EURORDIS
RARE DISEASES EUROPE

# EURORDIS THERAPEUTIC REPORT

May 2022

ISSUE 5

UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

# GENERAL NEWS

## EURORDIS Black Pearl Awards nominations are out!

*Nominations* for our next edition of the **EURORDIS Black Pearl Awards are now open**!

Take a moment to think about the individuals, organisations and companies who are going the extra mile to make a difference in rare diseases. **Help us:**

- **Identifying** the people whose hard work and contributions to the rare disease community deserve to be honoured;
- **Celebrating** their dedication and commitment to the cause;
- **Providing** them with international **recognition** for their hard work and incredible accomplishments!

The *12 Award Categories* are presented to patient advocates and organisations, policy makers, scientists, companies, and the media.

Your nominations will also help raise awareness in the run-up to **Rare Disease Day**, taking place on **28th February 2023**. We look forward to receiving your nominations soon and don't forget that you can nominate yourself or your company/organisation too!

For more information, and to watch last year's ceremony, visit the *EURORDIS Black Pearl Awards* website.

## IN THIS ISSUE

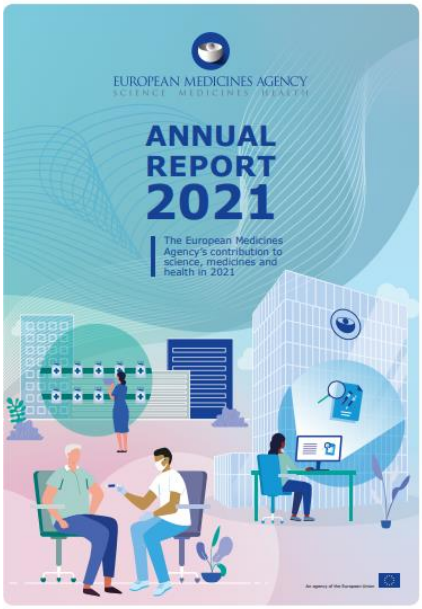


EURORDIS Black Pearl AWARDS

***Nominate now!***

## EMA Annual report 2021

The European Medicines Agency (EMA) is responsible for the scientific evaluation, supervision and safety monitoring of medicines in the European Union. Now, you can find the just published *2021 annual report*, which highlights the Agency's most significant achievements in 2021. It also contains reflections by EMA staff and its partners and stakeholders on topics of major interest in medicine and health and key figures, including core statistics that highlight the main outcomes of the Agency's activities and interesting trends and changes observed in recent years, such as patient involvement at the EMA.




In 2021, EMA recommended **92 medicines for marketing authorization, 19 orphan medicines**. The Agency recommended four vaccines and five treatments for COVID-19. Throughout the year, EMA approved 33 new manufacturing sites for COVID-19 vaccines, leading to a substantial increase in vaccine manufacturing capacity and supply.

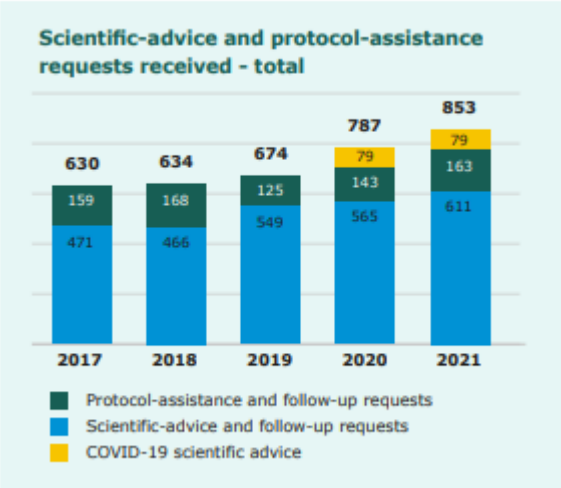
EMA continued to closely monitor the safety of medicines on the market and take action when needed. The product information for 502 centrally authorised medicines was updated on the basis of new safety data in 2021. Here are some key figures on the authorisation and safety monitoring of medicines for human use in 2021.

For more detailed information, *download the full annual report 2021*.

## The role of patients in scientific advice and protocol assistance

The role of patients in scientific advice is critical to inform medicines developers and regulators on what is most important for the community.

Patients can be invited to contribute written comments or to participate in meetings to discuss the medicine development plan proposed by the company. All documents and meetings are held in English and the EMA covers the costs of travel and accommodation.




