EURORDIS
THERAPEUTIC REPORT

June 2021

ISSUE 6

UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

EMA's 2020 Annual Report is out!

The European Medicine Agency (EMA) has just published the *2020 annual report*, which highlights the Agency's most significant achievements in 2020. It also contains reflections by EMA staff and its partners and stakeholders on topics of major interest in medicine and health and key figures, including core statistics that highlight the main outcomes of the Agency's activities and interesting trends and changes observed in recent years, such as patient involvement at the EMA.

For more information have a look at the *report here!*

IN THIS ISSUE

#30millionreasons for European Action

There are *30 million people living with a rare disease in Europe*. Yet no country can tackle the challenges of rare diseases alone. Their future depends on policy makers taking European action now. Every person living with a rare disease is a reason for Europe to take action on rare diseases that leaves no one behind by 2030.

Your voice counts! Help us make sure policy makers make the right decision for our future! There are *3 things* you can do to help ensure action is taken at European level:

- Tell Urusla von der Leyen, the President of the European Commission, YOUR reason why Europe needs to take action for a better future for people living with a rare disease by 2030.
- Share #30millionreasons on social media and in your newsletters.
- Ask your MEP to join the Parliamentary Network of Advocates on rare diseases.

Taking these actions will help build the support for European action on rare diseases across Europe. We need to show that, although each disease is rare, we have #30millionreasons for Europe to take action.

For more information, please *share your reason here*!

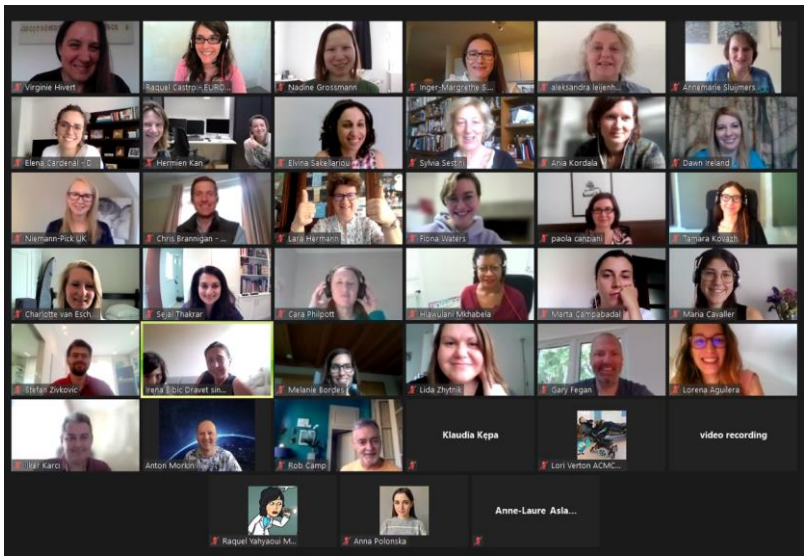
EURORDIS Open Academy

The objective of the *EURORDIS Open Academy* is to build the capacity of rare disease patient advocates at large, as well as a select number of researchers and clinicians, so that they can go on to advocate for rare diseases at both local or international levels. By providing training, EURORDIS empowers patients and ensures they have the confidence and knowledge needed to bring their expertise to discussions on health care, research and medicines development with policy makers, industry and scientists.

The *EURORDIS Open Academy* encompasses the *EURORDIS Summer School*, *EURORDIS Winter School*, *EURORDIS Digital School* and *EURORDIS Leadership School.*

EURORDIS Summer School

Since its launch in 2008, the *EURORDIS Summer School on Medicines Research & Development* has taken place every year in Barcelona. Exceptionally these past years took place online due to COVID-19. This year from 21-25 June! *EURORDIS Summer School* is now integrated within the *EURORDIS Open Academy*, and it is a programme targeted to patient advocates and researchers to be trained in different aspects of medicines development, from clinical trial methodology and EU regulatory process to the process of health technology assessment.
Remember that you have the option to **take part in the free online training!** Online modules are available for anyone to use! For more information, please see *EURORDIS Open Academy website*.



Congratulations to all the participants!

