EURORDIS
THERAPEUTIC REPORT
September
ISSUE 8
UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

EU Network Training Centre (EUNTC)

Are you staff of the European medicines regulatory network or an external expert involved in EU regulatory procedures and EMA activities? Remember to *register* for access to the **EU Network Training Centre** (EUNTC)!

The EUNTC is an initiative set up by the Heads of Medicines Agencies (HMA) and EMA, in collaboration with the EU medicines agencies regulatory network. The aim is **to ensure that good scientific and regulatory practice is spread across the EU medicines agencies regulatory network**.

On a pilot basis, some EUNTC training materials are **also accessible to international regulators** and may **become available to a wider audience**. Some training materials are **publicly accessible.**

More information is available *here*.

IN THIS ISSUE

New IRDiRC guidebook for drug repurposing for rare diseases

The **IRDiRC Drug Repurposing Guidebook: making better use of existing drugs to tackle rare diseases'** has been published in Nature Reviews Drug Discovery.

This guidebook, authored by the IRDiRC Task Force "Drug Repurposing Guidebook", **facilitates drug repurposing for rare diseases** by organizing available tools into a standardized framework.
The Task Force worked for 18 months with more than 25 experts from the field of RD to help reach the IRDiRC goal 2: '1000 new therapies for rare diseases will be approved, the majority of which will focus on diseases without approved options' by 2027.

Find the article *here*.

Last call to apply 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 **27th of October 2023**. Apply *here*!

Get involved in *rare disease day!*

RAREDISEASEDAY.ORG

HTx – Next Generation HTA

HTx - Next Generation HTA is a **project aiming to create a framework for the Next Generation Health Technology Assessment** (HTA), to **support** patient-centred, societally oriented, real-time decision-making on **access to and reimbursement for health technologies** throughout Europe and EURORDIS is a project partner.

The main objectives of the project are the following:

- To **facilitate the development of methodologies** to deliver more customized information on the effectiveness and cost-effectiveness of complex and personalised combinations of health technologies.
- To **provide methods to support personalised treatment advice** that will be shared with patients and their physicians.
- In close collaboration with the **European Network for HTA (EUnetHTA)** and its stakeholders **pilot the implementation of these methods in Europe.**

What is EUnetHTA?

EUnetHTA was established to create an **effective and sustainable network for HTA across Europe** and help develop reliable, timely, transparent, and transferable information to **contribute to HTA in European countries**. EUnetHTA supports collaboration between European HTA organisations that brings value at the European, national, and regional level through:

- The facilitation of efficient HTA resource use.
- The creation of a sustainable system of HTA knowledge sharing.
- The promotion of good practice in HTA methods and processes.

Read more information about the HTx- Generation HTA *here* and EunetHTA *here*.

HTx Patient toolbox to boost patient advocates involvement

A **Patient Toolbox to help patient advocates get involved in the project** and the future of HTA has been developed based on the experiences of EURORDIS Open Academy School on Medicines Research & Development participants.

The Toolbox **aims to explain the different aspects of the research** being performed through a series of videos, written materials, webinars, presentations, and face-to-face training sessions. From the challenges of real-world data to the intricacies of developing prediction models and predicting risks of complication, it covers everything you need to know to get involved in the future HTA.

Find out more about the patient toolbox *here*!

