EURORDIS
THERAPEUTIC REPORT
February 2022
ISSUE 2
UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

New Rare Barometer survey out!

EURORDIS Rare Barometer survey on diagnosis is out, make your voice heard and *answer it now, here!*! This survey should take you around 20 minutes to complete and it is available in 26 different languages! Your invaluable input will help us understand and improve the diagnosis journey of those who live with a rare disease.

The aim of the survey is to understand the journey people living with a rare disease go through when seeking a diagnosis for their rare disease, for example by measuring the time taken to obtain a diagnosis, or the consequences of being undiagnosed or misdiagnosed. The survey is open to all people living with a rare disease and their family members.

For more information, please *read here!*

IN THIS ISSUE

EURORDIS stands in solidarity with Ukraine

EURORDIS-Rare Diseases Europe stands in solidarity with the Ukrainian people and would like to extend support to the Ukrainian rare disease community. There are an estimated 2 million people in Ukraine who live with rare diseases. Of them, children require the most support and effective treatment. As a community that is less mobile and often more dependent on regular care, the wartime destruction of vital infrastructure, such as hospitals and care centres, threatens the lives of this vulnerable population. EURORDIS is calling on the European Union, the United Nations, WHO Europe and other UN agencies, humanitarian organisations and the international community at large to protect the most vulnerable, who are caught in the conflict, unable to flee and without access to humanitarian aid.

The current situation should not undermine the reality that the needs of people living with a rare disease are real, huge, and unmet. EURORDIS will facilitate a coordinated effort with European Rare Disease Federations and will support patient organisations in Ukraine as best we can to understand the challenges they are facing and to help policy makers and the international community understand the challenges people living with a rare disease face on the ground.

For more information, please *read here the press release* and just published *article* titled '*Urgent support and aid needed for Ukrainian patients with Rare Diseases and their families*'.

Register now and ***submit your abstract!*** *Deadline 31st March!*

Rare Disease Day 2022

Last 28 February was *Rare Disease Day*! The campaign continues to grow each year since it was first launched in 2008. Thousands of events were organised over 100 countries and regions to mark the occasion raising awareness and generating change for the 300 million people worldwide living with a rare disease, their families and carers!
More than 650 buildings were illuminated as an action of great support for Rare Disease Day keeping the global chain of lights and awareness strong (more than 100 from 2021!), please see below some!
Check the social media success using the official hashtag *#RareDiseaseDay* and the *website!*

Another event organised by the NGO Committee for Rare Diseases with the support of the Swedish Government, and its co-founding organisations, Agrenska, Rare Diseases International and EURORDIS-Rare Diseases Europe, was *the 2022 Global Rare Disease Day event* in Dubai. This event was the first public opportunity to celebrate the adoption in December 2021 of the first-ever *United Nations Resolution on Addressing the Challenges of Persons Living with a Rare Disease and their Families*. It also explored ways to increase international collaboration and synergies to make rare diseases a policy priority at all levels.

Ministerial Conference on Innovation and Care Pathways: For a European policy on rare diseases

Last 28th of February in Paris took place at the Ministry of Solidarites and Health the *Ministerial Conference on Innovation and Care Pathways: For a European policy on rare diseases*. The aim of this high-level conference, in accord with the Presidency Trio, was to put forward recommendations to further develop European regulations concerning rare diseases.

The conference provided the occasion to define the EU roadmap for this matter and to collectively prepare to implement a European plan for rare diseases by 2030. The event marked a major milestone in *EURORDIS #30millionreasons campaign* and a first occasion for multi-stakeholder discussions – including the recorded or physical presence of representatives of 12 Member State Ministries of health - on the proposal for a European Action Plan on Rare Diseases. For more information check here the *recording and the programme.*

11th EURORDIS Black Pearl Awards

The *11th edition of the EURORDIS Black Pearl Awards* took place online last 8th February. The EURORDIS Black Pearl Awards is an annual awards ceremony to launch the month of Rare Disease Day. Since 2012, EURORDIS has organised this event to recognise the major achievements and outstanding commitment of patient advocates, patient organisations, policy makers, scientists, companies and media who strive to make a difference for the rare disease community. Please check here the *recording* and the programme *EURORDIS Black Pearl Awardees 2022.*
Congratulations to all the awardees!

