EURORDIS
THERAPEUTIC REPORT
November
ISSUE 10
UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

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GENERAL NEWS

New e-learning course on survey design for patient organisations

EURORDIS Open Academy has launched a **new e-learning course on survey design for rare disease patient organisations** with the aim of empowering patients organisations **to create impactful surveys,** collect insights and drive positive change within the rare disease community.

The course is **for patient representatives** who want to understand how to best capture and act on the insights of their rare disease patient community, and anyone interested in developing own survey design skills, especially in the context of patient/people-centered methods.

Join *here* the new course!

IN THIS ISSUE

Multi-stakeholder workshop on soft tissue and bone sarcoma

The European Medicines Agency (EMA) and the European Organisation of Research and Treatment of Cancer (EORTC) are organising a **multi-stakeholder workshop** on soft tissue and bone sarcoma, specifically addressing **how we can develop new treatments in ultra-rare sarcomas,** as a model for ultra-rare tumours.

This workshop **brings together academia, learned societies, patients, non-profit organisations,** and **medicines regulators** to explore clinical and scientific aspects related to the development of medicines for ultra-rare cancers.

Registrations are open until 8th of January *here*!

5th c4c Multistakeholder meeting on Paediatric Irritability

Next conect4children (c4c) **International Multi-Stakeholder Meeting** is taking place on **18 and 19 March, 2024** after the European College of Neuropsychopharmacology (ECNP) New Frontiers Meeting 2024.

The meeting will address the topic of **Paediatric Irritability** and is organised in **hybrid format** that will take place in **Nice, France** and **online**.

Participation is upon invitation only following expression of interest. Apply *here* no later than January 15th!

EURORDIS Black Pearl AWARDS

EURORDIS Photo Award!
submit your photo!

In the spotlight: EURORDIS Rare Barometer

What is the Rare Barometer Programme?

Rare Barometer programme is a EURORDIS **global survey initiative,** available is 23 languages, that aims to make the **voice of rare disease patients stronger** by collecting the experiences and opinions of people living with a rare disease and their close family members on topics that directly affect them. All **responses are anonymous** and are kept in secure storage only accessible to our research team.

This initiative is **open to anyone from any country in the world** who is **living with a rare disease,** as well their **family** members and **carers**.

Click *here* to know more!

Make Your Voice Heard! – Rare Barometer guide

EURORDIS has crafted a **guide for members of EURORDIS-Rare Diseases Europe to actively participate in Rare Barometer surveys,** harness the experience and opinions of their communities, wield their survey results and **meaningfully use them in their advocacy work and actions.**

This guide offers an exclusive peek into the methodology behind Rare Barometer and **equips member organisations with insights** into:

- **Shaping Questionnaires**: how to participate in the design of Rare Barometer global questionnaires.
- **Community Engagement**: discover when and how you can motivate your community to participate in Rare Barometer survey, and reach enough respondents to receive your tailored survey results.
- **Utilising Survey Outcomes**: explore avenues to leverage survey results for impactful actions at local, European, and global levels.
- **Accessing Resources**: gain access to a wealth of valuable resources to further empower your organisation in participating in Rare Barometer surveys, or conduct your own surveys.

Learn more about the *Make your voice heard! Rare Barometer guide*.

Pharmacovigilance Risk Assessment Committee (PRAC) November 2023

Minutes September 2023
Agenda November 2023
Meeting Highlights November 2023

Minimising the risk of medicines containing pseudoephedrine

PRAC recommends **measures to minimise the risk of serious side effects with medicines containing pseudoephedrine**

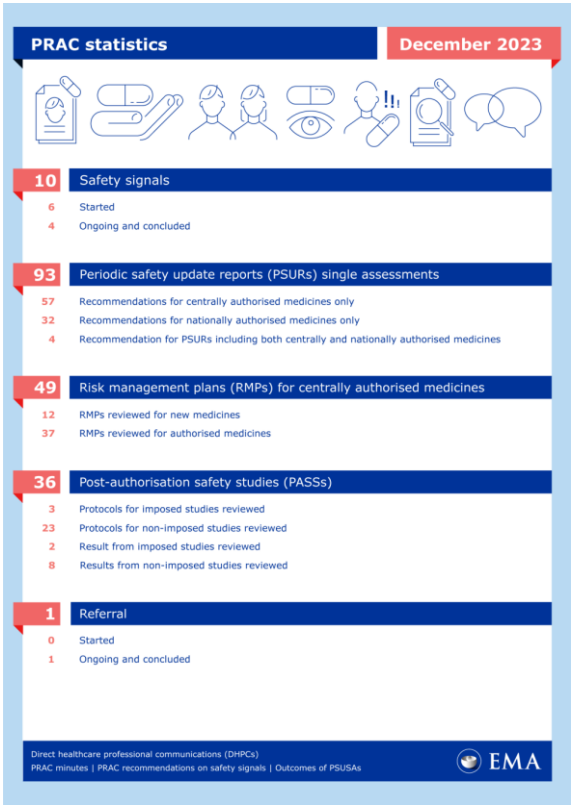
Pseudoephedrine is a stimulant that is **often used as a decongestant in people who have a cold or allergies**. Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) are rare conditions that can involve reduced blood supply to the brain, potentially causing serious, life-threatening complications.