Pharmacovigilance Risk Assessment Committee (PRAC) September 2023

Minutes July 2023
Agenda September 2023
Meeting Highlights September 2023

New safety information for Omega-3-acid ethyl esters

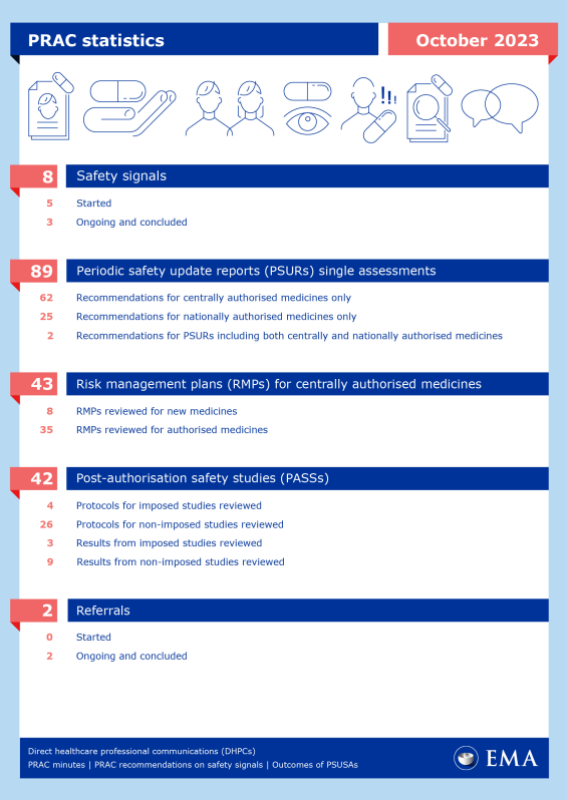
The PRAC agreed to add **atrial fibrillation** (irregular, rapid contraction of the heart) as a **common side effect** to the product information for **medicines containing omega-3-acid ethyl esters**.

Medicines containing this compound are **indicated for the treatment of hypertriglyceridaemia** when a modification of diet and lifestyle alone are not sufficient to bring down levels of triglyceride.

The PRAC considered systematic reviews and meta-analyses of randomised controlled clinical trials which highlighted a **dose-dependent increased risk of atrial fibrillation in patients with established cardiovascular diseases or cardiovascular risk factors treated with omega-3-acid ethyl esters** compared to placebo.

An **update to the product information** has been recommend informing healthcare professionals and patients of the risk of atrial fibrillation.

More information is available *here*.



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

277 Orphan designations included in authorised indication

244 Authorised OMPs

97 To be used in children

6 Removed from the market

84 Marketed, but no longer "orphans"

To date

154

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

25 October 2023

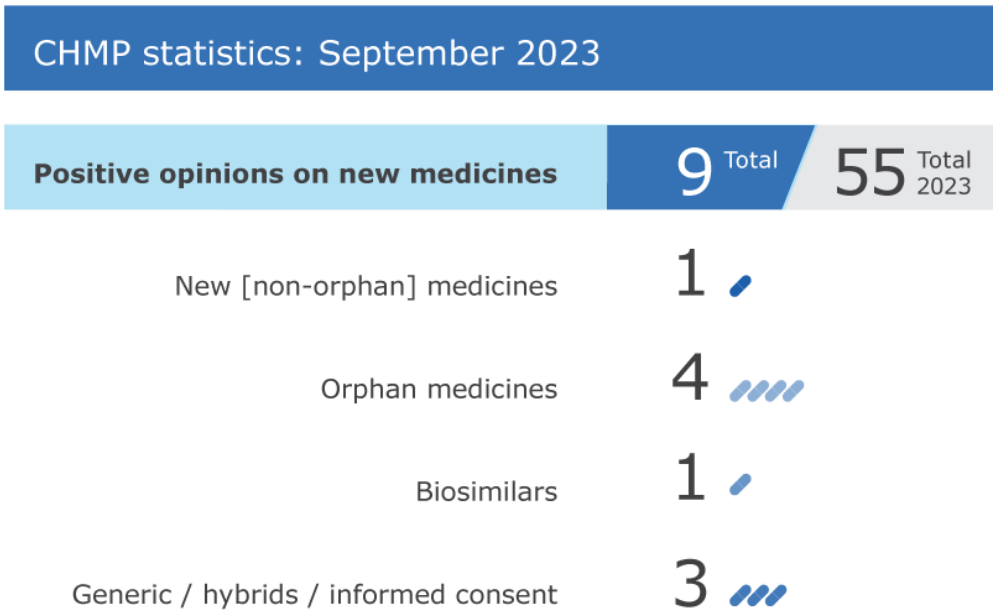
CHMP Meeting Highlights September 2023

Minutes August 2023
Agenda September 2023
Meeting Highlights September 2023

In September, the CHMP recommended **9 new medicines for approval, 4 of them orphan medicines**:

- *Finlee* (*dabrafenib*) for the treatment of glioma, a type of brain tumour that begins in glial cells, the cells that surround and support nerve cells.
- *Vanflyta* (*quizartinib*), for the treatment of adult patients with diagnosed acute myeloid leukaemia, a cancer of the blood and bone marrow.
- *Yorvipath* (*palopegteriparatide*), a parathyroid hormone replacement therapy, for the treatment of chronic hypoparathyroidism in adults.
- *Zilbrysq* (*zilucoplan*) for the treatment of generalised myasthenia gravis in adults.
- *Zoonotic Influenza Vaccine Seqirus* (surface antigen, inactivated, adjuvanted), for the active immunisation against H5N1 subtype of Influenza A virus.
- *Ebglyss (lebrikizumab),* for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents.
- *Herwenda* (*trastuzumab*) for the treatment of metastatic and early breast cancer and metastatic gastric cancer.
- *Aqumeldi* (*enalapril maleate*) for the treatment of heart failure.
- *Catiolanze* (*latanoprost*) for the reduction of elevated intraocular pressure.

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!

Medicinal Product	Marketing Authorisation Holder	Therapeutic Indication	Date of Marketing Authorisation
Hemgenix® *(etranacogene dezaparvovec)*	CSL Behring Gmbh	Haemophilia B	20/02/2023
Tibsovo® *(ivosidenib)*	Les Laboratoires Servier	Acute Myeloid Leukaemia and cholangiocarcinoma	12/05/2023
Hyftor® *(sirolimus)*	Plusultra pharma GmbH	Facial angiofibroma	15/05/2023
Ztalmy® *(ganaxolone)*	Marinus Pharmaceuticals Emerald Limited	Epileptic seizures in children with CDKL5	26/07/23
Talvey® (*talquetamab*)	Janssen-Cilag International N.V.	Multiple Myeloma	21/08/2023
Tepkinly® *(epcoritamab)*	AbbVie Deutschland GmbH & Co. KG	Diffuse large B-cell lymphoma (DLBCL)	22/09/2023

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 July 2023
Agenda September 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.

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

Minutes September 2023
Agenda September 2023
Meeting May 2023-July 2023

CAT highlights May– July meeting update

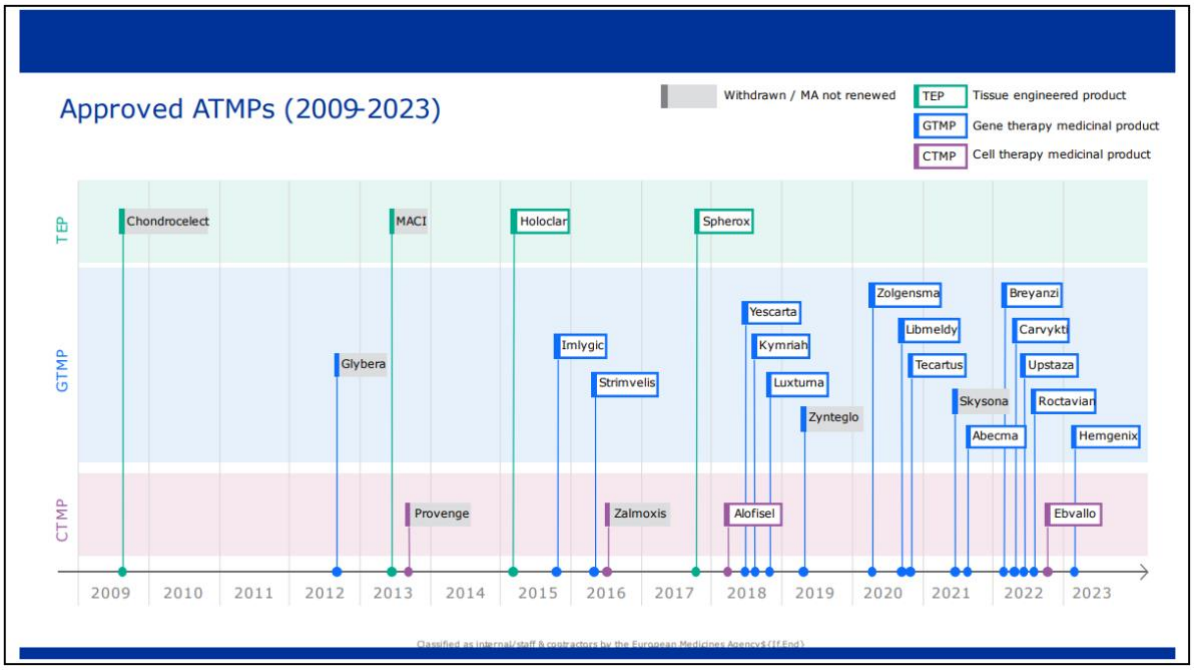
This report provides information on ATMP approvals and extension of indications of authorised ATMPs, as well as statistical data on product-related activities.