Adapted from *EMA Annual Report 2021*

In 2021, EMA received a **total of 690 requests for scientific advice**, among these, 79 were for COVID-19 medicines or vaccines, the same as in 2020. Protocol assistance is the special form of scientific advice for developers of designated orphan medicines for rare diseases. The requests for **protocol assistance increased by 14%, from 143 requests in 2020 to 163 in 2021.**

Patients participated as experts in several scientific advice and protocol assistance procedures**. In 2021 a total of 90 patients were involved in different procedures.**

For more information, please see *EMA Annual Report 2021.*

# Pharmacovigilance Risk Assessment Committee (PRAC) May 2022

Minutes August 2021
Agenda May 2022
Meeting Highlights May 20222

## Withdrawal of marketing authorisation for amfepramone medicines

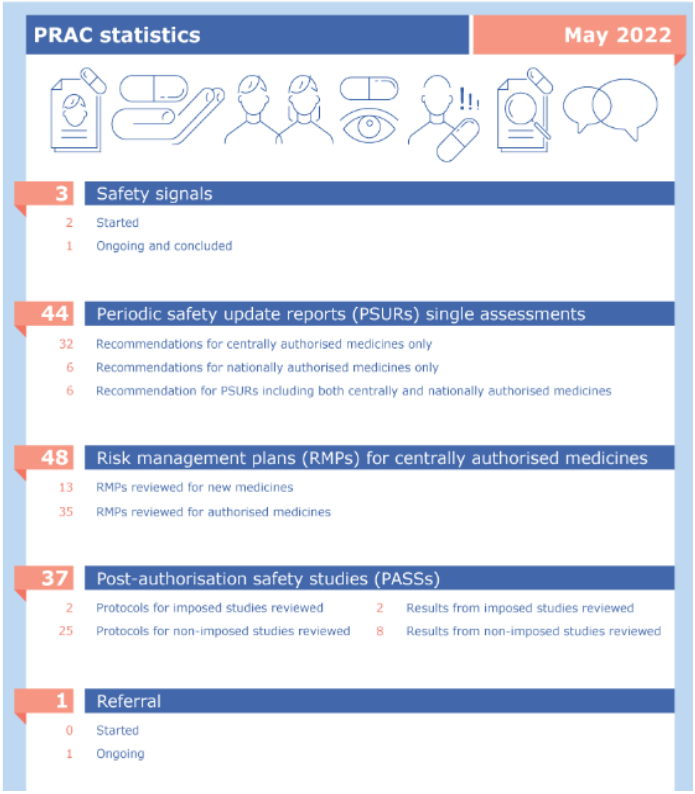
*EMA's safety committee (PRAC)* has recommended the **withdrawal of EU *marketing authorisations* for amfepramone obesity medicines.**

The recommendation follows a review which found that measures to restrict the use of these medicines for safety reasons have not been sufficiently effective. It found that the medicines were being used for longer than the recommended maximum period of 3 months, thereby potentially increasing the risk of serious side effects, such as pulmonary arterial hypertension (high blood pressure in the arteries of the lungs) and dependency.

The medicines were also being used in patients with a history of heart disease or psychiatric disorders, increasing their risk of heart and psychiatric problems. In addition, there was evidence of use during pregnancy, which could pose risks to the unborn baby.

The *PRAC* therefore concluded that the benefits of amfepramone medicines do not outweigh their risks and recommended that the medicines be removed from the market in the EU.

For more information, please see *EMA website.*




### 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

**2577** Orphan designations

**254** Orphan designations included in authorised indication

**221** Authorised OMPs

**89** To be used in children

**6** Removed from the market

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

## To date

**141**

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

25 May 2022

# CHMP Meeting Highlights May 2022

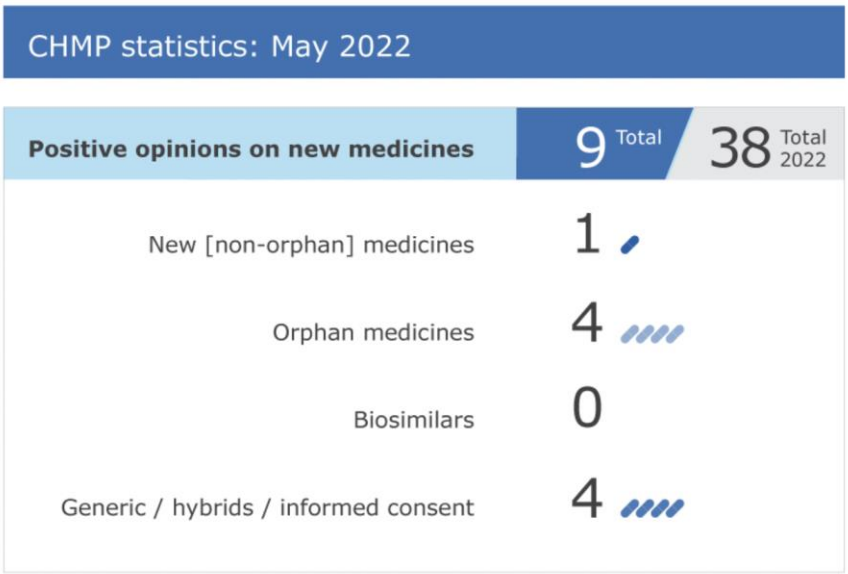
Minutes April 2022
Agenda May 2022
Meeting Highlights May 2022

