EURORDIS RARE DISEASES EUROPE

EURORDIS THERAPEUTIC REPORT

Summer Edition 2022

ISSUE 7

UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

EURORDIS training opportunities

If you a rare disease patient advocate interested in bringing your expertise to discussions on health care, research and medicines development apply now to attend and discover the new format of the *EURORDIS Open Academy Schools 2023*.
Save the date, **Barcelona on the 19-23 June 2023**!
Apply now before 24 October!

Rare Disease Week is back! This second edition will take place for **four days in-person during the week commencing 6 February 2023 in Brussels.** Through Rare Disease Week, we will train patient advocates in the EU to present a strong and united message to MEPs and other EU policymakers on behalf of the rare disease community. Attendees will get to join interactive training sessions, meetings with policy makers, and networking events. Don't wait, *apply by 5 October!*

New paper out!

The EMA just published a paper on the '*Contribution of patient registries to regulatory decision making on rare diseases medicinal products in Europe'*. Patient registries have been recognised as important sources of data on healthcare practices, drug utilisation and clinical outcomes. They may help address these challenges by providing information on epidemiology, standards of care and treatment patterns of rare diseases.

This paper illustrates the utility of patient registries across the different stages of development of medicinal products, including orphans, to provide evidence in the context of clinical studies and to generate post-authorisation long term data on their effectiveness and safety profiles, leveraging the role of registries for orphan medicinal products' development and monitoring to ultimately improve patients' lives.
Read it here!

IN THIS ISSUE

Patient experience data in medicines development and regulatory decision-making: EMA Multi-stakeholder workshop

Last 21st September took place face to face at the EMA a multistakeholder workshop that brought together patients, healthcare professionals, academia, regulators, and industry to discuss ways to improve the collection and use of patient experience data to achieve patient-centred medicine development and regulation. The main objectives of the workshop were to:

- Achieve a common understanding on what constitutes 'patient experience data', including patient engagement, patient preferences and patient reported outcomes.
- Reflect on current methods for collecting and incorporating patient data into medicines development and regulatory assessments
- Consider how direct patient data collection from real-world healthcare can be leveraged and used
- Agree on priorities to enhance the collection and use of patient experience data

Yann Le Cam, presented 'How patient engagement can contribute to the development and approval of medicines'. For more information, please see here the agenda, presentations and recording of the workshop.

Biosimilar medicines can be interchanged

The EMA and the Heads of Medicines Agencies (HMA) have issued a joint statement confirming that biosimilar medicines approved in the European Union (EU) are interchangeable with their reference medicine or with an equivalent biosimilar. A biosimilar is a biological medicine highly similar to another already approved biological medicine (the 'reference medicine'). Interchangeability in this context means that the reference medicine can be substituted by a biosimilar without a patient experiencing any changes in the clinical effect. While interchangeable use of biosimilars is already practiced in many Member States, this joint position harmonises the EU approach. It brings more clarity for healthcare professionals and thus helps more patients to have access to biological medicines across the EU.

The statement, is based on the experience gained in clinical practice, where it has become common that doctors switch patients between different biological medicinal products. Approved biosimilars have demonstrated similar efficacy, safety and immunogenicity compared with their reference medicines, and analysis of more than one million patient-treatment years of safety data did not raise any safety concerns. Thus, EU experts considered that when a biosimilar is granted approval in the EU, it can be used instead of its reference product (or vice versa) or replaced by another biosimilar of the same reference product. For more information, please read here.

Accelerating Clinical Trials in the EU: publication of 2022-2026 workplan

The European Commission (EC), the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) have published the 2022-2026 workplan of the initiative Accelerating Clinical Trials in the EU (ACT EU). ACT EU, launched in January 2022, seeks to transform how clinical trials are initiated, designed and run.

The aim is to further develop the EU as a focal point for clinical research, promote the development of high-quality, safe and effective medicines, and to better integrate clinical research in the European health system. The ACT EU workplan is structured in line with the ten priority actions for ACT EU and has been prepared based on the recommendations of the European medicines agencies network strategy to 2025 and the European Commission's Pharmaceutical Strategy for Europe. For more information, please visit here.

