EURORDIS RARE DISEASES EUROPE

EURORDIS THERAPEUTIC REPORT

November

ISSUE 10

UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

REMEDi4ALL Digital Academy webinar

The **REMEDi4ALL Digital Academy**, a wealth of online, on-demand training in drug repurposing, will be **launched officially in January 2025**. The academy is designed by a team of **experts with drug repurposing knowledge and patient-centred organisations**.

To mark the launch of the academy, **REMEDi4ALL will host a webinar on Wednesday, 29th Jan 2025, 12:30-13:30 CET.**

Join the launch of the REMEDi4ALL Digital Academy to find out more about it and how you can benefit from this new resource.

Register for the event *here*.

IN THIS ISSUE

General News 1
In the Spotlight: ERNs evaluations 2
Medicines Safety 3
Key figures Orphan medicines 4
Updates on EMA Committees
CHMP 5
COMP 6
PDCO 8
CAT 9
EMA's Management Board 10
PCWP 11
Glossary 12

c4c Multi-Stakeholder Meeting on paediatric Chronic Kidney Disease

conect4children (c4c) has organised its **sixth and last c4c International Multi-Stakeholder Meeting (MSM)** addressing the topic of paediatric Chronic Kidney Disease.
The meeting will have an **hybrid format**, and it will take place in Heidelberg, Germany, on **28 and 29 April 2025**, ahead of the ESCAPE Network Meeting.

Submit *here* your expression of interest to participate!

EURORDIS Photo Award 2025- submit your photo!

The **EURORDIS Photo Award 2025 is now open** for submissions!

Share your story through photography and help raise awareness of what it means to live with a rare disease. The contest is **open to all nationalities, ages** and **diseases**.

Submissions are open **until 31 January 2025**.
Submit your photo *now*!

EURORDIS Black Pearl AWARDS

EURORDIS Photo Award!
submit your photo!

In the spotlight: ERNs evaluations

What are the European Reference Networks (ERNs)?

European Reference Networks (ERNs) are **virtual networks that aim to improve the diagnosis, treatment, and care of patients with rare or complex diseases**. They are networks of **specialized clinical units of healthcare providers (HCPs) from across Europe**, enabling the **exchange of knowledge** and highly specialized resources across borders. The **networks cover a wide range of diseases**, including cranioencephalic and metabolic disorders, childhood cancer and rare epilepsies, and serve a large number of patients at European level.

About the ERNs evaluation results report

This report, published by the European Commission last November 2024, is a comprehensive **five-year evaluation of European Reference Networks (ERNs)** and its members, the Healthcare Providers (HCPs), across Europe, **focusing on their role in addressing complex and rare conditions**. 24 ERNs and 836 HCPs from 24 EU Member States and Norway participated in the evaluation.

The evaluation included **self-evaluations, document reviews, ERN interviews,** on-site **HCP audits** and **stakeholder interviews.** The results showed a **high level of commitment of ERNs to their objectives, with a significant proportion, 100% of ERNs and 89.7% of their members, achieving satisfactory results in the evaluation.**

Strengths were identified in the areas of Education and Training, Networks and Dissemination, Competence, Experience, and Patient-centred care, while Quality and Patient Safety, and Organization and Management are areas for improvement for both, ERNs, and HCPs respectively.

This report increases the **understanding of the essential role of the ERN system in addressing rare diseases and conditions across Europe**. It also presents **relevant information on the structure, maturity, activity, and impact** of the ERN system, and **identifies opportunities for improvement** based on the findings of the stakeholder interviews and the evaluation to further enhance the evaluation process and ensure the continued sustainability of the ERN system.

EURORDIS welcomes the milestone 5-year evaluations of the European Reference Networks as the **evaluations confirmed the ERNs to be "fit-for-purpose,"** with over 92% rated as "Excellent" or "Very Good." These results affirm the **remarkable progress of the ERNs**, which have been instrumental in sharing data across member centres, establishing disease registries, and fostering collaboration for patients with rare and complex conditions.

Read EURORDIS reflections on the evaluations *here* and the full report *here*.