Pharmacovigilance Risk Assessment Committee (PRAC) February 2022

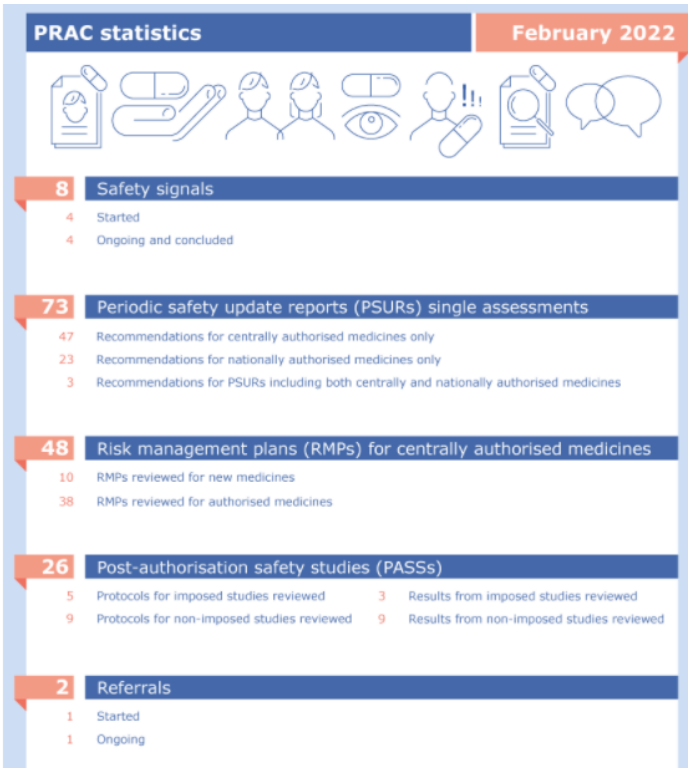
Minutes April 2021
Agenda February 2022
Meeting Highlights Feb 2022

Suspension of hydroxyethyl-starch solutions for infusion

EMA's safety committee (PRAC) has recommended that marketing authorisations for *hydroxyethyl-starch (HES)* solutions for infusion should be suspended across the European Union (EU). These products were authorised as an addition to other treatments for plasma volume replacements following acute (sudden) blood loss.

As a result of further reviews, the use of HES solutions for infusion was further restricted to accredited hospitals, and healthcare professionals prescribing or administering the medicines had to be trained in their appropriate use. Companies marketing HES solutions for infusion were also requested to conduct a drug utilisation study to check that the restrictions were adhered to in clinical practice, and to submit the results of this study to EMA.

The PRAC has now reviewed the results from this study, which show that HES solutions for infusion are still being used outside the recommendations included in the product information. In view of the serious risks that certain patient populations are still exposed to, **the PRAC has therefore recommended the suspension of the marketing authorisations for HES solutions for infusion in the EU.**