Pharmacovigilance Risk Assessment Committee (PRAC) July 2022

Minutes September 2021
Agenda June 2022
Meeting Highlights July 2022

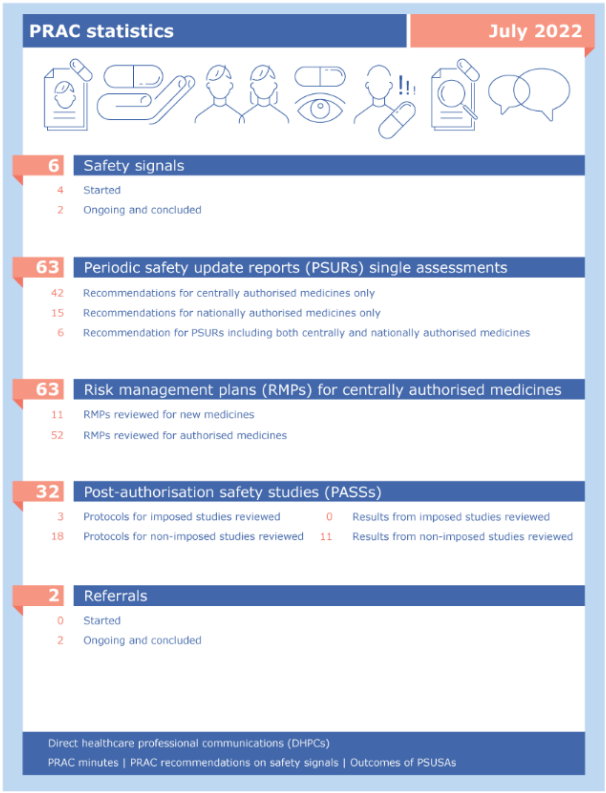
Risk of neurodevelopmental disorders with topiramate

EMA's safety committee (PRAC) has started a review of topiramate to assess new data on a potential risk of neurodevelopmental disorders in children who have been exposed to the medicine during pregnancy.

Topiramate is indicated for the treatment of epilepsy, either used alone (monotherapy) or in conjunction with other medicines (combination therapy), as well as for the prevention of migraine. The use of topiramate by pregnant women is already known to increase the risk of birth defects.

Recently, a *study* investigating the risk of neurodevelopmental disorders, including autism spectrum disorder and intellectual disability, associated with several anti-epileptic drugs, including topiramate, has been published. The study is based on Nordic registry data and includes more than 24,000 children exposed in utero to at least one anti-epileptic drug, including 471 who were exposed to topiramate. In light of the importance of this new information, the PRAC decided that further assessment is warranted to determine the scope and the best regulatory procedure to assess these potential risks.

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

2661 Orphan designations

263 Orphan designations included in authorised indication

230 Authorised OMPs

93 To be used in children

6 Removed from the market

74 Marketed, but no longer "orphans"

To date

150

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

21 September 2022

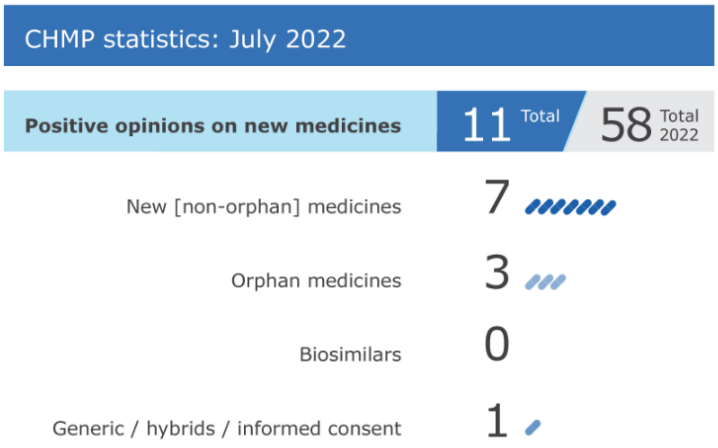
CHMP Meeting Highlights July 2022

Minutes July 2022
Agenda July 2022
Meeting Highlights July 2022

In July, the CHMP recommended **11 medicines for approval, 3 orphan medicines**:

- *Amvuttra (vutrisiran)* for the treatment of adults with hereditary transthyretin-mediated amyloidosis, a rare life-threatening disease that damages multiple nerves across the body.
- *Nulibry (fosdenopterin)* for the treatment of molybdenum cofactor deficiency type A, under exceptional circumstances. This is an ultra-rare condition that appears shortly after birth and leads to brain injury and death.
- Conditional marketing authorisation for *Tecvayli (teclistamab)* for the treatment of adults with relapsed and refractory multiple myeloma, who have received at least three prior therapies.
- *Celdoxome pegylated liposomal (doxorubicin hydrochloride)* for the treatment of metastatic breast cancer, advanced ovarian cancer, progressive multiple myeloma and Kaposi's sarcoma, a type of cancer that affects people with AIDS.
- *Illuzyce (lutetium (177lu) chloride),* a radiopharmaceutical precursor, is not intended for direct use in patients and must be used only for the radiolabelling of carrier medicines that have been specifically developed and authorised for radiolabelling with lutetium chloride.
- *Lupkynis (voclosporin*) for the treatment of lupus nephritis, an inflammation of the kidney caused by lupus.
- *Mounjaro (tirzepatide)* for the treatment of adults with type 2 diabetes mellitus.
- *Opdualag (relatlimab / nivolumab*), intended for the treatment of melanoma, a type of skin cancer, that has spread to other parts of the body and cannot be removed by surgery.
- *Tezspire (Tezepelumab),* intended as an add-on treatment in adult and adolescent patients with severe asthma.
- Vabysmo (faricimab), intended for the treatment of adults with neovascular age-related macular degeneration and visual impairment due to diabetic macular oedema.

The CHMP also recommended **5 extensions of therapeutic indication,** and recommended granting marketing authorisations for **1 biosimilar medicine,** *Thalidomide Lipomed (thalidomide)* received a positive opinion for the treatment of multiple myeloma.



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 July 2022 meeting update

Minutes May 2022
Agenda July 2022
Meeting July 2022

During the July plenary, the COMP adopted **21 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:

- Hutchinson-Gilford progeria syndrome, Global Medical Services Sp. z o.o.;
- Urea cycle disorders , Unicyte S.r.l.;
- Graft-versus-host-disease, MDC RegAffairs GmbH;
- Cryptococcosis, Insight Drug Regulatory;
- Mucopolysaccharidosis type IV A, (Morquio A syndrome), Fondazione Telethon;
- Frontotemporal dementia, Neuroplast B.V.;
- Myasthenia gravis, Pharma Gateway AB;
- Primary sclerosing cholangitis, Amsterdam UMC;
- Prevention of acute liver failure, Egetis Therapeutics AB;
- Nontuberculous mycobacterial lung disease, Regintel Limited;
- Nnontuberculous mycobacterial lung disease, Dlrc Pharma Services Limited;
- Amyotrophic lateral sclerosis, Clene Netherlands B.V.;
- Haemophilia A, S-Cubed Pharmaceutical Services ApS;
- Chondrosarcoma, TMC Pharma (EU) Limited;
- Familial adenomatous polyposis, Amsterdam UMC;
- Idiopathic hypersomnia, Propharma Group The Netherlands B.V.;
- Peripheral T-cell lymphoma, Pharma Gateway AB;
- Amyotrophic lateral sclerosis, Novartis Europharm Limited;
- Myelodysplastic syndrome, Syros Pharmaceuticals (Ireland) Limited;
- Osteosarcoma, Hephaistos-Pharma;
- Stargardt's disease, Alnylam Netherlands B.V.

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 **three** positive opinions at time of CHMP opinion:

- **Roctavian** (valoctocogene roxaparvovec) for treatment of haemophilia A, BioMarin International Limited.
- **Scemblix** (asciminib) for treatment of chronic myeloid leukaemia, Novartis Europharm Limited.
- **Vyvgart** (efgartigimod alfa) for treatment of myasthenia gravis, Argenx.