In May, the CHMP recommended **9 medicines for approval, 4 orphan medicines**:

- The CHMP gave a positive opinion under exceptional circumstances for a new gene therapy, ***Upstaza*** *(eladocagene exuparvovec)* to treat adult and paediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency, an ultra-rare genetic disorder affecting the nervous system.
- ***Xenpozyme*** *(olipudase alfa)* for the treatment of two types of Niemann-Pick disease, a rare metabolic disorder caused by acid sphingomyelinase deficiency (ASMD).
- A positive opinion under exceptional circumstances was adopted for ***Zokinvy*** *(ionafarnib),* the first treatment for children with progeroid syndromes, an ultra-rare genetic disease which causes premature aging and death.
- ***Kinpeygo*** *(budesonide),* a hybrid medicine indicated for the treatment of primary immunoglobulin A nephropathy in adults. Hybrid medicines rely in part on the results of pre-clinical tests and clinical trials of an already authorised reference product and in part on new data.
- ***Cevenfacta*** *(eptacog beta (activated))* for the treatment of bleeding episodes in patients with congenital haemophilia.

The CHMP also recommended **6 extensions of therapeutic indication,** and recommended granting marketing authorisations for **4 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.

Minutes March 2022
Agenda May 2022
Meeting May 2022

# COMP May 2022 meeting update

During the May plenary, the COMP adopted **22 positive opinions** on the designation of medicines as orphan medicinal products to the European Commission (EC). For further information, please see the *meeting report.*

Please find below the list of indications covered in the medicines that were recommended for orphan designation:

- Cystic fibrosis, AdRes EU B.V.;
- Angelman syndrome, Ionis Development (Ireland) Limited;
- Gain-of-function mutations of STIM1 and ORAI1 related diseases, ChemICare S.R.L.;
- SCN8A developmental and epileptic encephalopathy, Neurocrine Therapeutics Limited;
- Erythromelalgia, AlgoTherapeutix;
- ATTR amyloidosis, Turnkey Pharmaconsulting Ireland Limited;
- Soft tissue sarcoma, Thermosome GmbH;
- Myelodysplastic syndromes, Karyopharm Europe GmbH;
- Follicular lymphoma, AbbVie Deutschland GmbH & Co. KG;
- Hyperphenylalaninaemia, Orphix Consulting GmbH;
- Galactosaemia, Drug Development and Regulation S.L.;
- Partial deep dermal and full thickness burns, Evomedis GmbH;
- Primary IgA nephropathy, TMC Pharma (EU) Limited;
- TBR1-related disorder, Centre Hospitalier Universitaire Dijon Bourgogne;
- Osteogenesis imperfecta, 3R Pharma Consulting GmbH;
- Methylmalonic acidemia, Moderna Biotech Spain S.L.;
- Idiopathic pulmonary fibrosis, Regintel Limited;
- Chronic myeloid leukaemia, Aop Orphan Pharmaceuticals GmbH;
- Hereditary angioedema, Kalvista Pharmaceuticals (Ireland) Limited;
- Lymphatic malformations, Raremoon Consulting Esp S.L.;
- Retinopathy of prematurity, Granzer Regulatory Consulting & Services GmbH;
- Neuronal ceroid lipofuscinosis, Fondazione Telethon.

**Re-assessment of orphan designation at time of marketing authorisation**

When a designated orphan medicinal product receives a positive opinion for marketing authorisation from EMA's Committee for Medicinal Products for Human Use (CHMP), the COMP has the responsibility to review whether or not the medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation.

The COMP adopted **one positive opinion at time of CHMP opinion**.

