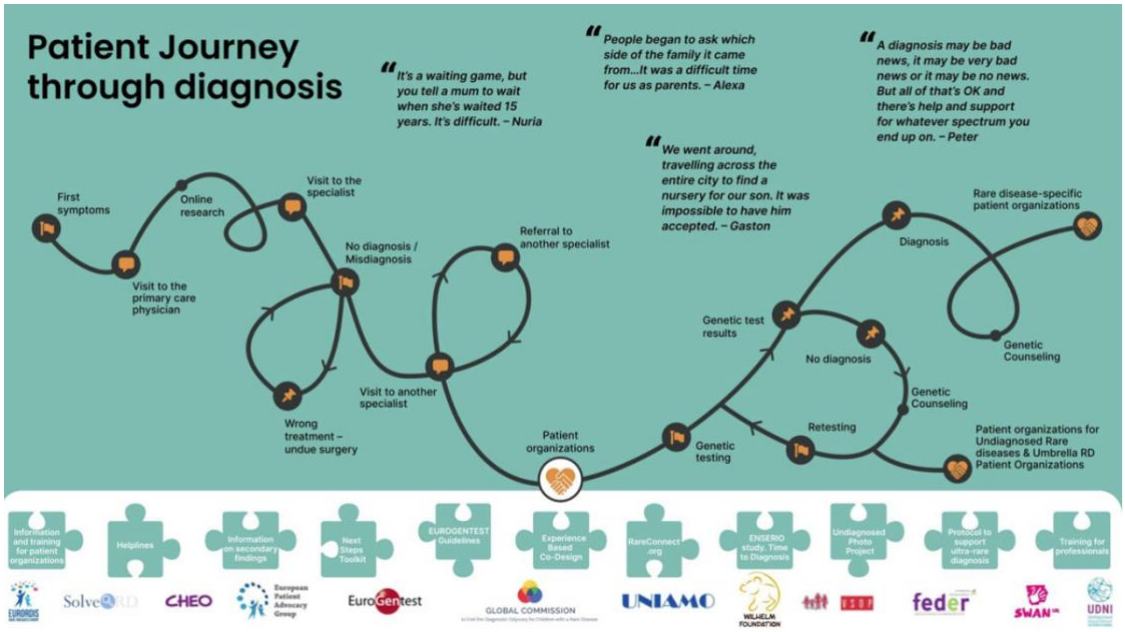
What is Solve RD?

Solve RD – Solving the Unsolved Rare Diseases was funded in 2018 by the European Commission for five years. It kicked off with ambitious goals set out by the *International Rare Diseases Research Consortium* to deliver diagnostic tests for most rare diseases by 2020 and fully integrates with the formation of ERNs. To date, *the Solve-RD Project* has analysed 21,348 datasets (phenotype and exome/genome sequencing data) from 6000 families. **The project has already solved 511 rare disease cases (8.5% diagnostic yield) for which a molecular cause was not previously known.**

Within the *Solve-RD project*, EURORDIS initiated the Community Engagement Task Force (CETF) – a multi-stakeholder community of patients, scientists and clinicians to support the needs of undiagnosed and recently diagnosed patients and leave a legacy of a strengthened undiagnosed community. The EURORDIS-led CETF has created an infographic setting out the patient journey to diagnosis. The infographic demonstrates the diagnostic odyssey many people experience on a daily basis and presents existing resources from CETF member organisations to support patients on this journey.

The infographic is available in 28 languages so far! For more information, please read *here and see below.*

Solve-RD infographic on the patient journey to diagnosis



Time to act!

The Solve-RD consortium and associated European Solve-RD network, including among others six European Reference Networks, EURORDIS, Orphanet and leading European Rare Disease Clinicians and Researchers in 20 countries, call upon all European RD stakeholders, including EU Member States, the European Commission, the Council of the European Union, the general public and private organisations active in the RD field, as well as the rare disease community at large **call to act now to seize the current once-in-a-generation opportunity to significantly improve RD diagnosis in Europe.**

This unique opportunity is characterized **by pan-European access to diagnostic technologies in particular Whole Exome Sequencing**, the just reached maturity of the European Refence Networks ecosystem, the looming opportunity to share RD data on European-wide scale within the forthcoming European Health Data Space, the upcoming RD-Partnership as well as - with Solve-RD - the availability of a scalable transnational diagnostics research platform.

Read the full critical action points *here!*

Pharmacovigilance Risk Assessment Committee (PRAC) April 2023

Minutes February 2023
Agenda April 2023
Meeting Highlights April 2023

Topiramate use in pregnancy under revision

EMA's safety committee (PRAC) has started a **review of topiramate and the risk of neurodevelopmental disorders in children** whose mothers were taking topiramate during pregnancy.

The review was triggered by a recent *study* which suggested a possible increase in the risk of neurodevelopmental disorders, in particular autism spectrum disorders and intellectual disability, in children whose mothers were taking topiramate during pregnancy.

The committee will now conduct an in-depth review of the available data on the benefits and risks of topiramate use in pregnant women and women of childbearing potential in the approved indications.

