

## GENERAL NEWS

### IRDiRC Orphan Drug Development Guidebook is out!

*The International Rare Diseases Research Consortium (IRDiRC)* has created a **Guidebook** to facilitate drug development for rare diseases by organizing available tools into a standardized framework. Virginie Hivert, EURORDIS Therapeutic Development Director, together with other colleagues have been working over the past 2-3 years in this project, which is now published in the format of a *Commentary in Nature Reviews Drug Discovery*. Read it [here](#)!

The aim of this Guidebook is to provide all types of developers (including Patient Organisations involved in R&D) with tools and recommendations in order to navigate the complexity of the medicines development ecosystem. By enhancing the use of available tools, delays in development timelines can be avoided, risks and costs reduced, and patient and regulatory acceptability improved.

In the context of *ECRD 2020*, an explanatory webinar on the *IRDiRC Orphan Drug Development Guidebook* will be available for the participants, don't miss this opportunity and [register here](#)!

For more information, please see [IRDiRC website](#), and please you can find the paper [here](#)!

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### IMI PARADIGM CEE Transferability Workshops

The *IMI PARADIGM project* (in which EURORDIS is a partner) is holding *3 online workshops* to collect input from patient representatives in Central & Eastern Europe (CEE) on tools/ practices to improve patient engagement in the medicines R&D process.

EURORDIS members from Bulgaria, Croatia, Czech Republic, Hungary, Poland, Romania, Slovakia, Slovenia are invited to attend! [Register now!](#)

For more information, please see [IMI PARADIGM website!](#)

THE 10<sup>th</sup> EUROPEAN CONFERENCE ON  
RARE DISEASES & ORPHAN PRODUCTS



ONLINE on 14-16 May 2020

THE JOURNEY OF LIVING WITH  
a RARE DISEASE in

2030

**ECRD2020 online**  
**don't miss it!**  
**Register today!**

## New survey on rare disease patients' experience of COVID-19 is out!

*EURORDIS Rare Barometer survey on rare disease patients' experience of COVID-19 is out!* This survey is essential for the rare disease community. It will enable us to measure how the virus is affecting rare disease patients' lives and give us the possibility to communicate facts and figures to decision-makers, so that people living with a rare disease are not left behind when handling this crisis or future crisis of this type. The survey will be open to people living with a rare disease and their family members from any country in the world. It is **translated in 23 languages**. Please complete [this survey](#), only takes 15 min!

The main objectives are:

- Evaluate the impact of COVID-19 on rare disease patients' medical care, social care and well-being.
- Identify measures and facilities that are helping rare disease patients to cope with the pandemic
- Identify aspects that may have a negative impact on rare disease patients care and well-being
- Identify potential long-term consequences of the pandemic

**Share your experience and tell us how of the COVID-19 pandemic is affecting you by *completing our survey*!**

## EURORDIS COVID-19 Information Resource Centre

With the fast-evolving situation surrounding COVID-19 in Europe and across the world, members of the rare disease community may be concerned about their health. [EURORDIS COVID-19 Information Resources Centre](#) is a collection of EURORDIS actions and communication around the COVID-19 pandemic. You can also find EURORDIS statements, sources of official information, and information/ activities organised in response to the pandemic that we have received through our network!

We are also producing a weekly update on the [development of products for the treatment of COVID-19](#). This document provides a selection of updates on the research and development of treatments for COVID-19. **Please note that no product against COVID-19 has been approved.** Please avoid self-prescription and always refer to your doctor before making any treatment decision.

EURORDIS open letter to policy makers: [Recommendations to protect people living with a rare disease during the COVID-19 pandemic](#). Through this open letter, we implore policy makers and authorities in Europe and around the world to take action to protect people living with a rare disease from becoming even more vulnerable during this crisis in line with the recommendations set out further below. **Use this open letter to policy makers to advocate in your country for the protection of people living with a rare disease during the COVID-19 pandemic.** In the letter, we set out challenges people living with a rare disease are currently facing and suggest proposals on how policymakers can best support the rare disease community during this time. This is just one of the EURORDIS COVID-19 statements, please visit all the resources available via the [EURORDIS COVID-19 Information Resource Centre](#)!