Recommendations include:

- Medicines containing pseudoephedrine are **not to be used** in patients with **high blood pressure** that is **severe or uncontrolled,** or with **severe acute** or **chronic kidney disease or failure.**
- Healthcare professionals should **advise patients to stop using** these medicines immediately and seek treatment if they develop **symptoms of PRES or RCVS**.

The product information for all pseudoephedrine-containing medicines will be updated to include the risks concerning PRES and RCVS and the new measures to be taken.

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

2773 Orphan designations

280 Orphan designations included in authorised indication

247 Authorised OMPs

98 To be used in children

6 Removed from the market

86 Marketed, but no longer "orphans"

To date

155

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

21 December 2023

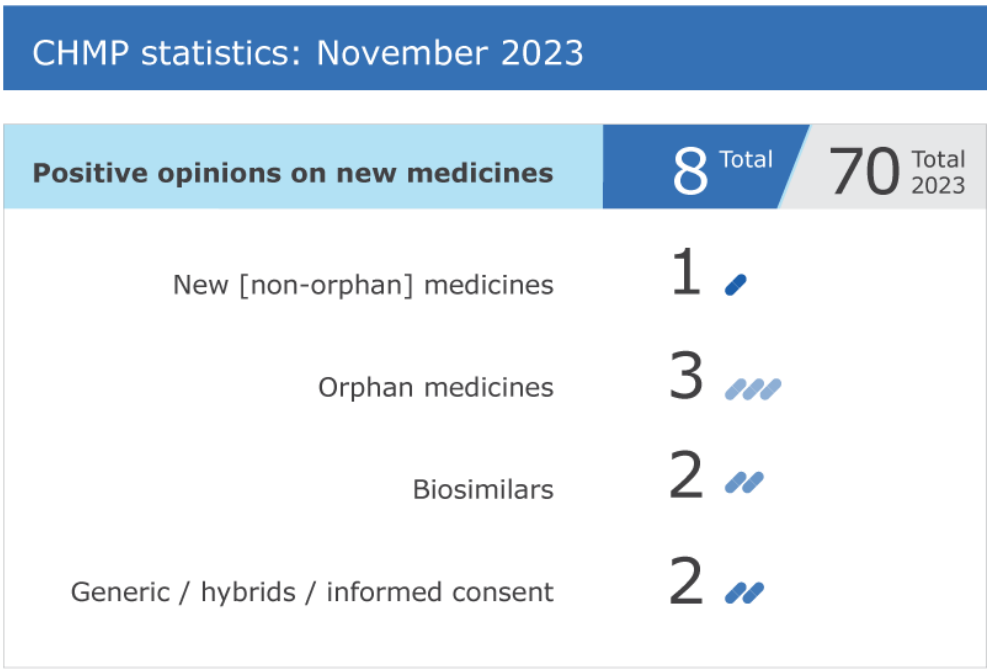
CHMP Meeting Highlights November 2023

Minutes October 2023
Agenda November 2023
Meeting Highlights November 2023

In October, the CHMP recommended **8 new medicines for approval, 3 of them orphan medicines**:

- *Omjjara* (*momelotinib*), for the treatment of myelofibrosis, a rare blood cancer that affects the bone marrow.
- *Rystiggo* (*rozanolixizumab*), intended for the treatment of generalised myasthenia gravis, a chronic autoimmune neuromuscular condition that causes muscle weakness in different parts of the body.
- *Spexotras* (*trametinib*) for the treatment of paediatric patients aged one year and older with glioma, a type of brain tumour that begins in glial cells (the cells that surround and support nerve cells).
- *Rimmyrah* (*ranibizumab*), for the treatment of neovascular age-related macular degeneration, a progressive retinal macular disease causing gradual vision impairment mainly in the elderly.
- *Uzpruvo* (*ustekinumab*), for the treatment of plaque psoriasis, psoriatic arthritis and Crohn's disease.
- *Azacitidine Kabi* (azacitidine), for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia.
- *Naveruclif* (*paclitaxel*), for the treatment of metastatic breast cancer, metastatic adenocarcinoma of the pancreas and non-small cell lung cancer.
- *Krazati* (*adagrasib*), for the treatment of adults with advanced non-small cell lung cancer with a G12C mutation in the KRAS gene whose disease has worsened after at least one systemic treatment.

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
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

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 October 2023
Agenda November 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.

Enpr-EMA annual workshop

The European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA) **is a network of research networks, investigators and centres** with recognised expertise in performing clinical trials in children. Enpr-EMA's main objective is to **facilitate clinical trials in order to increase the availability of authorised medicines for children**.

Last October 10th 2023 it took place **the annual workshop of Enpr-EMA** at the EMA's premises in Amsterdam. Enpr-EMA's **annual workshop is a unique opportunity** for networks as well as other stakeholders of paediatric clinical trials, such as healthcare professionals, parents, carers, patient representatives as well as medicine developers and regulators, **to learn about the network's priority activities.** The workshop **aims to facilitate inter-network and stakeholder collaboration** and to build competences at European level.

You can access the presentations from the event *here*, and the report from the workshop will shortly be published on the Enpr-EMA website with updates on Enpr-EMA's most recent activities and plans for the upcoming year.

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

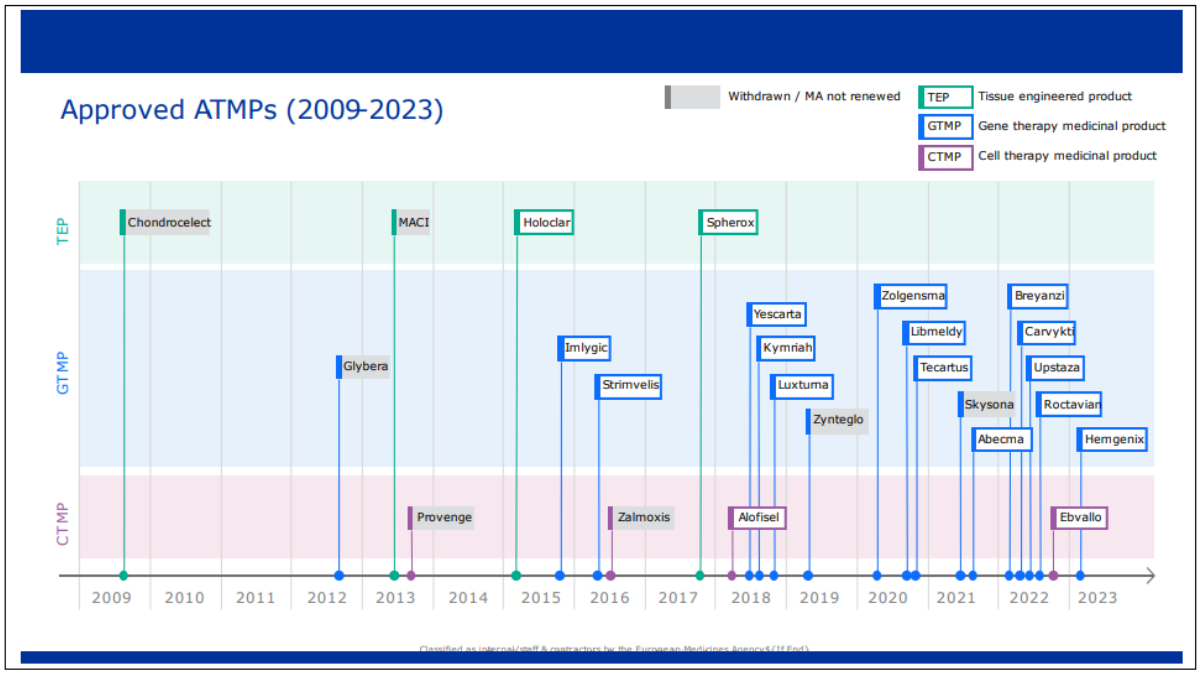
This report provides information on ATMP approvals and extension of indications of authorised ATMPs, as well as statistical data on product-related activities.

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*.



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.

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