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
Skytrofa ® (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) *Withdrawn by the company*	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
Lunsumio® (mosunetuzumab)	Roche Registration GmbH	Adults with follicular lymphoma	03/06/2022
Filsuvez® (birch bark extract)	Amryt Pharmaceuticals DAC	Adults and children aged 6 months or older with epidermolysis bullosa (EB)	21/06/2022
Xenpozyme® (olipudase alfa)	Genzyme Europe BV	Acid sphingomyelinase deficiency (ASMD)	24/06/2022
Kinpeygo® (budesonide)	Calliditas Therapeutics AB	Adults with primary immunoglobulin A nephropathy (IgAN)	15/07/2022
Zokinvy® (lonafarnib)	EigerBio Europe Limited	12 months and older living with progeria and laminopathies	18/07/2022

Medicinal Product	Marketing Authorisation Holder	Therapeutic Indication	Date of Marketing Authorisation
Upstaza® (eladocagene exuparvovec)	PTC Therapeutics International Limited	Adults and children aged 18 months and older with severe aromatic L-amino acid decarboxylase (AADC) deficiency	18/07/2022
Vyvgart® (efgartigimod alfa)	Argenx	Adults with myasthenia gravis	10/08/2022
Roctavian® (valoctocogene roxaparvovec)	BioMarin International Limited	Haemophilia A	24/08/2022
Scemblix® (asciminib)	Novartis Europharm Limited	Chronic myeloid leukaemia (CML)	25/08/2022

Please click also on the following links to see:

Orphan medicinal products authorised during 2022

Orphan medicinal products authorised since 2000

PDCO April to June 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*.

CAT highlights May – July meeting update

Minutes July 2022
Agenda July 2022
Meeting May-July 2022

From May to July the Committee for Advanced Therapies (CAT) finalised **14 scientific recommendations on the classification of advanced therapy medicinal products** (ATMPs).

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

Advanced therapy medicinal products approvals from May-July 2022.

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

- **Upstaza** (eladocagene exuparvovec) for the following indication: treatment of patients aged 18 months and older with a clinical, molecular, and genetically confirmed diagnosis of aromatic L-amino acid decarboxylase (AADC) deficiency with a severe phenotype. Based on the assessment of the CAT, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation under exceptional circumstances for the medicinal product Upstaza.

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

- **Roctavian** (valoctocogene roxaparvovec) for the following indication: treatment of severe haemophilia A (congenital factor VIII deficiency) in adult patients without a history of factor VIII inhibitors and without detectable antibodies to adeno associated virus serotype 5 (AAV5). Based on the assessment of the CAT, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a conditional marketing authorisation for the medicinal product Roctavian.

Extension of indication of authorised ATMPs

During its plenary meeting of **July 2022,** CAT adopted an extension of indication for:

- *Tecartus,* to include the treatment of adult patients 26 years of age and above with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL).

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 22nd September took place face to face *the Patients and Consumers' (PCWP) and 'Healthcare Professionals' (HCPWP) Working Parties meeting.*

During the meeting new chair and co-chair was elected. EMA's Patients' and Consumers' Working Party (PCWP) has elected Marilena Vrana of the European Heart Network (EHN) as new co-chair. The Healthcare Professionals' Working Party (HCPWP) has elected Rosa Giuliani of the European Society for Medical Oncology (ESMO) as new co-chair.

A discussion on the progress report on clinical trials and contribution to ICH guidance on good clinical practice was also discussed and the EMA shared feedback from the ATMPs dedicated webinar on 28 June, as well as updates on pharmacovigilance and new initiatives for risk minimisation.

For more information, please see the agenda *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.

Co-funded by
the Health Programme
of the European Union

Acknowledgements: This publication (or activity) has been funded with support from the European Union's Health Programme. This material only reflects the views of the author, and funders cannot be held responsible for any use which may be made of the information contained herein. Icons in this issue made by Freepik from www.flaticon.com

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 Health Programme
of the European Union

Acknowledgements: This publication (or activity) has been funded with support from the European Union's Health Programme. This material only reflects the views of the author, and funders cannot be held responsible for any use which may be made of the information contained herein. Icons in this issue made by Freepik from www.flaticon.com