

GENERAL NEWS

EPTRI Paediatric Administration Devices survey

The *European Paediatric Formulation Initiative (EuPFI)*, founded in 2007, is a group of members from the pharmaceutical industry, universities and hospitals, working together in a non-profit way to promote the preparation of better and safe medicines for children.

EuPFI in collaboration with EPTRI, developed *a Paediatric Administration Device survey* to improve the existing knowledge about the medical devices used by children and to help to find ways of making them more user-friendly and effective. This survey is **addressed to boys and girls between 10 to 18 years of age and their parents** and it is available in *7 different languages*. It takes approximately **10-15 minutes** to be completed and will be open until the **end of April!**

Share your experience with using medical devices and contribute to the creation of more efficient and tailored devices for children!

PARADIGM publication on metrics is out!

PARADIGM work on metrics has led to the publication of an article entitled: "*Evaluation of patient engagement in medicine development: a multi-stakeholder framework with metrics*" in the journal *Health Expectations*. This work has been led by VU-Athena Institute in the Netherlands, with participation of other consortium partners including EURORDIS and our colleague, Elisa Ferrer.

The framework published will allow participants to select what metrics they value and assess to what extent patient engagement has contributed. A framework tool was also developed and can be found here, *PARADIGM Toolbox*.

For more information, please read the *article!*

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Results of the Rare Barometer H-Care survey

The results of the *H-Care survey on patients' and carers' experience of medical care* for their rare diseases are now available in *23 languages*. The report includes: key results of the survey; three recommendations to improve the healthcare experience for all people living with a rare disease; and the methodology of the H-CARE Survey.

Also the results of the survey regarding the *development of a validated scale and of a Common Feedback Mechanism* to measure healthcare experience for rare diseases in Europe are out!

For more information, please read the *results here!*



COVID-19 vaccines in children

EURORDIS asked the EMA about vaccines in children, and in particular, children with rare diseases. Please see below EMA's answer:

EURORDIS Question: *The paediatric Investigation Plans for vaccines for COVID-19 are due in 2024. Children living with a rare disease are vulnerable populations as probably at higher risk of severe COVID-19. They might not want to wait until 2024. Which clinical development is planned? Are clinical efficacy and safety data needed (long development), or would immunogenicity data followed by for example an open label safety study suffices?*

EMA Answer: PIPs are due for 2024, but this is for the youngest part of the paediatric population, children of less than 2 years. For children first from 12 to 18, and then younger ones, immunogenicity data are requested and no large scale long duration clinical trial are requested. Immunogenicity studies are already in progress. This population could benefit from a vaccine before the end of 2021. It could take more time for the youngest ones, but for the very young (newborn and less than 2), it is unsure a vaccine is needed. The authorisation to use some of the adult vaccines in children is expected for the end of 2021.

For more information, please contact francois.houyez@eurordis.org and check the [EURORDIS COVID-19 Information Resource Centre](#).

EMA creates a pool of people who have had experienced COVID-19

The EMA Public and Stakeholders Engagement department created a pool of people who have had **personal and confirmed experience with COVID-19**. They would like to consult with them on COVID related materials and potential involvement in activities. EMA is contributing to global efforts during the COVID-19 pandemic by expediting the development and approval of safe and effective treatments and vaccines, supporting the continued availability of medicines, and providing reliable information to patients and healthcare professionals.

If you have had a personal and confirmed experience with COVID-19, and would like to join this pool, please contact maria.mavris@ema.europa.eu

New publication highlights how COVID-19 pandemic is affecting the rare disease community and our recommendations on integrated care

With the pandemic, the need for integrated care is more pressing than ever. The latest editorial of the International Journal for Integrated Care addresses how the pandemic is exacerbating the care coordination challenges faced by the rare disease community, based on the recent [EURORDIS Rare Barometer surveys](#). The article entitled: *'Learning from the Pandemic to Improve Care for Vulnerable Communities: The Perspectives and Recommendations from the Rare Disease Community'* also includes the key actions that the rare disease community recommends for integrated care to become a reality within this decade, extracted from the [EURORDIS position paper on Holistic Person-Centred Care](#).

For more information, please read the [article](#)!

Pharmacovigilance Risk Assessment Committee (PRAC) February 2021

Minutes November 2020
Agenda February 2021
Meeting Highlights Feb 2021

New safety information for Strimvelis and Zolgensma

As part of its advice on safety-related aspects to other EMA Committees, the PRAC discussed direct healthcare professional communications (DHPCs) containing important safety information for the following products:

- For *Strimvelis*, the DHPC warns doctors of the risk that the use of the gene therapy Strimvelis could lead to genetic mutations with the potential to cause cancer in patients who receive this medicine. Strimvelis is a medicine to treat severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID). This recommendation is based on a careful analysis of a single case of acute leukaemia (lymphoid T cell leukaemia) reported in a patient who was treated with Strimvelis almost 5 years prior to the cancer diagnosis. Doctors are advised to monitor patients long-term for cancerous changes with at least annual visits for the first eleven years and then at 13- and 15-years post treatment with Strimvelis.
- For *Zolgensma*, the DHPC warns doctors of the risk of thrombotic microangiopathy (an acute and lifethreatening condition characterised by thrombocytopenia, haemolytic anaemia and acute kidney injury) following administration of Zolgensma (onasemnogene abeparvovec), a gene therapy for patients with spinal muscular atrophy. The DHPC enhances awareness of this risk and advises on the need for prompt clinical management.

