

## GENERAL NEWS

### Reflection paper on the use of artificial intelligence in the lifecycle medicines

EMA has published a [draft reflection paper](#) outlining the current thinking on the use of artificial intelligence (AI) to support the safe and effective development, regulation and use of human and veterinary medicines. The reflection paper highlights that a **human-centric approach** should **guide all development and deployment** of AI and Machine learning (ML).

The paper is part of the [joint HMA-EMA Big Data Steering Group \(BDSG\)](#) initiatives to develop the European Medicines Regulatory Network's capability in data-driven regulation.

It is now **open for public consultation** until 31 December 2023.

Find more information [here!](#)

### First REMEDI<sub>4</sub>ALL Multi-Stakeholder Meeting

The first **REMEDI<sub>4</sub>ALL Multi-Stakeholder Meeting (MSM)** will address the topic of **Drug Repurposing, an Attractive Strategy in Pancreatic Cancer Treatment?**

It will take place on **14th November 2023** ahead of the **European Cancer Summit** in **Brussels**.

The meeting will be **on invitation only** following expression of interest. Interested participants can apply before **30th October 2023** by filling the Expression of Interest form available [here](#).

Get to know more about the project [here](#).

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### Applications are open for the 2024 Open Academy Schools!

Save the date to join us in **June 2024** in **Barcelona!**

If you are a **rare disease patient advocate** interested in bringing your expertise to discussions on **health care, research** and **medicines development** don't miss the opportunity to apply to the [EURORDIS Open Academy Schools 2024](#).

Applications will close on the **27<sup>th</sup> of October 2023**. Apply [here!](#)

## What is ERICA?

The aim of the **European Rare Disease Research Coordination and Support Action** consortium (ERICA), in which all 24 European Reference Networks (ERNs) take part, is to **build on the strength of the individual ERNs and create a platform that integrates all ERNs research and innovation capacity**. The ERICA consortium consists of 29 partners, amongst which all [24 ERNs](#), [EURORDIS](#), the [EJP RD](#), [Orphanet](#), [Mapi Trust Research](#), and [EATRIS](#). EURORDIS is a project partner and will deliver a framework for patient involvement in clinical trials in the ERNs by the end of the project in 2025.

Through knowledge sharing, engagement with stakeholders in the rare disease domain and assembly of transdisciplinary research groups working across the global health spectrum, **ERICA strives to reach the following goals:**

- new intra- and inter-ERN rare disease competitive networks
- effective data collection strategies
- better patient involvement
- enhanced quality and impact of clinical trials
- increased awareness of ERNs innovation potential.



ERICA will **strengthen research and innovation capacity** by integration of ERN research activities, outreach to European research infrastructures to synergistically increase impact, and innovation. This will **result in efficient access and safe therapies for the benefit of patients suffering from rare diseases and complex conditions**.

For more information, please check the [website](#) and follow the project on social media!

## PROMs Repository

The ERICA Patient Reported Outcome Measures (PROMs) Repository is the **first attempt to identify and centralize Clinical Assessment Outcomes questionnaires** of relevance **for rare diseases** and constitutes a milestone in the Europe-wide standardization of Patient-Centered Outcome Measures (PCOMs) and PROMs for rare diseases.

It has been made possible through the **joint collaboration** between *Orphanet*, *Mapi Research Trust/ICON* and *ERN EuroBloodNet* (VHIR, APHP), and the active contribution of ERNs and ePAGs.

For more information on the methodology for the constitution and future evolution of the repository read [here](#) and [here](#).

The central repository is a dynamic and evolutive service and should be regarded as a centralized and standardized access gate to more in depth information contained in [PROQOLID™](#).

In May 2023 the content of the repository was enriched with Observer-Reported Outcome Measures (ObsROMs), with PROMs & ObsROMs measuring quality of life as well as PROMs & ObsROMs recently developed for rare diseases.

Your **contribution is crucial to identify new measures and keep alive and up-to date the repository**. If you know about PROMs, ObsROMs or other Patient Centered-Clinical Outcomes Assessment (PC-COA) measures (Clinician-Reported Outcome Measure (ClinROM) and Performance Outcome (PerfO)) developed or validated for any rare diseases not included yet in the repository, **please contribute [here!](#)**



## Pharmacovigilance Risk Assessment Committee (PRAC) July 2023

Minutes July 2023  
Agenda July 2023  
Meeting Highlights July 2023

### Data revision on paternal exposure to valproate

The EMA is reviewing data on the **potential risk of neurodevelopmental disorders (NDDs) in children** conceived by **fathers taking valproate medicines**. The review is focussing on data from a *retrospective observational study* conducted by companies as an obligation following a previous review of valproate use during pregnancy.