Pharmacovigilance Risk Assessment Committee (PRAC) November 2024

Minutes October 2024
Agenda November 2024
Meeting Highlights November 2024

Evidence not supporting Doxycycline link with risk of suicidality

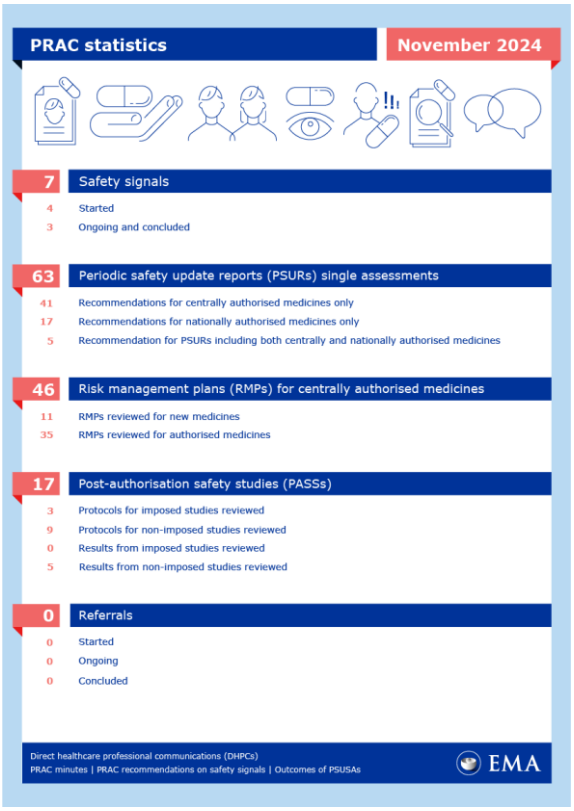
The PRAC has concluded that the **currently available evidence is not sufficient to establish a causal relationship between** the use of the antibiotic **doxycycline and the risk of suicidality**.

Doxycycline is a broad-spectrum antibiotic, widely used to treat a wide range of infections caused by bacteria such as acne, urinary and lower respiratory tract infections, dental infections, and skin infections. It is also used to prevent the development of certain infections, such as malaria.

A **safety signal on the risk of suicidality,** suicidal thoughts or actions with doxycycline was **raised based on reported cases**. The PRAC started its review in November 2023 and also requested a study based on real-world evidence. After **reviewing all available evidence,** the PRAC considered that it is **not sufficient to establish a causal relationship** and that **no update to the product information of doxycycline is warranted**.

Suicide-related events in relation to doxycycline will be **closely monitored** and any new evidence will be discussed in the Periodic Safety Update Reports (PSURs).

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

3031 Orphan designations

301 Orphan designations included in authorised indication

268 Authorised OMPs

104 To be used in children

6 Removed from the market

97 Marketed, but no longer "orphans"

To date

165

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

19 December 2024

CHMP Meeting Highlights November 2024

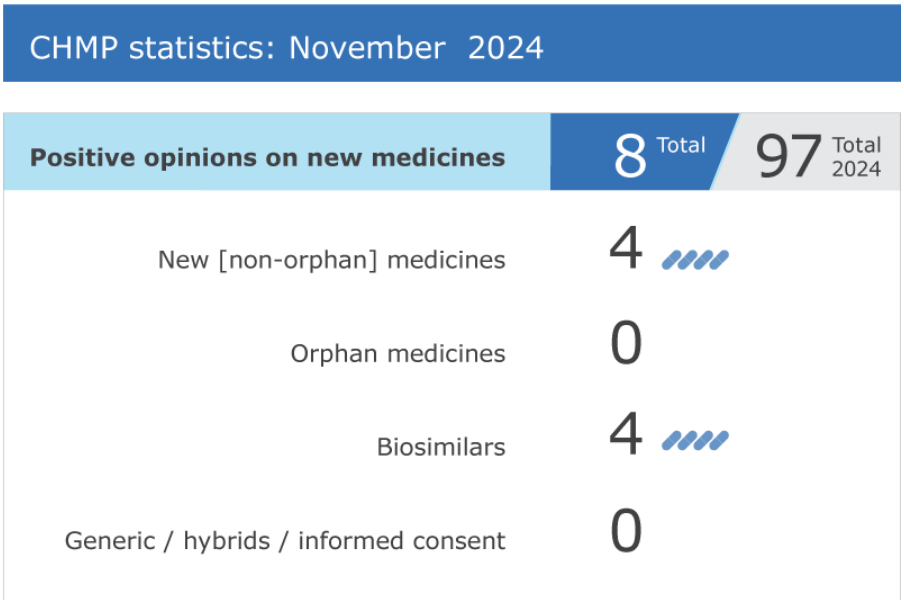
Minutes September 2024
Agenda November 2024
Meeting Highlights November 2024

In November, the CHMP recommended **7 new medicines for approval, none of them orphan medicines**.

Non-orphan medicines, biosimilars, generics/hybrids/informed consent:

- *Augtyro (repotrectinib)*, for the treatment of adults and adolescents with advanced solid tumours, and adults with locally advanced or metastatic non-small cell lung cancer.
- *Gohibic* (*vilobelimab*), for the treatment of adult patients with SARS-CoV2-induced acute respiratory distress syndrome who are receiving systemic corticosteroids as part of standard of care and receiving invasive mechanical ventilation with or without extracorporeal membrane oxygenation.
- *Lazcluze* (*lazertinib*) for the first-line treatment of adult patients with advanced non-small cell lung cancer in combination with amivantamab.
- *Baiama* (*aflibercept*) and its duplicate *Ahzantive*, for the treatment of neovascular age-related macular degeneration, and visual impairment due to macular oedema secondary to retinal vein occlusion, diabetic macular oedema or myopic choroidal neovascularisation.
- *Obodence* (*denosumab*), for the treatment of osteoporosis and bone loss.
- *Xbryk* (*denosumab*), for the prevention of skeletal-related events in adults with advanced malignancies involving bone, and the treatment of giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

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



New chair elected for EMA's Human Medicines Committee

At its September 2024 meeting, EMA's Committee for Human Medicinal Products (CHMP) elected Bruno Sepodes as its new chair. Professor Sepodes started his three-year mandate on 21 September.