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

2527 Orphan designations

251 Orphan designations included in authorised indication

218 Authorised OMPs

89 To be used in children

6 Removed from the market

71 Marketed, but no longer "orphans"

To date

141

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

21 March 2022

CHMP Meeting Highlights February 2022

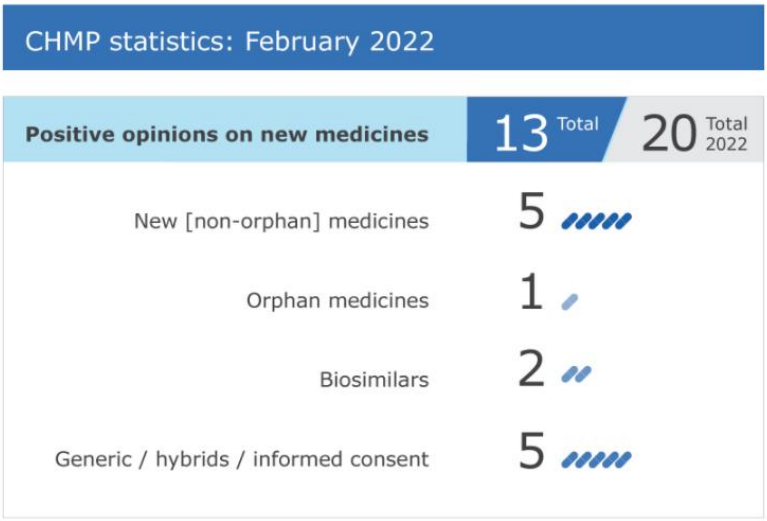
Minutes December 2021
Agenda February 2022
Meeting Highlights Feb 2022

In February, the CHMP recommended **13 medicines for approval, 1 orphan medicine**:

- *Kimmtrak** (tebentafusp) for the treatment of uveal melanoma, a type of eye cancer.
- *PreHevbri* (Hepatitis B vaccine (recombinant, adsorbed)) was granted a positive opinion for the active immunisation against hepatitis B virus infection.
- *Kapruvia* (difelikefalin) for the treatment of moderate-to-severe pruritus associated with chronic kidney disease.
- *Orgovyx* (relugolix) for the treatment of prostate cancer.
- *Quviviq* (daridorexant) for the treatment of insomnia.
- *Vydura* (rimegepant) for the prophylaxis and acute treatment of migraine.

The CHMP also recommended **9 extensions of therapeutic indication,** and recommended granting marketing authorisations for **2 biosimilars and 5 generic medicines**.

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.

Minutes December 2021
Agenda February 2022
Meeting February 2022

COMP February 2022 meeting update

During the February 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.*

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

- Sickle cell disease, Pharma Gateway AB;
- Collagen VI-related myopathies, Fondazione Telethon;
- Mucopolysaccharidosis type II (Hunter syndrome), Diamond Pharma Services Ireland Limited;
- Phenylalanine hydroxylase deficiency, Diamond Pharma Services Ireland Limited;
- Fragile X syndrome, Purposeful I.K.E.;
- Erythropoietic protoporphyria, Mitsubishi Tanabe Pharma GmbH;
- Tenosynovial giant-cell tumour, local and diffuse type, Synox Therapeutics Limited;
- Argininosuccinic aciduria, Unicyte S.R.L;
- Spinal cord injury, Ros Lynch;
- Narcolepsy, Laboratoires Delbert;
- Idiopathic pulmonary fibrosis, Unither Therapeutik GmbH.

Re-assessment of orphan designation at time of marketing authorisation

When a designated orphan medicinal product receives a positive opinion for marketing authorisation from EMA's Committee for Medicinal Products for Human Use (CHMP), the COMP has the responsibility to review whether or not the medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation.

The COMP adopted **2 positive opinions at time of CHMP opinion**:

- *Ayvakyt* (avapritinib) for treatment of mastocytosis, Blueprint Medicines (Netherlands) B.V.
- *Kimmtrak* (tebentafusp) for treatment of uveal melanoma, Immunocore Ireland Limited.

Summaries of positive opinions on orphan designations are available on the *EMA website*.

Medicinal Product	Marketing Authorisation Holder	Therapeutic Indication	Date of Marketing Authorisation
Tavneos ® (avacopan)	Vifor Fresenius Medical Care Renal Pharma France	Adult patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)	11/01/2022
Voraxaze ® (glucarpidase)	SERB SAS	Adults and children (aged 28 days and older) with delayed methotrexate elimination or at risk of methotrexate toxicity	11/01/2022
Lonapegsomatropin Ascendis Pharma® (lonapegsomatropin)	Ascendis Pharma Endocrinology Division A/S	Children who do not produce enough growth hormone (GHD)	11/01/2022
Oxbryta® (voxelotor)	Global Blood Therapeutics Netherlands B. V.	Haemolytic anaemia, and +12 years old sickle cell disease	14/02/2022
Ngenla® (somatrogon)	Pfizer Europe MA EEIG	Children and adolescents with growth hormone deficiency	14/02/2022