Initial results of the study may indicate an increased risk of NDDs in children born to men taking valproate in the three months before conception. However, the PRAC has identified important limitations with the data from the study.

The **PRAC will review the required data** as they become available and make an **EU-wide recommendation**.

More information is available [here](#).

| PRAC statistics   | July 2023  |
|---|--|
|   |  |
| <b>7</b>  | <b>Safety signals</b>  |
| 6   | Started  |
| 1   | Ongoing/concluded  |
| <b>78</b>   | <b>Periodic safety update reports (PSURs) single assessments</b>                       |
| 50  | Recommendations for centrally authorised medicines only                                |
| 25  | Recommendations for nationally authorised medicines only                               |
| 3   | Recommendations for PSURs including both centrally and nationally authorised medicines |
| <b>56</b>   | <b>Risk management plans (RMPs) for centrally authorised medicines</b>                 |
| 8   | RMPs reviewed for new medicines  |
| 48  | RMPs reviewed for authorised medicines   |
| <b>30</b>   | <b>Post-authorisation safety studies (PASSs)</b>                                       |
| 3   | Protocols for imposed studies reviewed   |
| 2   | Results from imposed studies reviewed  |
| 16  | Protocols for non-imposed studies reviewed   |
| 9   | Results from non-imposed studies reviewed  |
| <b>0</b>  | <b>Referrals</b>   |
| 0   | Started  |
| 0   | Ongoing/concluded  |
| <small>Direct healthcare professional communications (DHPCs)<br/>PRAC minutes   PRAC recommendations on safety signals   Outcomes of PSUSAs</small> |  |

#### 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



**2782**  
Orphan  
designations



**276**  
Orphan designations  
included in authorised  
indication



**243**  
Authorised  
OMPs



**97**  
To be used in  
children



**6** Removed from  
the market

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

## To date

**158**

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

22 September 2023

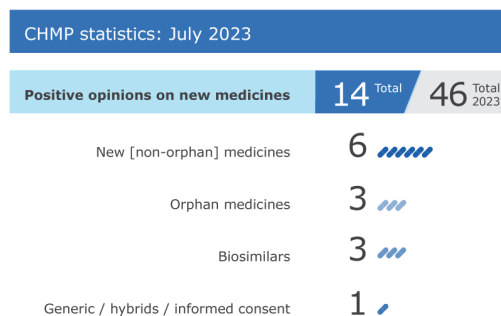
## CHMP Meeting Highlights July 2023

Minutes June 2023  
Agenda July 2023  
Meeting Highlights July 2023

In July, the CHMP recommended **14 new medicines for approval, 3 of them orphan medicines:**

- **Talvey** (talquetamab) for the treatment of adult patients with relapsed and refractory multiple myeloma, a rare cancer of the bone marrow that affects plasma cells.
- **Teplinly** (epcoritamab) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, a fast-growing cancer of the lymphatic system.
- **Tevimbra** (tislelizumab), for the treatment of adult patients with unresectable, locally advanced or metastatic oesophageal squamous cell carcinoma after prior platinum-based chemotherapy.
- **Abrysvo** (bivalent, recombinant), a vaccine to protect small infants and older people against lower respiratory tract disease caused by respiratory syncytial virus (RSV).
- **Apretude** (cabotegravir), for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired human immunodeficiency virus type 1 (HIV-1) infection.
- **Degarelix Accord** (degarelix acetate), for the treatment of prostate cancer.
- **Enrylaze** (crisantaspase) for the treatment of acute lymphoblastic leukaemia, a type of blood cancer that starts from white blood cells called lymphocytes in the bone marrow, and lymphoblastic lymphoma, an aggressive type of non-Hodgkin lymphoma.
- **Inaqovi** (decitabine/cedazuridine) for the treatment of acute myeloid leukaemia, a disease in which cancer cells are found in the blood and the bone marrow.
- **Litfulo** (ritlecitinib) for the treatment of severe alopecia areata, a disease that causes hair loss on the scalp or other parts of the body.
- **Lyfnua** (gefapixant), intended for the treatment of refractory or unexplained chronic cough.
- **Orserdu** (elacestrant) for the treatment of postmenopausal women and men with locally advanced or metastatic breast cancer.
- **Tyenne** (tocilizumab), intended for the treatment of rheumatoid arthritis, active systemic juvenile idiopathic arthritis, juvenile idiopathic polyarthritis, giant cell arteritis, chimeric antigen receptor T cell-induced cytokine release syndrome, and COVID-19.
- **Tyruko** (natalizumab), for active relapsing remitting multiple sclerosis, a disease of the brain and spinal cord in which inflammation destroys the protective covering around nerves and the nerves themselves.
- **Yesafili** (aflibercept), for age-related macular degeneration, affecting the central part of the retina at the back of the eye, and different types of visual impairment.