Minutes October 2024
Agenda November 2024

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*.

New chair elected for EMA's Orphan Medicinal Products Committee

EMA's Committee for Orphan Medicinal Products (COMP) elected a new chair. Tim Leest started his three-year mandate on 16 September.

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
Adzynma® *(rADAMTS13 Purpura)*	Takeda Manufacturing Austria AG	Congenital thrombotic thrombocytopenic purpura (cTTP)	01/08/2024
Winrevair® *(Sotatercept)*	Merck Sharp & Dohme B.V.	Pulmonary arterial hypertension (PAH)	22/08/2024
Iqirvo® *(Elafibranor)*	Ipsen Pharma	Liver Cirrhosis, Biliary	19/09/2024
Vyloy® *(Zolbetuximab)*	Astellas Pharma Europe B.V.	Stomach Neoplasms Esophageal Neoplasms	19/09/2024
Akantior® *(Polyhexanide)*	SIFI SPA	Acanthamoeba Keratitis	22/08/2024

***Ordspono*®** *(Odronextamab)*	Regeneron Ireland Designated Activity Company (DAC)	Follicular lymphoma or diffuse large B-cell lymphoma (DLBCL)	22/08/2024
***Elahere*®** *(Mirvetuximab soravtansine)*	AbbVie Deutschland GmbH & Co. KG	Advanced cancers of the ovaries fallopian tubes and the peritoneum	14/11/2024

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 October 2024
Agenda November 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 October 2024
Agenda November 2024
Meeting August 2024-October 2024

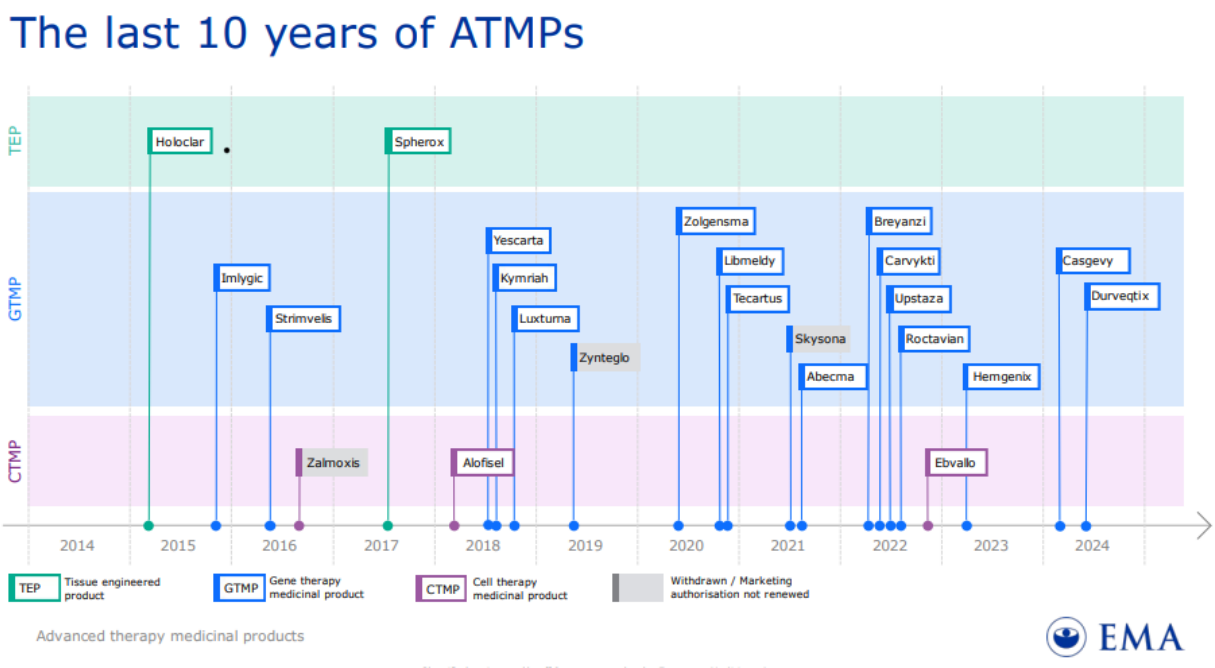
CAT highlights August 2024– October 2024 meeting update

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*.

During the period covered, the CAT has not approved any new ATMP.

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



EMA's Management Board

Minutes June 2024
Agenda October 2024
Meeting Highlights October 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.

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 20th November 2024 took place *the Patients and Consumers' (PCWP) and 'Healthcare Professionals' (HCPWP) Working Parties meeting* at the EMA.

Topics discussed during the meeting included European Medicines Agency data related initiatives, digitalisation and artificial intelligence tools, sustainability of the network, working party related activities, and clinical trial updates.

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.

Co-funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HaDEA. Neither the European Union nor the granting authority can be held responsible for them.

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

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HaDEA. Neither the European Union nor the granting authority can be held responsible for them.