EURORDIS Winter School

The *EURORDIS Winter School on Scientific Innovation and Translational Research* aims of deepening patient representatives' understanding of how pre-clinical research translates into real benefits for rare disease patients. It equips participants with knowledge and skills, so they are empowered to effectively participate in discussions with the researchers, policymakers, and companies responsible for research or research infrastructures.
The applications for the next edition of the Winter School will be launched soon. Stay tuned!
You can also learn more about rare disease research at a time and place that suits you by taking the free online modules which includes a lesson and quiz! For more information, please visit EURORDIS website.

Pharmacovigilance Risk Assessment Committee (PRAC) June 2021

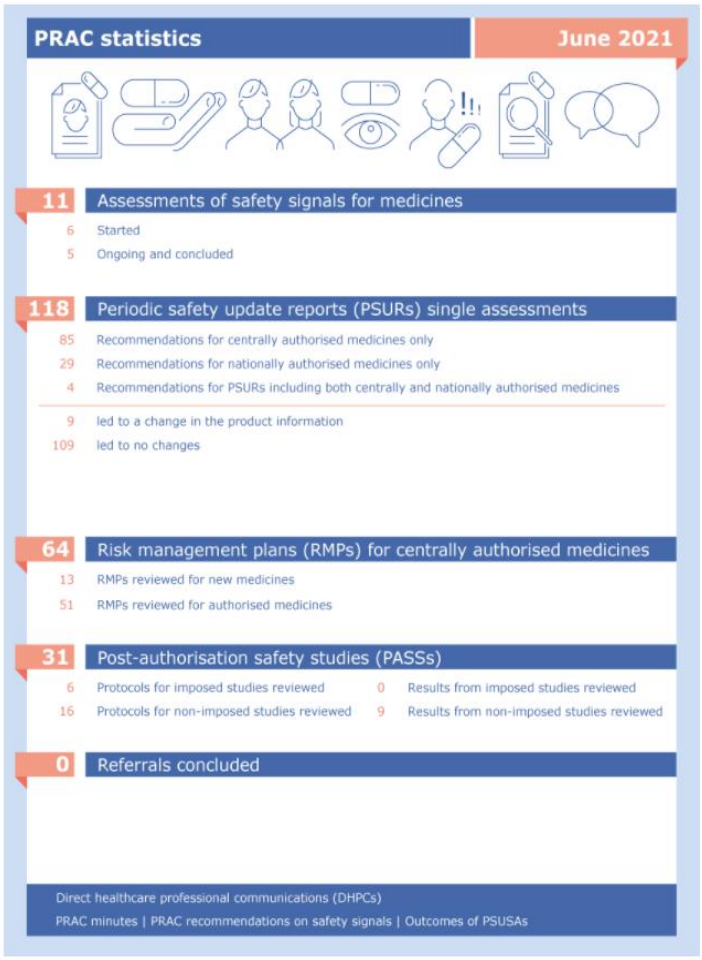
Minutes November 2020
Agenda June 2021
Meeting Highlights June 2021

PRAC concludes review of signal of increased risk of major cardiovascular events and cancer with Xeljanz

The PRAC has recommended an update to the product information for Xeljanz to include a new recommendation for its use. Xeljanz is used to treat adults with moderate to severe rheumatoid arthritis (inflammation of the joints), psoriatic arthritis (red, scaly patches on the skin with inflammation of the joints) and ulcerative colitis (inflammation and ulcers of the colon and rectum).

The Committee has concluded its review of a safety signal regarding major adverse cardiovascular events and cancer (excluding non-melanoma skin cancer). The PRAC is reminding healthcare professionals to carefully evaluate a patient's individual benefit-risk profile when deciding to prescribe or continue the treatment with Xeljanz. It also advises healthcare professionals that Xeljanz should only be used in patients over 65 years of age, patients who are current or past smokers, patients with other cardiovascular risk factors, and patients with other malignancy risk factors, if no suitable treatment alternative is available.