Following this review, the PRAC will give its recommendation as to whether marketing authorisations of topiramate-containing products should be maintained, varied, suspended or revoked.

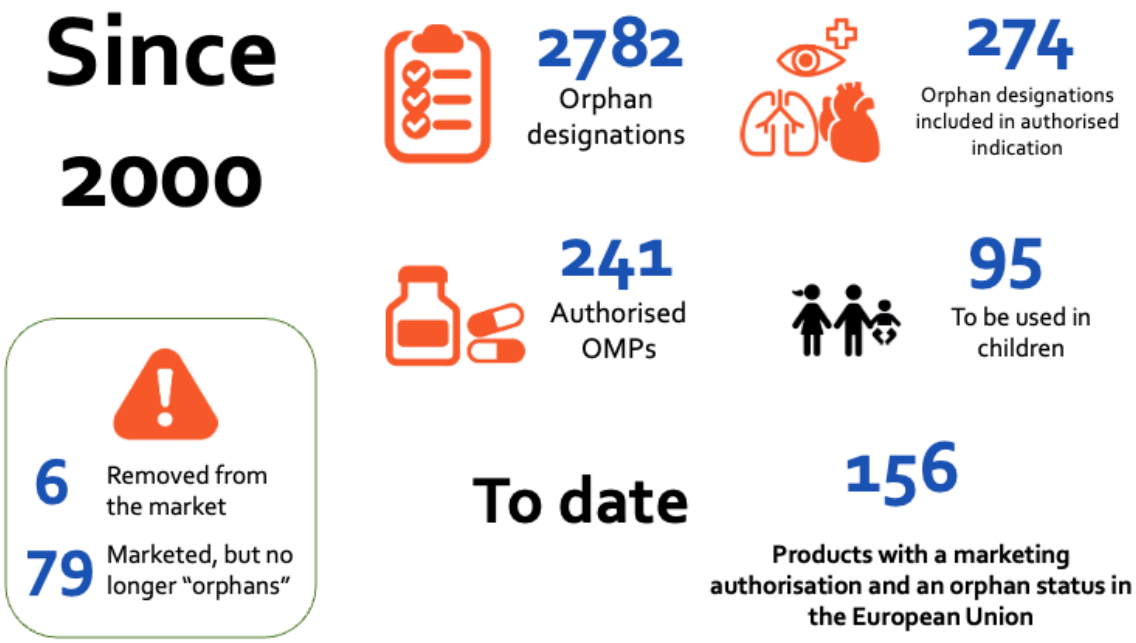
More information is available *here*.

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



18 May 2023

CHMP Meeting Highlights April 2023

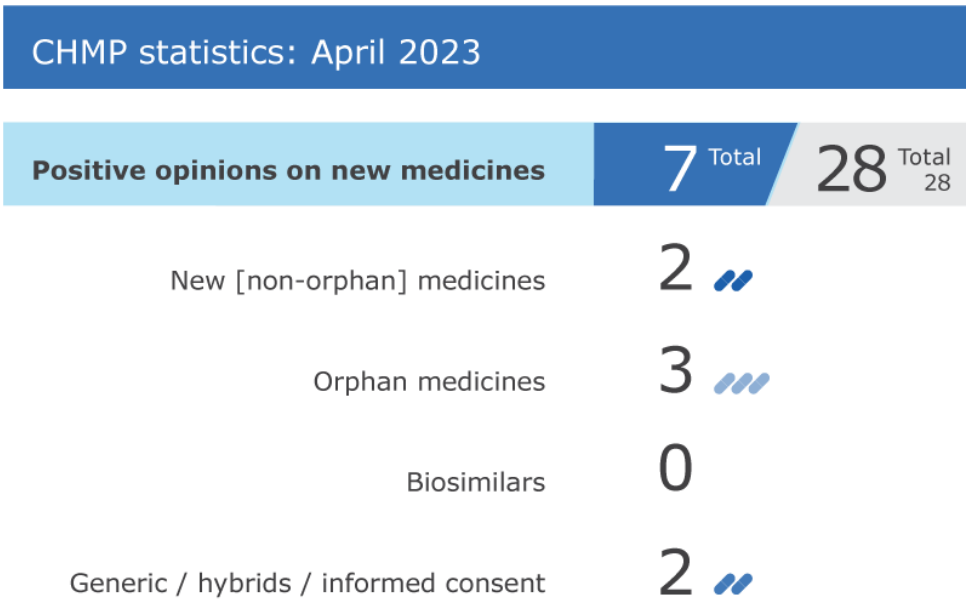
Minutes February 2023
Agenda April 2023
Meeting Highlights April 2023

In April, the CHMP recommended **7 new medicines for approval, 3 of them orphan medicines**:

- *Columvi* (*glofitamab*) under conditional marketing authorisation 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.
- *Jaypirca* (*pirtobrutinib*) under conditional marketing authorisation 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.
- *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.
- *Arexvy* (*recombinant, adjuvanted*), the first hybrid vaccine for active immunisation to protect adults aged 60 years and older against lower respiratory tract disease caused by respiratory syncytial virus (RSV).
- *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.
- *Opfolda* (*miglustat*) for the treatment of glycogen storage disease type II (Pompe disease) in combination with cipaglucosidase alfa.