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



2394
Orphan
designations



232
Orphan designations
included in authorised
indication



199
Authorised
OMPs



77
To be used in
children



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

To date

128

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

16 March 2021

CHMP Meeting Highlights February 2021

Minutes January 2021
Agenda February 2021
Meeting Highlights Feb 2021

In February, the CHMP recommended **6 medicines for approval, 2 orphan medicines**:

- **Evrysdi** (risdiplam), the first treatment that can be given orally to patients with certain types of spinal muscular atrophy, a rare and often fatal genetic disease that causes muscle weakness and progressive loss of movement.
- **Orladeyo** (berotralstat) received a positive opinion for the prevention of recurrent attacks of hereditary angioedema (rapid swelling under the skin).
- *Conditional marketing authorisation* for **Jemperli** (dostarlimab) for the treatment of certain types of recurrent or advanced endometrial cancer.
- **Two biosimilar medicines**, **Abevmy** (bevacizumab) and **Lextemy** (bevacizumab), received a positive opinion for the treatment of carcinoma of the colon or rectum, breast cancer, non-small cell lung cancer, renal cell cancer, epithelial ovarian, fallopian tube or primary peritoneal cancer, and carcinoma of the cervix.
- **One generic medicine** **Abiraterone Accord** (abiraterone) received a positive opinion for the treatment of metastatic prostate cancer.

The CHMP also recommended five extensions of therapeutic indication.

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

New pilot project for early contact with patients

The CHMP started a new pilot project to enhance engagement with patients at the start of review of all marketing authorisation applications for **orphan medicines**. This one-year pilot will enable patients to share their views on aspects such as quality of life, treatment options and unmet medical needs with the CHMP so they can be aware of all aspects from the beginning. For further details on this project, read the full [project overview document](#).

CHMP statistics: February 2021		
Positive opinions on new medicines	6 Total	20 Total 2021
New [non-orphan] medicines	1	
Orphan medicines	2	
Biosimilars	2	
Generic / hybrids / informed consent	1	



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 February 2021 meeting update

During the February plenary, the COMP adopted **10 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:

- Krabbe disease, Pharma Gateway AB;
- Gastrointestinal stromal tumours, Immunicum AB;
- Dravet syndrome, Premier Research Group S.L.;
- ATTR amyloidosis, Voisin Consulting S.A.R.L.;
- Glioma, Rapport Global Strategic Services Ireland Limited;
- PIK3CA-related overgrowth spectrum, Novartis Europharm Limited;
- Mucopolysaccharidosis type I, Artemida Pharma Europe Limited;
- Cystic fibrosis, IDEA Innovative Drug European Associates (Ireland) Limited;
- Small cell lung cancer, Molecular Biology And Integral Biomathics;
- Friedreich's ataxia, Ptc Therapeutics International Limited

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**:

- [Pemazyre](#) (pemigatinib) for treatment of biliary tract cancer, Incyte Biosciences Distribution B.V.
- [Sogroya](#) (somapacitan) for treatment of growth hormone deficiency, Novo Nordisk A/S.

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

For further information on the work of the COMP for this 2021, please see the [work plan](#).

Orphan medicines in 2021

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

Please click also on the following links to see:

[Orphan medicinal products authorised during 2021](#)

[Orphan medicinal products authorised since 2000](#)

PDCO February meeting to be updated next issue

PDCO January 2021 meeting update

Minutes December 2020
Agenda January 2021
Meeting Report January 2021

In January, the PDCO adopted **16 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.

