

## GENERAL NEWS

### EMA recommended second COVID-19 vaccine for authorization in the EU

EMA recommended granting a conditional marketing authorisation for the [COVID-19 vaccine Moderna](#), developed by Moderna, to prevent coronavirus disease 2019 (COVID-19) in people from 18 years of age.

EMA's human medicines committee (CHMP) has completed its rigorous evaluation of the vaccine concluding by consensus that sufficiently robust data on the quality, safety and efficacy of the vaccine are now available to recommend a formal conditional marketing authorisation.

For more information, please see the [EMA website](#).

### EURORDIS COVID-19 Information Resources Centre

François Houyez, Information & Access to Therapies Director & Health Policy Advisor, participated in the two EMA Public Stakeholder meetings on the development, authorisation and roll-out of safe & effective COVID-19 vaccines in the EU that took place online last [11<sup>th</sup> December](#), and [8<sup>th</sup> January](#). During the meeting he raised five crucial points that related, in particular, to the vaccine from the perspective of people living with a rare disease. Watch the full [video](#)! Please also read EURORDIS comments "[Putting the COVID-19 vaccines in context for people with rare diseases](#)".

For more information on the research and development of COVID-19 vaccines, please read the [EURORDIS January update here](#).

For more information, please read the [EURORDIS COVID-19 Information Resources Centre](#).

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# In the spotlight: Newborn screening

## What is Newborn Screening?

*Newborn Screening (NBS)* is a comprehensive system that includes multidimensional components, including testing, diagnosis, communication of information to parents, follow up care and storage of samples for secondary use. Recent and continued scientific and technological advancements have opened up the discussion on the expansion of NBS programmes to include rare diseases that could be screened using new sequencing techniques.

## Newborn Screening key principles

The *EURORDIS Newborn Screening Working Group (NBS-WG)* was set up to review current policy and practice in the field of NBS, in order to develop principles for harmonious uptake/adoption of the NBS programs across the Member States with a view to delivering maximum benefit and improving outcomes for babies born with rare diseases. Members of NBS-WG include representatives from patient organizations, international screening societies and international and national federations with a focus on NBS.

For the first time, EURORDIS, alongside its Council of National Alliances, Council of European Federations and its members, have set out *11 Key Principles* to support an harmonised European approach to Newborn Screening. The vast inequalities across Europe, coupled with technological and scientific advances highlight the urgent need to move forward from the status quo.

1. Screening should identify opportunities to help the newborn and the family as broadly as possible. That is, screening should identify actionable diseases including treatable diseases.
2. NBS should be organised as a system with clearly defined roles, responsibilities, accountability and communication pathways that are embedded into the national health care system and recognised as a mechanism for earlier diagnosis of actionable conditions as part of the broader care pathway.
3. The family of the newborn who has been diagnosed through NBS should be provided with psychological, social and economic support by the competent national health authorities.
4. All stakeholders should be included in the different stages of the NBS process.
5. Transparent and robust governance for expanding NBS programmes is needed. Every country/region should have a clearly defined transparent, independent, impartial and evidence-based process for deciding which conditions are covered by the NBS programme that includes all stakeholders.
6. Governance of NBS programmes should be explicit, comprehensive, transparent and accountable to national authorities.
7. The evaluation process on the inclusion/exclusion of diseases in NBS programmes needs to be based on the best available evidence, reflecting health economic evidence but not determined only by health economics.
8. Information and education of all stakeholders on rare diseases and the whole NBS process is essential for a broad and fair implementation of NBS programmes.
9. European-wide standards addressing the timing, sample collection methods, follow-up, and information shared with parents are needed to guarantee uniformity and quality throughout the process.
10. Blood spot samples should be stored in national biobanks for research purposes while ensuring appropriate safeguards for data protection and data access are in place.
11. ERN affiliated centres should be integrated in the care pathways of the different Healthcare systems and should be considered as preferential partners in providing recommendations on NBS policies.

For more information, please read *EURORDIS position paper*.