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 19-20 September 2023 took place online *the Patients and Consumers' (PCWP) and 'Healthcare Professionals' (HCPWP) Working Parties meeting.* Topics discussed in the two day meeting included the involvement of patient and HCP representatives in various EMA working groups, updates on crisis preparedness, big data, medicine shortages, patient information, clinical trials and EMA communications, and updates from recent international activities.

For more information, please see the agenda and presentations of the meeting *here*.

EMA Glossaries

The EMA just published a *medical terms simplifier* that gives plain-language descriptions of medical terms commonly used in information about medicines.

A *glossary of regulatory terms* that gives definitions for the main terms used on the EMA website and in their documents has also been published.

For more information, please check the *glossaries here.*

GLOSSARY

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

Advanced therapies or advanced-therapy medicinal products (ATMPs)
ATMPs are new medical products based on genes, cells and tissues, which offer new treatment opportunities for many diseases and injuries. There are four main groups:

- **Gene-therapy medicines**
  They are medicines that contain genes leading to a therapeutic effect. They work by inserting 'recombinant' genes into cells, usually to treat a variety of diseases, including genetic disorders, cancer or long-term diseases. A recombinant gene is a stretch of DNA that is created in the laboratory, bringing together DNA from different sources.
- **Somatic-cell therapy medicines**
  These contain cells or tissues that have been manipulated to change their biological characteristics. They can be used to cure, diagnose or prevent diseases;
- **Tissue-engineered medicines**
  These contain cells or tissues that have been modified so they can be used to repair, regenerate or replace tissue.
- **Combined advanced-therapy medicines**
  These are medicines that contain one or more medical devices as an integral part of the medicine. An example of this is cells embedded in a biodegradable matrix or scaffold.

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

Compliance check
It is performed to verify that all the measures agreed in a *Paediatric Investigation Plan* (PIP) and reflected in the Agency's decision have been conducted in accordance with the decision, including the agreed timelines. Full compliance with all studies/measured contained in the PIP is one of several prerequisites for obtaining the rewards and incentives provided for in Articles 36 to 38 of the Paediatric Regulation.

Conditional marketing authorisation
It is granted to a medicine that addresses unmet medical needs of patients on the basis of less comprehensive data than normally required. The available data must indicate that the medicine's benefits outweigh its risks and the applicant should be in a position to provide the comprehensive clinical data in the future.

Designation, orphan medicinal product
A status assigned to a medicine intended for use against a rare condition. The medicine must fulfil certain criteria for designation as an orphan medicine so that it can benefit from incentives such as protection from competition once on the market.

European Public Assessment Report (EPAR)
It is a lay-language document, which provides a summary of the grounds on which the EMA/CHMP based its recommendation for the medicine to receive a marketing authorisation. This happens when a manufacturer develops a generic medicine based on a reference medicine, but with a different strength or given by a different route.

Hybrid application for marketing authorisation
Hybrid applications rely partly on the results of tests on the reference medicine and partly on new data from clinical trials.

Informed consent application for marketing authorisation
An informed consent application makes use of data from the dossier of a previously authorised medicine, with the marketing authorisation holder of that medicine giving consent for the use of their data in the application.