- COVID-19 vaccine (Ad26.COV2-S (recombinant)), from Janssen-Cilag International NV, for the prevention of coronavirus disease 2019 (COVID-19);
- Baricitinib, from Eli Lilly and Company Limited, for the treatment of coronavirus disease 2019 (COVID-2019);
- Secukinumab, from Novartis Europharm Limited, for the treatment of systemic lupus erythematosus;
- Imetelstat, EMEA-001910-PIP03-20, from Geron Corporation, for the treatment of acute myeloid leukemia and treatment of myelodysplastic syndromes, including juvenile myelomonocytic leukemia;
- Seltorexant, Janssen-Cilag International NV, for the treatment of major depressive disorder;
- Tacrolimus, from Proveca Pharma Limited, for the prevention of solid organ transplant rejection and treatment of solid organ transplant rejection;
- Rozibafusp alfa, from Amgen Europe B.V., for the treatment of systemic lupus erythematosus;
- Rimegepant, from Biohaven Pharmaceuticals, Inc., for the treatment of migraine headaches;
- Telitacicept, from RemeGen, Ltd., for the treatment of systemic lupus erythematosus;
- Linear single strand of deoxyribonucleic acid (encoding human retinitis pigmentosa GTPase regulator [RPGR]) packaged in a recombinant adeno-associated virus protein capsid of serotype 5 (AAV5-hRKp.RPGR), from MeiraGTx UK II Ltd, for the treatment of retinitis pigmentosa;
- Bimekizumab, from UCB Biopharma SRL, for the treatment of hidradenitis suppurativa;
- Crovalimab, from Roche Registration GmbH, for the treatment of atypical haemolytic uremic syndrome and treatment of paroxysmal nocturnal haemoglobinuria;
- Delgocitinib, from LEO Pharma A/S, for the treatment of dermatitis and eczema;
- Respiratory Syncytial Virus (RSV) PreF3 recombinant Fusion protein, from GlaxoSmithKline Biologicals SA, for the prevention of RSV-associated lower respiratory tract illness through maternal immunisation;
- Crinecerfont, from Neurocrine Therapeutics Ltd, for the treatment of congenital adrenal hyperplasia;
- (S)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran 3-yl) pyrimidine-5-carboxamide (PF-06865571), from Pfizer Europe MA EEIG, for the treatment of non-alcoholic steatohepatitis (NASH).

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 February 2021 meeting update

Minutes November 2020
Agenda February 2021
Meeting Report February 2021

In February 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 products were classified as **tissue engineered products**:

- Autologous bone marrow aspirate concentrate, intended for bone repair in a variety of bony defects such as fractures, arthroplasty, bone cysts, osteonecrosis or avascular necrosis;
- *In vitro* expanded autologous human articular chondrocytes, intended for the repair of symptomatic, localised, full-thickness cartilage defects of the knee joint in patients with closed epiphyseal growth plates.

CAT noted the **withdrawal** of the marketing authorisation application of autologous human chondrocytes, *in vitro* expanded, which was intended for the repair of cartilage defects of the knee joint.

New safety information for Strimvelis and Zolgensma and a referral procedure for Zynteglo.

The CAT adopted the recommendation from the Pharmacovigilance Risk Management Committee (PRAC) and the direct healthcare professional communications (DHPCs) containing important safety information for Strimvelis and Zolgensma. For more information, please read PRAC section (page 9).

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 March meeting

Last 2nd and 3rd March 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). The meeting was introduced by EMA's new Executive Director, Emer Cooke.

The meeting focused on the following:

- Update on COVID-19 vaccines and therapeutics
- European Reference Network model in the European Data Space
- Advanced Therapy Medicinal Products (ATMPs)
- Personalised medicine approaches for the next generation of medicines
- Big Data
- ICH Guidances on Good Clinical Practice (E6/E8)
- Overview of the 2020 Satisfaction Survey results on interactions with EMA

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

EMA third public stakeholder meeting on COVID-19 vaccines

Next 26th March the EMA will organise a third virtual [meeting](#) to provide an update to EU citizens about the continued assessment, approval and safety monitoring of COVID-19 vaccines, as well as their expected impact at community level. The event will also allow the public and stakeholders to further inform EMA of their needs, expectations and any concerns.

The [event](#) will be broadcasted live, please see the [agenda](#).

EURORDIS and the European Patients Forum (EPF) signed a jointly letter asking the EMA to organise a multi-stakeholder meetings open to the public on vaccines to prevent SARS-CoV-2 infection, please read the [letter 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/measures contained in the PIP is one of several prerequisites for obtaining the rewards and incentives provided for in Articles 36 to 38 of the Paediatric Regulation.

Conditional marketing authorisation

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

Designation, orphan medicinal product

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

European Public Assessment Report (EPAR)

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

Hybrid application for marketing authorisation

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

Informed consent application for marketing authorisation

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

Orphan Legislation

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



Paediatric Investigation Plan (PIP)

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

Paediatric Use Marketing Authorisation (PUMA)

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

Patient-reported outcomes (PROs)

Measurements based on data provided directly by patients regarding their health condition without interpretation of the patient's response by a clinician or anyone else.

Patient-reported outcome measures (PROMs)

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

Periodic Safety Update Reports (PSURs)

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

Post-authorisation efficacy studies (PAES)

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

Post-authorisation safety studies (PASS)

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

Prevalence

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

Public summaries of PDCO evaluations of PIPs

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

Referral procedures for safety reasons

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

Risk Management Plans (RMPs)

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

Scientific advice/protocol assistance

Through scientific advice, companies can ask the EMA for advice on whether they are conducting the appropriate tests and studies during the clinical development of a given product. In the case of orphan medicines for the treatment of rare diseases, it also includes advice on 1) the demonstration of significant benefit for the designated orphan indication and on 2) similarity or clinical superiority over other medicines; which are criteria for the authorisation of an orphan medicine.



Significant benefit

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

Safety signal

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

Similar active substance

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

Scientific Advisory Group (SAG)

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

Waiver

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