## Pharmacovigilance Risk Assessment Committee (PRAC) March 2020

Minutes October 2019  
Agenda March 2020  
Meeting Highlights March 2020

### PRAC starts review of certain ifosfamide cancer medicines

EMA's safety committee (PRAC) has started a review of medicines containing ifosfamide. Ifosfamide is used to treat different types of cancers, including various solid tumours and blood cancers such as lymphomas (cancer of white blood cells). The medicine is given into a vein and is available as a ready-made and a concentrate for solution, and powder for solution for infusion. Following studies suggesting that the risk of encephalopathy (brain disorder) with the solution is higher than the risk with the powder, the PRAC will assess the available data on this risk.

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

### PRAC 2020 work plan

For further information on the work of the PRAC for this 2020, see the [work plan](#).

### PRAC recommends suspension of ulipristal acetate

The PRAC has recommended, as a precautionary measure during ongoing review of liver injury risk, that women should stop taking 5-mg ulipristal acetate (Esmya and *generic medicines*) for uterine fibroids. Ulipristal acetate is also authorised as a single-dose medicine for emergency contraception. This review does not affect the single-dose ulipristal acetate emergency contraceptive (ellaOne and other trade names) and there is no concern out liver injury with these medicines.

A [2018 PRAC review concluded](#) that there is a risk of rare but serious liver injury with ulipristal acetate medicines for uterine fibroids, and measures were implemented to minimise the risk. However, as the new case of serious liver injury occurred despite adherence to these measures, the Committee has started a new review. The start of this new review follows a recent case of liver injury, which led to liver transplantation in a patient taking the medicine.

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



**2265**  
Orphan  
designations



**212**  
Orphan designations  
included in authorised  
indication



**179**  
Authorised  
OMPs



**69**  
To be used in  
children



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

To date

**110**

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

15 Abril 2020

## ORPHAN MEDICINAL PRODUCTS AUTHORISED 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)	Anylam Netherlands B.V.	Acute hepatic porphyria	02/03/2020

Please click also on the following links to see:

[Orphan medicinal products authorised during 2020](#)

[Orphan medicinal products authorised since 2000](#)

## CHMP Meeting Highlights March 2020

Minutes January 2020  
Agenda March 2020  
Meeting Highlights March 2020

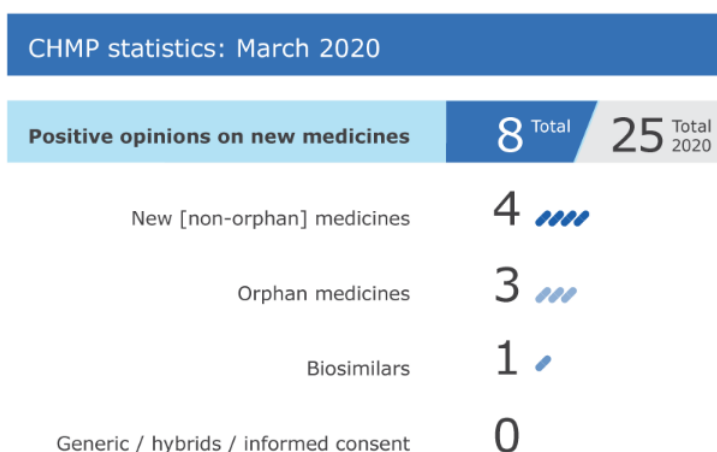
In March, the CHMP recommended **8 medicines for approval, three orphan medicines**:

- The Committee recommended granting a conditional marketing authorisation for *Zolgensma (onasemnogene abeparvovec)*, an advanced therapy medicinal product (ATMP) for the treatment of babies and young children with spinal muscular atrophy, a rare and often fatal genetic disease that causes muscle weakness and progressive loss of movement.
- *Sarclisa (isatuximab)* for the treatment of multiple myeloma, a cancer of the bone marrow.
- *Pretomanid FGK (pretomanid)* for the treatment of tuberculosis in combination with bedaquiline and linezolid.
- The CHMP also adopted a positive opinion for *Aectura Breezhaler (indacaterol / mometasone furoate)* and *Bemrist Breezhaler (indacaterol / mometasone furoate)* for the treatment of asthma.
- *Zeposia (ozanimod)* received a positive opinion for the treatment of adult patients with relapsing remitting multiple sclerosis with active disease.
- *Fluad Tetra (influenza vaccine (surface antigen, inactivated, adjuvanted))* for prophylaxis against influenza.
- The biosimilar medicine *Nepexto (etanercept)* received a positive opinion for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis, non-radiographic axial spondyloarthritis), plaque psoriasis and paediatric plaque psoriasis.

Six recommendations on extensions of therapeutic indication were also granted.

For further details, read the full [CHMP meeting highlights](#).

For further information on the work of the CHMP for this 2020, see the [work plan](#).



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 March 2020 meeting update

During the March plenary, the COMP adopted **11 positive opinions** on the designation of medicines as orphan medicinal products to the European Commission (EC). For further information, please see the [meeting report](#).

For further information on the work of the COMP for this 2020, see the [work plan](#).

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

- DNA plasmid encoding IL-12 p35 and p40 genes for treatment of ovarian cancer, FGK Representative Service GmbH
- Haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate for treatment in haematopoietic stem cell transplantation, CATS Consultants GmbH
- Rozanolixizumab for treatment of myasthenia gravis, UCB Pharma
- Tislelizumab for treatment of hepatocellular carcinoma, BeiGene Ireland Limited
- Adeno-associated viral vector serotype 3B encoding human multidrug resistance protein 3A for treatment of progressive familial intrahepatic cholestasis, Vivet Therapeutics S.A.S.
- Adeno-associated virus vector serotype hu37 encoding human factor VIII for treatment of haemophilia A, Bayer AG
- Anti-(integrin beta-3) human monoclonal antibody for prevention of fetal and neonatal alloimmune thrombocytopenia due to human platelet antigen-1a incompatibility, FGK Representative Service GmbH;
- Cusatuzumab for treatment of acute myeloid leukaemia, Janssen-Cilag International N.V.
- Florbetaben (18F) for diagnosis of AL amyloidosis, Life Molecular Imaging GmbH;
- Glucagon analogue linked to a human immunoglobulin Fc fragment for treatment of insulin autoimmune syndrome, JVM Europe B.V.
- Mitapivat sulfate for treatment of pyruvate kinase deficiency, Agios Netherlands B.V.

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

**PDCO March 2020 meeting to be updated in the next issue**

Minutes November 2019  
Agenda February 2020  
Meeting Report February 2020

## PDCO February 2020 meeting update

In February, the PDCO adopted **17 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.