## Pharmacovigilance Risk Assessment Committee (PRAC) December 2020

Minutes October 2020  
Agenda December 2020  
Meeting Highlights Dec 2020

### First monthly summary safety report for COVID-19 vaccine Comirnatys

EMA's safety committee (PRAC) will evaluate summary safety reports submitted monthly by marketing authorisations holders of COVID-19 vaccines. The first such report will be for Comirnaty. The company is expected to submit their monthly summary safety report in mid-January. The PRAC will evaluate and discuss it during its PRAC plenary virtual meeting at the end of January.

During the pandemic, marketing authorisation holders for COVID-19 vaccines are expected to submit monthly summary safety reports, in line with the [risk management plan](#) and as described in the [safety monitoring plan for COVID-19 vaccines](#) prepared by EMA and the national competent authorities of the EU Member States. The plan outlines how relevant new information emerging after the authorisation and roll-out of COVID-19 vaccines will be collected and promptly reviewed.

The monthly summary safety report will include, among others, information on reported suspected adverse reactions, including adverse events of special interest (AESIs). The submission of such reports complements the submission of periodic safety update reports (PSURs).

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 PRAC



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



**2361**  
Orphan  
designations



**228**  
Orphan designations  
included in authorised  
indication



**195**  
Authorised  
OMPs



**77**  
To be used in  
children



**5** Removed from  
the market  
**66** Marketed, but no  
longer "orphans"

To date

**124**

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

20 Jan 2021

## CHMP Meeting Highlights December 2020

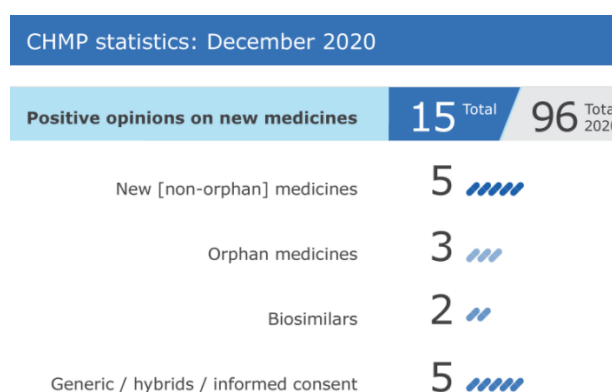
Minutes November 2020  
Agenda December 2020  
Meeting Highlights Dec 2020

In December, the CHMP recommended **15 medicines for approval, three orphan medicines:**

- Marketing authorisation *under exceptional circumstances* for **Lumoxiti** (moxetumomab pasudotox) for the treatment of relapsed or refractory hairy cell leukaemia, a cancer of a type of white blood cell called B-lymphocytes.
- **Inrebic** (fedratinib) for the treatment of primary myelofibrosis (an uncommon type of bone marrow cancer) and of myelofibrosis secondary to polycythaemia vera (a type of blood cancer) or essential thrombocythaemia (a rare chronic blood cancer).
- **Sibnalyal** (potassium citrate / potassium hydrogen carbonate) for the treatment of distal renal tubular acidosis, a rare genetic disorder that affects the ability of the kidneys to remove acid from the blood.
- *Conditional marketing authorisation* for **Enhertu** (trastuzumab deruxtecan) for the treatment of metastatic HER2-positive breast cancer.
- **Heplisav B** (hepatitis B surface antigen) for the active immunisation against hepatitis B virus infection.
- *Conditional marketing authorisation* for **Retsevmo** (selpercatinib) for the treatment of cancers that display a rearranged during transfection (RET) gene fusion: RET-fusion positive non-small cell lung cancer, RET-fusion positive thyroid cancer and RET-mutant medullary-thyroid cancer.
- **Rukobia** (fostemsavir) received a positive opinion for the treatment of multidrug resistant HIV-1 infection.
- **Tukysa** (tucatinib) received a positive opinion for the treatment of HER2-positive locally advanced or metastatic breast cancer.