- ***Yescarta*** (axicabtagene ciloleucel) for treatment of follicular lymphoma, Kite Pharma EU B.V

Summaries of positive opinions on orphan designations are available on the *EMA website*.

| Medicinal Product | Marketing Authorisation Holder | Therapeutic Indication | Date of Marketing Authorisation |
|---|---|---|---|
| *Tavneos* ® (avacopan) | Vifor Fresenius Medical Care Renal Pharma France | Adult patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) | 11/01/2022 |
| *Voraxaze* ® (glucarpidase ) | SERB SAS | Adults and children (aged 28 days and older) with delayed methotrexate elimination or at risk of methotrexate toxicity | 11/01/2022 |
| *Lonapegsomatropin Ascendis Pharma*® (lonapegsomatropin) | Ascendis Pharma Endocrinology Division A/S | Children who do not produce enough growth hormone (GHD) | 11/01/2022 |
| *Oxbryta*® (voxelotor) | Global Blood Therapeutics Netherlands B. V. | Haemolytic anaemia, and +12 years old sickle cell disease | 14/02/2022 |
| *Ngenla*® (somatrogon) | Pfizer Europe MA EEIG | Children and adolescents with growth hormone deficiency | 14/02/2022 |
| *Kimmtrak*® (tebentafusp) | Immunocore Ireland Limited | Adult patients with unresectable or metastatic uveal melanoma | 01/04/2022 |
| *Uplizna*® (inebilizumab) | Viela Bio | Adults with neuromyelitis optica spectrum disorders (NMOSD) | 25/04/2022 |
| *Carvykti*® (ciltacabtagene autoleucel) | Janssen-Cilag International NV | Adults with multiple myeloma | 25/05/2022 |

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

*Orphan medicinal products authorised during 2022*

*Orphan medicinal products authorised since 2000*

PDCO April & May meeting to be updated when info available

Minutes February 2022
Agenda March 2022
Meeting Report March 2022

## PDCO March 2022 meeting update

In March, the PDCO adopted **8 positive opinions** agreeing *paediatric investigation plans (PIPs)* for the medicines below. The PIP 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.

- Ibutamoren mesylate, from Lumos Pharma, Inc., for the treatment of growth hormone deficiency;
- Zinc gluconate / alisitol / retinyl palmitate, from Vanessa Research Magyarorszag Kft, for the treatment of microvillus inclusion disease;
- Peptide derivative of glucagon-like-peptide 1 and glucagon with fatty acid side chain (BI 456906), from Boehringer Ingelheim International GmbH, for the treatment of obesity;
- Mitapivat, from Agios Netherlands B.V., for the treatment of thalassaemia;
- Deucravacitinib, from Bristol-Myers Squibb International Corporation, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- Adeno-associated viral vector serotype rh.10 expressing beta-galactosidase, from Lysogene, for the treatment of GM1 gangliosidosis;
- Virus-like particle of SARS-CoV-2 spike protein (recombinant, adjuvant) (CoVLP), from Medicago Inc., for the prevention of coronavirus disease 2019 (COVID-19);ç
- SARS-CoV-2 virus, beta-propiolactone inactivated, from Valneva Austria GmbH, for the prevention of coronavirus disease 2019 (COVID-19);

The PDCO also adopted opinions on **product-specific waivers, modifications to an agreed PIP and compliance check** that can be consulted in the *meeting report.*

For a comprehensive list of opinions and decisions on PIPs, please check the *EMA website.*

Minutes October 2021
Agenda December 2021
Meeting Report December 2021

CAT from January to May meeting to be updated when info available

# CAT December 2021 meeting update

In December the Committee for Advanced Therapies (CAT) finalised **4 scientific recommendations on the classification of advanced therapy medicinal products** (ATMPs) depicted below.

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

The following product **fulfil the definition of a gene therapy medicinal product:**

- CD 19 CAR T-cells transduced with lentiviral vector, intended for the treatment of adults and children with B-cell non-Hodgkin's lymphoma and acute lymphoblastic leukaemia;
- Recombinant adeno-associated virus, serotype 2, containing human ND4 codon-optimised gene, intended for the treatment of Leber's hereditary optic neuropathy.

The following products fulfil the definition of a somatic cell therapy medicinal product:

- Allogeneic adipose-derived mesenchymal stromal cells, ex-vivo expanded, intended for the treatment of osteoarthritis of the knee;
- Allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured, intended for the treatment of paediatric and adult patients undergoing partially human leucocyte antigen (HLA) compatible allogeneic haematopoietic stem cell transplantation to accelerate adaptive immunological reconstitution.

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.*

## First EMA PCWP & HCPWP meeting with all eligible organisations of 2022!

Last 2nd and 3th of March took place *the first annual meeting of 2022* which brought together all eligible patient and consumer and healthcare professionals organisations and members of the Patients' and Consumers' Working Party (PCWP) and Healthcare Professionals' Working Party (HCPWP).

The first day of the meeting provided an update on EMA projects and initiatives, including:

- *accelerating clinical trials in the EU (ACT EU),*
- *big data;*
- *electronic product information (ePI);*
- *the Agency's extended mandate.*

The second day of the meeting enabled discussion on *advanced therapy medicinal products (ATMPs)* and sharing members' voices. The meeting closed with looking ahead to 2022 to 2025.

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