- Bintrafusp alfa, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system neoplasms, haematopoietic and lymphoid tissue neoplasms);
- Pneumococcal polysaccharides (serotypes 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20B, 22F, 23F and 33F) individually biotinylated and complexed with a carrier protein (recombinant fusion construct of rhizavidin and Streptococcus pneumoniae derived proteins SP1500 and SP0785) [ASP3772], from Astellas Pharma Europe, B.V., for the prevention of disease caused by Streptococcus pneumonia
- Pracinostat, from Helsinn Birex Pharmaceuticals limited, for the treatment of acute myeloid leukemia
- N-(3-{6-Amino-5-[2-(N-methylprop-2-enamido)ethoxy]pyrimidin-4-yl}-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide (LOU064), from Novartis Europharm Limited, for the treatment of chronic spontaneous urticaria
- Polymyxin B, from The GARDP Foundation, for the treatment of infections due to aerobic Gram-negative bacteria
- Temozolomide, from Accord Healthcare S.L.U., for the treatment of malignant glioma
- Dihomo-γ-linolenic acid (DS107), from DS Biopharma Ltd., for the treatment of atopic dermatitis
- 2-[[2-ethyl-6-[4-[2-(3-hydroxyazetidin-1-yl)-2-oxoethyl]piperazin-1-yl]-8-methylimidazo[1,2-a]pyridin-3-yl](methyl)amino]-4-(4-fluorophenyl)-1,3-thiazole-5-carbonitrile (GLPG1690), from Galapagos NV, for the treatment of interstitial pulmonary diseases with fibrosis; or human monoclonal antibody, from Momenta Pharmaceuticals, Inc., for the treatment of myasthenia gravis
- Leriglitazone, from Minoryx Therapeutics S.L., for the treatment of adrenoleukodystrophy
- Ladarixin, from Dompé farmaceutici SpA, for the treatment of type 1 diabetes mellitus
- Lenadogene nolpharovec (GS010), from GenSight-Biologics, for the treatment of Leber hereditary optic neuropathy (LHON)
- Pegcetacoplan, from Apellis Ireland Limited, for the paroxysmal nocturnal haemoglobinuria
- Cenobamate, from Arvelle Therapeutics Netherlands B.V., for the treatment of epilepsy
- Alpha1-proteinase inhibitor (human) (A1-PI), from CSL Behring GmbH, for the prevention of graft-versus-host disease
- Lebrikizumab, EMEA-002536-PIP01-18, from Dermira Inc., for the treatment of atopic dermatitis;
- (S)-(2-(5-chloro-4-methyl-1H-benzo[d]imidazol-2-yl)-2-methylpyrrolidin-1-yl)(4-methoxy-2-(2H1,2,3-triazol-2-yl)phenyl)methanone hydrochloride (daridorexant), EMEA-002121-PIP03-19, from Idorsia Pharmaceuticals Deutschland GmbH, for the treatment of insomnia
- Pneumococcal Polyssacharide Serotype 6A conjugated to CRM197 carrier protein adsorbed on aluminium Phosphate, from Pfizer MA EEIG, for the prevention of disease caused by Streptococcus pneumoniae.

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 March 2020 meeting to be updated in the next issue

Minutes January 2020  
Agenda February 2020  
Meeting Report Feb 2020

## CAT February 2020 meeting update

In February the Committee for Advanced Therapies (CAT) finalised 7 **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](#).

For further information on the work of the CAT for this 2020, see the [work plan](#).

The following products were classified as **gene therapy medicinal products**:

- Adeno-associated viral vector serotype 5 encoding for the human Retinitis Pigmentosa GTPase Regular (RPGR) gene, intended for the treatment of X-linked retinitis pigmentosa due to defects in RPGR.
- Adeno-associated viral vector serotype 9 encoding for a codon-optimised human aspartylglucosaminidase (AGA) gene, intended for the treatment of aspartylglucosaminuria due to a loss-of-function mutation in the AGA gene.

The following products were classified as advanced therapy medicinal products. *CAT was unable to consider if these products meet the definition of somatic cell therapy or tissue engineering product due to shortcomings in the information provided regarding the claimed mode of action:*

- Allogeneic viable Wharton's jelly derived mesenchymal stem cells, intended for the treatment of:
  - Age-related macular degeneration
  - Bone non-union
  - Chorioretinal disorders
  - Epidermolysis bullosa
  - Hypoxic-ischemic encephalopathy

For more information, see also the [EMA news release](#).



# 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 first 2020 meeting

Last 3&4 March took place the [first meeting of 2020](#) which has 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). During these two days meeting at the European Medicines Agency's (EMA) it was discussed:

- strategies for future activities, including the Regulatory Science Strategy and the Network Strategy to 2025
- review of ICH guidelines for clinical trials and GCP
- big data taskforce recommendations addressing aspects related with data sharing and data protection
- feedback from the various scientific committees
- update on Electronic product information (ePI) activities
- CIOMS guidelines on patient involvement
- shortages

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

## PCWP and HCPWP 2019-2022 Work Plan



Adapted from EMA's [work plan 2019 - 2022](#)

## 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.