The CHMP also recommended granting marketing authorisations for two biosimilar medicines, four generic medicines and one hybrid medicine. Nine recommendations on extensions of therapeutic indication were also granted.

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 December 2020 meeting update

Minutes September 2020  
Agenda December 2020  
Meeting Report Dec 2020

During the December plenary, the COMP adopted **12 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:

- Idiopathic hypersomnia, Jazz Pharmaceuticals Ireland Limited;
- Congenital muscular dystrophy, Maxia Strategies-Europe Limited;
- Idiopathic pericarditis, Granzer Regulatory Consulting & Services;
- Primary biliary cholangitis, GenKyoTex S.A.;
- Fabry disease, Consejo Superior De Investigaciones Cientificas;
- Myotrophic lateral sclerosis, Morrison & Foerster;
- Angelman syndrome, DlrC Pharma Services Limited;
- Phelan-McDermid syndrome, DlrC Pharma Services Limited;
- Pitt-Hopkins syndrome, DlrC Pharma Services Limited;
- Dermatomyositis, Pfizer Europe MA EEIG;
- Mucopolysaccharidosis type II (Hunter's syndrome), Shire Pharmaceuticals Ireland Limited;
- Invasive candidiasis, Mundipharma Corporation (Ireland) Limited.

### 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. After the October plenary, the COMP adopted by written procedure **2 positive opinions at time of CHMP opinion**:

- [Blincyto](#) (blinatumomab) for treatment of acute lymphoblastic leukaemia, Amgen Europe B.V.
- [Elzonris](#) (tagraxofusp) for treatment of blastic plasmacytoid dendritic cell neoplasm, TMC Pharma. The opinion was adopted by written procedure after the November Meeting.

Summaries of positive opinions on orphan designations are available on the [EMA website](#).

# Orphan medicines in 2020

Medicinal Product	Marketing Authorisation Holder	Therapeutic Indication	Date of Marketing Authorisation
<b>Isturisa®</b> (osilodrostat)	Novartis Europharm Limited	Cushing Syndrome	09/01/2020
<b>Polivy®</b> (polatuzumab vedotin)	Roche Registration GmbH	Diffuse large B-cell lymphoma (DLBCL)	16/01/2020
<b>Givlaari®</b> (givosiran)	Alnylam Netherlands B.V.	Acute hepatic porphyria	02/03/2020
<b>Trepulmix®</b> (treprostinil)	SciPharm Sàrl	Chronic thromboembolic pulmonary hypertension (CTEPH)	03/04/2020
<b>Zolgensma®</b> (onasemnogene abeparvovec)	AveXis EU Limited	Spinal muscular atrophy (SMA)	18/05/2020
<b>Reblozyl®</b> (luspatercept)	Celgene Europe B.V.	Beta thalassaemia & Myelodysplastic syndromes	25/06/2020
<b>Daurismo®</b> (glasdegib)	Pfizer Europe MA EEIG	Newly-diagnosed acute myeloid leukaemia (AML)	26/06/2020
<b>Pretomanid FGK®</b> (pretomanid)	FGK Representative Service GmbH	Adults with drug-resistant tuberculosis	31/07/2020
<b>Hepcludex®</b> (bulevirtide)	MYR GmbH	Chronic (long-term) hepatitis delta virus (HDV) infection in adults	31/07/2020
<b>Idefix®</b> (imlifidase)	Hansa Biopharma AB	Prevent the body from rejecting a newly transplanted kidney	25/08/2020
<b>Kaftrio®</b> (ivacaftor / tezacaftor / elexacaftor)	Vertex Pharmaceuticals (Ireland) Limited	Cystic fibrosis	21/08/2020
<b>Blenrep®</b> (belantamab mafodotin)	GlaxoSmithKline (Ireland) Limited	Multiple Myeloma	25/08/2020
<b>Ayvakyt®</b> (avapritinib)	Blueprint Medicines (Netherlands) B.V.	Gastrointestinal stromal tumour (GIST)	24/09/2020
<b>Arikayce liposomal®</b> (amikacin sulfate)	Insmed Netherlands B.V.	Adults with a lung infection caused by Mycobacterium avium complex (MAC)	27/10/2020
<b>Adakveo®</b> (crizanlizumab)	Novartis Europharm Limited	Sickle cell disease aged 16 years and older	28/10/2020
<b>Oxlumo®</b> (lumasiran)	Alnylam Netherlands B.V.	Primary hyperoxaluria type 1	19/11/2020
<b>Obiltoxaximab SFL®</b> (obiltoxaximab)	SFL Pharmaceuticals Deutschland GmbH	Inhalational anthrax due to Bacillus anthracis	18/11/2020
<b>Libmeldy®</b> (autologous CD34+ cells encoding ARSA gene)	Orchard Therapeutics (Netherlands) BV	Metachromatic leukodystrophy (MLD)	17/12/2020
<b>Fintepla®</b> (fenfluramine)	Zogenix ROI Limited	Seizures associated with Dravet syndrome	18/12/2020