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



Click on the image to get the latest issue of [Human Medicines Highlights](#), a newsletter published by EMA address to organisations representing patients, consumers and healthcare professionals summarising key information on medicines for human use.

COMP will no longer publish meeting reports, all the information now in the minutes

## COMP

The Committee for Orphan Medicinal Products (COMP) is the European Medicines Agency's (EMA) committee responsible for recommending orphan designation of medicines for rare diseases.

The COMP was established in 2000, in line with [Regulation \(EC\) No 141/2000](#) and is responsible for evaluating applications for [orphan designation and reviewing it at time of marketing authorisation](#). This designation is for medicines to be developed for the diagnosis, prevention or treatment of **rare diseases** that are life-threatening or very serious. In the European Union (EU), a disease is defined as rare if it affects fewer than 5 in 10,000 people across the EU. The European Commission decides whether to grant an orphan designation for the medicine based on the COMP's opinion.

An orphan designation allows a pharmaceutical company to benefit from incentives from the EU, such as reduced fees and protection from competition once the medicine is placed on the market.

The COMP also advises and assists the European Commission on matters related to orphan medicines, including:

- developing and establishing an EU-wide policy;
- drawing up detailed guidelines;
- liaising internationally.

COMP is planning the following activities for the year 2023:

- Defining the requirements for major contribution to patient care at orphan designation as well as at marketing authorisation stage and draft a concept paper outlining the conclusions as guidance to sponsors.
- Work on the flexibility in the definition of orphan conditions to be more in line with innovative scientific development (for example the use of biomarker or tissue-agnostic therapies).
- Continue the pilot of RWE studies to support COMP decision-making including identification of use cases.

Read [here](#) the full work plan for more information.



COMP members celebrating rare diseases day 2023!

# Orphan medicines in 2023

| Medicinal Product   | Marketing Authorisation Holder          | Therapeutic Indication                         | Date of Marketing Authorisation |
|---|---|--|---------------------------------|
| <b><i>Hemgenix</i></b> <sup>®</sup><br>( <i>etranacogene dezaparvovec</i> ) | CSL Behring GmbH                        | Haemophilia B                                  | 20/02/2023                      |
| <b><i>Tibsovo</i></b> <sup>®</sup><br>( <i>ivosidenib</i> )                 | Les Laboratoires Servier                | Acute Myeloid Leukaemia and cholangiocarcinoma | 12/05/2023                      |
| <b><i>Hyftor</i></b> <sup>®</sup><br>( <i>sirolimus</i> )                   | Plusultra pharma GmbH                   | Facial angiofibroma                            | 15/05/2023                      |
| <b><i>Ztalmy</i></b> <sup>®</sup><br>( <i>ganaxolone</i> )                  | Marinus Pharmaceuticals Emerald Limited | Epileptic seizures in children with CDKL5      | 26/07/23                        |
| <b><i>Talvey</i></b> <sup>®</sup><br>( <i>talquetamab</i> )                 | Janssen-Cilag International N.V.        | Multiple Myeloma                               | 21/08/2023                      |

Please click also on the following links to see:

[Orphan medicinal products authorised during 2023](#)

[Orphan medicinal products authorised since 2000](#)

PDCO no longer publishes meeting reports. All the information now can be found in the minutes!

Minutes June 2023  
Agenda July 2023

## PDCO

The *Paediatric Committee (PDCO)* is the European Medicines Agency's (EMA) scientific committee responsible for activities on medicines for children and to support the development of such medicines in the European Union by providing scientific expertise and defining paediatric needs.

The *PDCO* was established in line with the *Paediatric Regulation*, which came into effect in 2007, to improve the health of children in Europe by facilitating the development and **availability of medicines for children** aged 0 to 17 years.

The *PDCO*'s main role is to assess the content of *paediatric investigation plans* (PIPs), which determine the studies that companies must carry out in children when developing a medicine. This includes assessing applications for a full or partial **waiver** and for **deferrals**.

The *PDCO* is not responsible for *marketing authorisation applications* for medicines for use in children, which is in the remit of the CHMP.