The CHMP also recommended **11 extensions of therapeutic indication**, and recommended granting marketing authorisations for **1 generic medicines**.

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 is planning the following activities for the year 2023:

- Defining the requirements for major contribution to patient care at orphan designation as well as at marketing authorisation stage and draft a concept paper outlining the conclusions as guidance to sponsors.
- Work on the flexibility in the definition of orphan conditions to be more in line with innovative scientific development (for example the use of biomarker or tissue-agnostic therapies).
- Continue the pilot of RWE studies to support COMP decision-making including identification of use cases.

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

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
Pombiliti® *(cipaglucosidase alfa)*	Amicus Therapeutics Europe Limited	Glycogen Storage Disease Type II	16/05/2023

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 March 2023
Agenda April 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 is planning the following activities for the year 2023:

- Conduct 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.
- Publish guidance on the pilot phase for the stepwise PIP.
- Publish a document reflecting on practical considerations related to the use of extrapolation from a regulatory and HTA perspective; linked to the priority activity reflected in the *joint workplan of EUnetHTA21 and EMA*.

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

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

Minutes February 2023
Agenda April 2023
Meeting November 2022-January 2023

CAT highlights Nov– Jan 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.

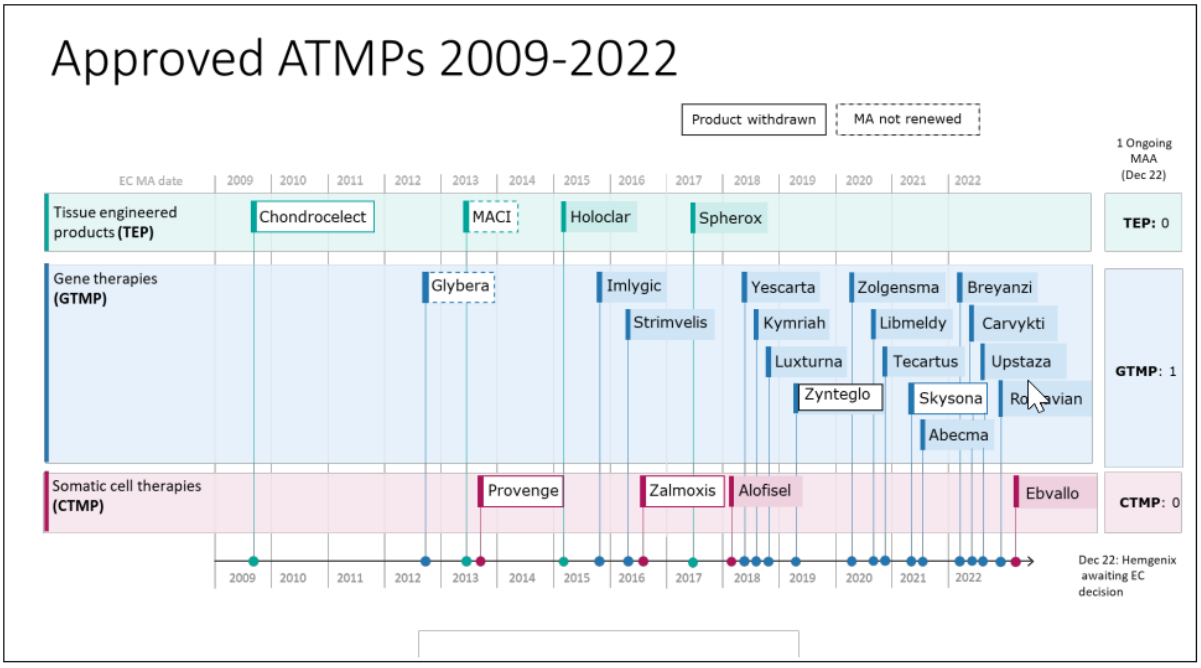
The outcome of these assessments can be found here: *Summaries of scientific recommendations on classification of ATMPs*.

Advanced therapy medicinal products approvals from November 2022-January 2023.

During its plenary meeting of **December 2022,** CAT adopted a positive draft opinion for:

- Conditional marketing authorisation for *Hemgenix (etranacogene dezaparvovec)* for the following indication: treatment of severe and moderately severe Haemophilia B (congenital Factor IX deficiency) in adult patients without a history of Factor IX inhibitors.

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



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 3rd March 2023 took place face to face *the Patients and Consumers' (PCWP) and 'Healthcare Professionals' (HCPWP) Working Parties meeting. The meeting has focused on the following topics:*

- reorganisation of EMA Working parties;
- feedback from EMA scientific committees.
- medical device expert panels;
- biosimilars and interchangeability;
- EMA policy for multilingualism.

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

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.

Co-funded by
the European Union

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