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

2428 Orphan designations

236 Orphan designations included in authorised indication

203 Authorised OMPs

79 To be used in children

5 Removed from the market

68 Marketed, but no longer "orphans"

To date

130

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

8 July 2021

CHMP Meeting Highlights June 2021

Minutes May 2021
Agenda June 2021
Meeting Highlights June 2021

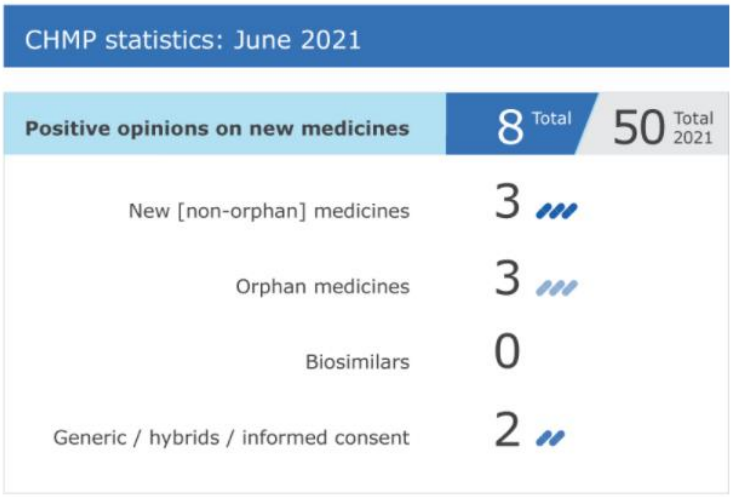
In June, the CHMP recommended **8 medicines for approval, 3 orphan medicines**:

- *Conditional marketing authorisation* for *Abecma* (idecabtagene vicleucel) a gene therapy for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three previous therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody.
- *Voxzogo* (vosoritide) for the treatment of achondroplasia in patients two years of age and above whose epiphyses are not closed
- *Minjuvi* (tafasitamab) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT).
- *Bimzelx* (bimekizumab) for the treatment of moderate to severe plaque psoriasis.
- *Byooviz* (ranibizumab) for the treatment of neovascular (wet) age-related macular degeneration, visual impairment due to diabetic macular oedema, proliferative diabetic retinopathy, visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO), and visual impairment due to choroidal neovascularisation.
- *Evrenzo* (roxadustat) for the treatment of anaemia symptoms in patients with chronic kidney disease.

The CHMP recommended granting marketing authorisations for two generic medicines.

The CHMP also recommended **6 extensions of therapeutic indication.**

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 April 2021
Agenda June 2021
Meeting Report June 2021

COMP June 2021 meeting update

During the June plenary, the COMP adopted **22 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:

- Growth hormone deficiency, Parexel International (Irl) Limited;
- Medulloblastoma, Y-Mabs Therapeutics A/S;
- Non-traumatic spontaneous intracerebral haemorrhage, Worphmed S.r.l.;
- Amyotrophic lateral sclerosis, Prilenia Therapeutics B.V.;
- Primary biliary cholangitis, Zydus France;
- Perivascular epithelioid tumours, YES Pharmaceutical Development Services GmbH;
- Follicular lymphoma, Novartis Europharm Limited;
- Pantothenate kinase-associated neurodegeneration, Premier Research Group S.L.;
- Propionic acidaemia, Premier Research Group S.L.;
- Allan-Herndon-Dudley syndrome, Raremoon Consulting Esp S.L.;
- SLC13A5-epileptic encephalopathy deficiencies, Raremoon Consulting Esp S.L.;
- Otoferlin gene-mediated hearing loss, Boyd Consultants Limited;
- Frontotemporal dementia, Pharma Gateway AB;
- Neuronal ceroid lipofuscinosis, University of Padua;
- Multiple myeloma, Pfizer Europe MA EEIG;
- Achondroplasia, YES Pharmaceutical Development Services GmbH;
- Graft-versus-host disease, Biocon Pharma Ireland Limited;
- Glycogen storage disease type III, Ultragenyx Germany GmbH;
- Adenosine triphosphate binding cassette transporter protein subfamily C member 6 deficiency, Inozyme Pharma Ireland Limited;
- Familial chylomicronaemia syndrome, Pharma Gateway AB;
- Chronic myeloid leukaemia, Sun Pharmaceutical Industries Europe B.V.;
- Biliary tract cancer, Voisin Consulting.