Please click also on the following links to see:

Orphan medicinal products authorised during 2022

Orphan medicinal products authorised since 2000

PDCO November to February meetings to be updated when info available

Minutes June 2021
Agenda October 2021
Meeting Report October 2021

PDCO October 2021 meeting update

In October, the PDCO adopted **9 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.

- Peptide derivative of glucagon-like-peptide 1 and glucagon with fatty acid side chain (BI 456906), from Boehringer Ingelheim International GmbH, for the treatment of nonalcoholic steatohepatitis;
- Marzeptacog alfa (activated), from Catalyst Biosciences, Inc., for the treatment of haemophilia A and haemophilia B;
- Satralizumab, from Roche Registration GmbH, for the treatment of myasthenia gravis;
- Ravulizumab, from Alexion Europe SAS, for the treatment of neuromyelitis optica spectrum disorders;
- Magrolimab, from Gilead Sciences International Ltd, for the treatment of acute myeloid leukaemia and treatment of myelodysplastic syndromes (including juvenile myelomonocytic leukaemia);
- Lutetium (177Lu) oxodotreotide, from Advanced Accelerator Applications, for the treatment of gastroenteropancreatic neuroendocrine tumours;
- 2'-O-(2-methoxyethyl) phosphorothioate antisense oligonucleotide targeting CD49d RNA (ATL1102), from Antisense Therapeutics Limited, for the treatment of Duchenne muscular dystrophy;
- Evenamide, from Newron Pharmaceuticals SpA, for the treatment of schizophrenia;
- Neisseria meningitidis serogroup B Protein-based active substance / Recombinant Neisseria meningitidis serogroup B protein 1 / Recombinant Neisseria meningitidis serogroup B protein 3 / Recombinant Neisseria meningitidis serogroup B protein 2, from Sanofi Pasteur, for the prevention of meningococcal disease.

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*.

Minutes October 2021
Agenda December 2021
Meeting Report December 2021

CAT January&February meeting to be updated when info available

CAT December 2021 meeting update

In December the Committee for Advanced Therapies (CAT) finalised **4 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 **fulfil the definition of a gene therapy medicinal product:**

- CD 19 CAR T-cells transduced with lentiviral vector, intended for the treatment of adults and children with B-cell non-Hodgkin's lymphoma and acute lymphoblastic leukaemia;
- Recombinant adeno-associated virus, serotype 2, containing human ND4 codon-optimised gene, intended for the treatment of Leber's hereditary optic neuropathy.

The following products fulfil the definition of a somatic cell therapy medicinal product:

- Allogeneic adipose-derived mesenchymal stromal cells, ex-vivo expanded, intended for the treatment of osteoarthritis of the knee;
- Allogeneic T-cell precursors, mobilised peripheral blood-derived, ex vivo cultured, intended for the treatment of paediatric and adult patients undergoing partially human leucocyte antigen (HLA) compatible allogeneic haematopoietic stem cell transplantation to accelerate adaptive immunological reconstitution.

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.*

First EMA PCWP & HCPWP meeting with all eligible organisations of 2002!

Last 2nd and 3th of March took place *the first annual meeting of 2022* 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 first day of the meeting provided an update on EMA projects and initiatives, including:

- *accelerating clinical trials in the EU (ACT EU)*,
- *big data*;
- *electronic product information (ePI)*;
- *the Agency's extended mandate.*

The second day of the meeting enabled discussion on *advanced therapy medicinal products (ATMPs)* and sharing members' voices. The meeting closed with looking ahead to 2022 to 2025.

For more information, please see the *agenda, the presentations and the recordings 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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GLOSSARY

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.

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