Orphan Legislation
Regulation (EC) No 141/2000 on orphan medicinal products

Paediatric Investigation Plan (PIP)
It sets out a programme for the development of a medicine in the paediatric population. It aims to generate the necessary quality, safety and efficacy data through studies to support the authorisation of the medicine for use in children of all ages. These data have to be submitted to the EMA, or national competent authorities, as part of an application for a marketing authorisation for a new medicine, or for one covered by a patent.

Paediatric Use Marketing Authorisation (PUMA)
It is a dedicated marketing authorisation for medicinal products indicated exclusively for use in the paediatric population, or subsets thereof, with, if necessary, an age-appropriate formulation. It has been designed to promote paediatric development of already authorised products which are no longer covered by a patent. Benefits are 8 years of data protection and 10 years market protection

Patient-reported outcomes (PROs)
Measurements based on data provided directly by patients regarding their health condition without interpretation of the patient's response by a clinician or anyone else.

Patient-reported outcome measures (PROMs)
They are instruments, scales, or single-item measures that have been developed to measure PROs, for example a self-completed questionnaire to assess pain.

Periodic Safety Update Reports (PSURs)
Periodic reports that the evaluate the benefit-risk balance of a medicine as evidence is gathered in clinical use. They are submitted by marketing authorisation holders at defined time points after the authorisation.

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Post-authorisation efficacy studies (PAES)
PAES are studies relating to authorised medicinal products conducted within the therapeutic indication with the aim of addressing well-reasoned scientific uncertainties on aspects of the evidence of benefits of a medicine that could not be resolved before authorisation or were identified afterwards.

Post-authorisation safety studies (PASS)
A PASS is carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC is responsible for assessing the protocols of imposed PASSs and for assessing their results.

Prevalence
In the context of the Orphan Legislation, the prevalence refers to the number of persons with the condition at the time the application is made, divided by the population of the European Union (EU) at that time. It requires demonstration through authoritative references that the disease or condition for which the medicinal product is intended affects not more than 5 in 10,000 persons in the EU, when the application is made.

Public summaries of PDCO evaluations of PIPs
They describe the applicant's proposal for the development of their medicine in children, the PDCO's conclusion on the potential use of the medicine in the paediatric population, the plan agreed between the committee and the applicant at the completion of the procedure (including any partial waivers or deferrals) and the next steps.

Referral procedures for safety reasons
A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or a class of medicines on behalf of the European Commission or a Member State.

Risk Management Plans (RMPs)
RMPs are regulatory documents submitted by medicine developers when they apply for marketing authorisation and include information on the medicine's safety profile; how its risks will be prevented or minimised in patients; plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine; risk factors for developing adverse reactions; measuring the effectiveness of risk-minimisation measures.

Scientific advice/protocol assistance
Through scientific advice, companies can ask the EMA for advice on whether they are conducting the appropriate tests and studies during the clinical development of a given product. In the case of orphan medicines for the treatment of rare diseases, it also includes advice on1) the demonstration of significant benefit for the designated orphan indication and on 2) similarity or clinical superiority over other medicines; which are criteria for the authorisation of an orphan medicine.

Significant benefit
Demonstrating a significant benefit, this is demonstrating a "clinically relevant advantage or a major contribution to patients" is one of the criteria that medicines for the treatment of rare diseases must fulfil to benefit from 10 years of market exclusivity once they have been authorised. For further information, read the *workshop report: Demonstrating significant benefit of orphan medicines*, held at the EMA in December 2015.

Safety signal
A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature, but their presence does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of a safety signal is required to establish whether or not there is a causal relationship between the medicine and the adverse event.

Similar active substance
It means an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of them) and which acts via the same mechanism.

Scientific Advisory Group (SAG)
SAGs have been established to provide an independent recommendation on scientific/technical matters related to products under evaluation through centralised regulatory procedures and referrals by the CHMP or any other scientific issue relevant to the work of the Committee.

Waiver
A waiver can be issued if there is evidence that the medicine concerned is likely to be ineffective or unsafe in the paediatric population, or that the disease or condition targeted occurs only in adult populations, or that the medicine, or the performance of trials, does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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