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 **5 positive opinions at time of CHMP opinion**:

- Bylvay (*odevixibat*) for treatment of progressive familial intrahepatic cholestasis.
- Darzalex (*daratumumab*) for treatment of AL amyloidosis, Janssen-Cilag International NV.
- IMCIVREE (*setmelanotide*) for treatment of leptin receptor deficiency, TMC Pharma (EU) Limited
- IMCIVREE (*setmelanotide*) for treatment of pro-opiomelanocortin deficiency, TMC Pharma (EU) Limited.
- Skysona (*elivaldogene autotemcel*) for treatment of adrenoleukodystrophy, bluebird bio (Netherlands) B.V.

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

Medicinal Product	Marketing Authorisation Holder	Therapeutic Indication	Date of Marketing Authorisation
Elzonris® (tagraxofusp)	Stemline Therapeutics B.V.	Adults with blastic plasmacytoid dendritic cell neoplasm (BPDCN)	07/01/2021
Inrebic® (fedratinib)	Celgene Europe BV	Adults with myelofibrosis (a rare form of blood cancer)	08/02/2021
Lumoxiti® (moxetumomab pasudotox)	AstraZeneca AB	Adults with hairy cell leukaemia, a cancer of the white blood cells	08/02/2021
Evrysdi® (risdiplam)	Roche Registration GmbH	5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies	26/03/2021
Pemazyre® (pemigatinib)	Incyte Biosciences Distribution B.V.	Adults with cholangiocarcinoma	26/03/2021
Sogroya® (somapacitan)	Novo Nordisk A/S	Growth hormone deficiency	31/03/2021
Enspryng® (satralizumab)	Roche Registration GmbH	Neuromyelitis Optica Spectrum disorders (NMOSD)	24/06/2021

Please click also on the following links to see:

Orphan medicinal products authorised during 2021

Orphan medicinal products authorised since 2000

PDCO June meeting to be updated next issue

Minutes April 2021
Agenda April 2021
Meeting Report April 2021

PDCO April 2021 meeting update

In April, the PDCO adopted **11 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.

- 3,4-Dimethoxy-N-methylbenzohydroxamic acid / Deferoxamine mesylate / Alpha-ketoglutaric acid /Arginine / Alanine / Glycine / Aspartic acid / Tryptophan / N-acetyl-histidine (monohydrate) /Histidine / Calcium chloride (dihydrate) / Magnesium chloride (hexahydrate) / Potassium chloride /Sodium chloride, from Dr. Franz Köhler Chemie GmbH, for cardioplegia;
- Sotatercept, from Acceleron Pharma, for the treatment of pulmonary arterial hypertension;
- Human plasma derived c1-inhibitor, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of hereditary angioedema;
- Iscalimab, from Novartis Europharm Limited, for the prophylaxis of solid organ transplant rejection;
- Ravulizumab, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Erdafitinib, from Janssen-Cilag International N.V., for the treatment of all conditions included in the category of malignant neoplasms (except urothelial carcinoma, haematopoietic and lymphoid tissue neoplasms);
- Talazoparib, from Pfizer Europe MA EEIG, for the treatment of Ewing sarcoma;
- Atropine sulfate, from Nevakar Inc., for the treatment of myopia;
- Bamlanivimab, from Eli Lilly and Company Limited, for the treatment of Coronavirus disease 2019 (COVID-19);
- Etesevimab, from Eli Lilly and Company Limited, for the treatment of Coronavirus disease 2019 (COVID-19);
- Zorecimeran, from CureVac AG; for the prevention of Coronavirus disease 2019 (COVID-19).

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 further information on the work of the PDCO for this 2021, please see the *work plan.*

For a comprehensive list of opinions and decisions on PIPs, please check the *EMA website.*

PDCO June meeting to be updated next issue

Minutes April 2021
Agenda May 2021
Meeting Report May 2021

PDCO May 2021 meeting update

In May, the PDCO adopted **12 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.