PDCO is planning the following activities for the year 2023:

- Conduct the pilot on RWE studies including through DARWIN EU to support PDCO decision-making including identification of use cases where the evidence from real word data can support the scientific assessment.
- Publish guidance on the pilot phase for the stepwise PIP.
- Publish a document reflecting on practical considerations related to the use of extrapolation from a regulatory and HTA perspective; linked to the priority activity reflected in the *joint workplan of EUnetHTA21 and EMA*.

Read [here](#) the full work plan for more information.



# AUTHORISED ADVANCED THERAPIES

CAT updates are now quarterly- will be updated when EMA publishes

Minutes June 2023  
Agenda July 2023  
Meeting May 2023-July 2023

## CAT highlights May– July meeting update

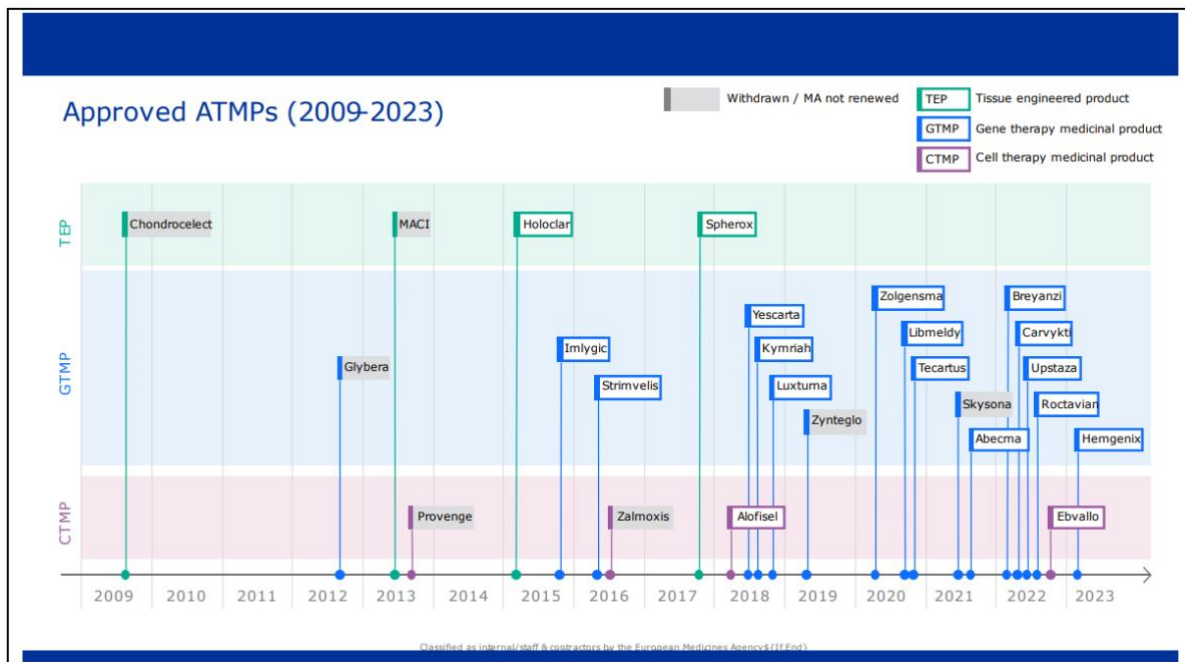
This report provides information on ATMP approvals and extension of indications of authorised ATMPs, as well as statistical data on product-related activities.

The outcome of these assessments can be found here: [Summaries of scientific recommendations on classification of ATMPs](#).

There are **no approvals of Advanced therapy medicinal products** in the period covered by this report.

There are **no extension of indication of authorised ATMPs**.

For more information, see also the [EMA meeting report](#).



# PATIENTS' AND CONSUMERS' WORKING PARTY

The Patients' and Consumers' Working Party (PCWP), established in 2006, serves as a platform for exchange of information and discussion of issues of common interest between EMA and patients and consumers. It provides recommendations to EMA and its human scientific committees on all matters of interest in relation to medicines.

For more information, see also the [PCWP mandate, objectives and rules of procedure](#).



## EMA PCWP & HCPWP meeting working parties joint meeting

Last 28<sup>th</sup> June 2023 took place face to face [the Patients and Consumers' \(PCWP\) and 'Healthcare Professionals' \(HCPWP\) Working Parties meeting](#). The meeting has focused on providing update on various EMA activities including clinical trials, pharmacovigilance, EMA communication and reporting. For more information, please see the agenda and presentations of the meeting [here](#).

The PCWP met also the 27<sup>th</sup> June to discuss its operations under the new mandate. For more information, read [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](#).

**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 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.