Please click also on the following links to see:

[Orphan medicinal products authorised during 2020](#)

[Orphan medicinal products authorised since 2000](#)

## PDCO December 2020 meeting update

Minutes November 2020  
Agenda December 2020  
Meeting Report December 2020

In December, the PDCO adopted **14 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.

- Arimoclomol (citrate), from Orphazyme A/S, for the treatment of amyotrophic lateral sclerosis;
- Autologous peripheral blood T cells CD4- and CD8-selected and CD3- and CD28-activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (KTE-X19), from Kite Pharma EU B.V., for the treatment of mature B-cell neoplasms;
- Lenacapavir, from Gilead Sciences International Ltd., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Allopurinol / verinurad, from AstraZeneca AB, for the treatment of chronic kidney disease;
- Esketamine (hydrochloride), from Celon Pharma S.A., for the treatment of bipolar depression and treatment of major depressive disorder;
- Retinol (Vitamin A), from orphanix GmbH, for the prevention of bronchopulmonary dysplasia;
- Carfilzomib, from Amgen Europe BV, for the treatment of acute lymphoblastic leukaemia;
- Autologous tumour-infiltrating lymphocytes (LN-144/LN-145), from Iovance Biotherapeutics, Inc., for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- (S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride (KH176), from Khondrion BV, for the treatment of mitochondrial respiratory chain/oxidative phosphorylation defects;
- Obinutuzumab, from Roche Registration GmbH, for the treatment of systemic lupus erythematosus;
- Sparsentan, from Trave Therapeutics Ireland Ltd., for the treatment of IgA nephropathy;
- Dexmedetomidine (hydrochloride), from BioXcel Therapeutics, Inc., for the treatment of bipolar disorder and treatment of schizophrenia;
- Sparsentan, from Trave Therapeutics Ireland Ltd., for the treatment of focal segmental glomerular sclerosis;
- 3-((1R,3S,5S)-3-((7-((5-methyl-1H-pyrazol-3-yl)amino)-1,6-naphthyridin-5-yl)amino)-8-azabicyclo[3.2.1]octan-8-yl)propanenitrile (TD-1473), EMEA-002757-PIP01-19, from Theravance Biopharma Ireland Limited, for the treatment of ulcerative colitis.

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 December 2020 meeting update

Minutes October 2020  
Agenda December 2020  
Meeting Report Dec 2020

In December the Committee for Advanced Therapies (CAT) finalised 6 **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 was classified as **gene therapy medicinal products**:

- Autologous CD34+ cells transduced with a lentiviral vector encoding human cystinosin, intended for the treatment of cystinosis.
- Delolimogene mupadenorepvec (oncolytic adenovirus expressing two immunostimulatory transgenes (TMZ-CD40L and 4-1BBL)), intended for the treatment of cancer.