- Macitentan, from Janssen-Cilag International N.V., for the treatment of functional single ventricle heart disease with total cavo-pulmonary connection;
- Finerenone, from Bayer AG, for the treatment of heart failure;
- Ralinepag, from United Therapeutics Corporation, for the treatment of pulmonary arterial hypertension;
- Allogeneic skin-derived ABCB5-positive mesenchymal stem cells, from RHEACELL GmbH & Co. KG, for the treatment of epidermolysis bullosa;
- Adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401), from Ultragenyx Germany GmbH, for the treatment of glycogen storage disease type Ia;
- Maralixibat Chloride, from Mirum Pharmaceuticals Inc., for the treatment of biliary atresia;
- Odevixibat, from Albireo AB, for the treatment of Alagille syndrome;
- Recombinant monoclonal antibody to sialic acid-binding Ig-like lectin 8, from Allakos Inc, for the treatment of eosinophilic gastrointestinal inflammatory disorders;
- Cilgavimab (AZD1061), from AstraZeneca AB, for the prevention or treatment of COVID-19;
- Tixagevimab (AZD8895), from AstraZeneca AB for the prevention or treatment of COVID-19;
- Pralsetinib, from Roche Registration GmbH, for the treatment of thyroid neoplasms;
- Autologous selected renal cells, from ProKidney, for the treatment of chronic kidney 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 further information on the work of the PDCO for this 2021, please see the *work plan.*

For a comprehensive list of opinions and decisions on PIPs, please check the *EMA website*.

CAT June meeting to be updated next issue

Minutes April 2021
Agenda May 2021
Meeting Report May 2021

CAT May 2021 meeting update

In May the Committee for Advanced Therapies (CAT) finalised **6 scientific recommendations on the classification of advanced therapy medicinal products** (ATMPs) depicted below.

The outcome of these assessments can be found here: *Summaries of scientific recommendations on classification of ATMPs*.

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

- Oncolytic adenovirus, intended for the treatment of histologically and radiologically confirmed progressive neuroendocrine neoplasm (NEN) of gastrointestinal, pancreatic or bronchial origin with multiple liver metastases;
- DNA plasmid encoding several neoepitopes from the tumour of a patient, a live wild-type modified vaccinia strain Ankara and a monoclonal antibody against Cytotoxic T-lymphocyte associated protein 4, intended for the treatment of cancer;
- Recombinant adeno-associated virus encoding for the human α-sarcoglycan-protein, intended for the treatment of patients with a confirmed diagnosis of Limb-Girdle muscular dystrophy Type 2D/R3.

The following product was classified as a somatic cell therapy medicinal product:

- Autologous antigen presenting cells loaded with SARS-CoV-2 antigen, intended to be used as vaccines against SARS-CoV-2.

The following product was classified as a tissue-engineered product:

- Autologous cultured chondrocytes, intended for the repair of cartilage defects.

The following product was classified as a tissue engineered product and a combined ATMP:

- Autologous mesenchymal stem cells combined with a matrix pre-loaded with BMP2, intended to treat femoral osteochondral lesion (grade III to IV).

CAT noted the publication of the *Questions and Answers on the principles of GMP* for the manufacturing of starting materials of biological origin used to transfer genetic material for the manufacturing of ATMPs.

For further information on the work of the CAT for this 2021, please see the *work plan.*

For more information, see also the *EMA meeting report.*

PATIENTS' AND CONSUMERS' WORKING PARTY

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

For more information, see also the *PCWP mandate, objectives and rules of procedure.*

PCWP and HCPWP June meeting

Last 1st and 2nd June took place a *2 days virtual meeting* 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).

During the first day, the Agency together with the European Commission (EC) presented on the future extension of EMA's mandate. The meeting also focused on communication and stakeholder engagement and on COVID-19 vaccines, therapeutics and safety surveillance.

On the second day, the discussion focused on stakeholders' involvement in Scientific Advisory Groups (SAGs), and an update on the regulatory science research agenda and on Big Data. The final part of the meeting is dedicated to an update on the electronic Product Information (ePI).

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

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

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GLOSSARY

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.

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.

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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.

Co-funded by the Health Programme of the European Union

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