The following products were classified as **somatic cell therapy medicinal products**:

- Autologous tumour-infiltrating lymphocytes, intended for the treatment of advanced melanoma.
- Allogeneic cord tissue-derived mesenchymal stromal cells, intended for the treatment of inflammatory and immunological diseases (acute graft-versus-host disease, systemic lupus erythematosus, systemic sclerosis, acute respiratory distress syndrome).

The following products were classified as **tissue engineered products and combined ATMPs**:

- 3D bio-printed bionic pancreas composed of islets of Langerhans and non-viable printable porcine-derived matrix plus porcine-derived decellularised blood vessel, intended for the treatment of late-chronic pancreatitis.
- 3D bio-printed bionic pancreas composed of insulin- and glucagon-releasing cells and nonviable printable porcine-derived matrix plus porcine-derived decellularised blood vessel, intended for the treatment of brittle diabetes mellitus type I.

CAT noted the **withdrawal** of the marketing authorisation application of autologous human chondrocytes, in vitro expanded, which was intended for the repair of cartilage defects of the knee joint.

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](#).



## PCWP and HCPWP November meeting

Last 16<sup>th</sup> November took place a virtual meeting update on [COVID-19 pandemic](#) 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 meeting focused on the following:

- Update on Agency's response to the COVID-19 pandemic
- Patient / Healthcare Professionals' participation in EMA Covid-19 Taskforce (ETF)
- Pharmacovigilance aspects on COVID therapeutics & vaccines
- Information materials on COVID-19 vaccines

For more information, please see the [agenda](#).

## EMA second public stakeholder meeting on COVID-19 vaccines

Last 8<sup>th</sup> January the EMA organised a second virtual [meeting](#) to explain the processes for the [development, evaluation, approval and safety](#) monitoring of COVID-19 vaccines in the EU, including EMA's specific role. It gave the opportunity to the public and stakeholder groups to speak and share their needs, expectations and any concerns.

The [event](#) was broadcasted live, please see the [agenda](#), [presentations](#) and [recording here](#).

EURORDIS and the European Patients Forum (EPF) signed a jointly letter asking the EMA to organise a multi-stakeholder meetings open to the public on vaccines to prevent SARS-CoV-2 infection, please read the [letter here!](#)

## Accelerated assessment

Rapid assessment of medicines in the centralised procedure aimed at facilitating patient access to new medicines that address an unmet medical need. Accelerated assessment usually takes 150 evaluation days, rather than 210.

## Advanced therapies or advanced-therapy medicinal products (ATMPs)

ATMPs are new medical products based on genes, cells and tissues, which offer new treatment opportunities for many diseases and injuries. There are four main groups:

### Gene-therapy medicines

They are medicines that contain genes leading to a therapeutic effect. They work by inserting 'recombinant' genes into cells, usually to treat a variety of diseases, including genetic disorders, cancer or long-term diseases. A recombinant gene is a stretch of DNA that is created in the laboratory, bringing together DNA from different sources.

### Somatic-cell therapy medicines

These contain cells or tissues that have been manipulated to change their biological characteristics. They can be used to cure, diagnose or prevent diseases;

### Tissue-engineered medicines

These contain cells or tissues that have been modified so they can be used to repair, regenerate or replace tissue.

### Combined advanced-therapy medicines

These are medicines that contain one or more medical devices as an integral part of the medicine. An example of this is cells embedded in a biodegradable matrix or scaffold.

## Authorisation under exceptional circumstances

It allows patients access to medicines that cannot be approved under a standard authorisation as comprehensive data cannot be obtained, either because there are only very few patients with the disease, the collection of complete information on the efficacy and safety of the medicine would be unethical, or there are gaps in the scientific knowledge. These medicines are subject to specific post-authorisation obligations and monitoring.

## Compliance check

It is performed to verify that all the measures agreed in a [Paediatric Investigation Plan](#) (PIP) and reflected in the Agency's decision have been conducted in accordance with the decision, including the agreed timelines. Full compliance with all studies/measures 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 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.

## 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 on 1) 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.

