

## GENERAL NEWS

### New c4c train the trainers workshop for patients!

*Conect4children (c4c) is hosting an online 'train the trainers' workshop on 16 and 17 September 2020.*

EURORDIS is leading this workshop together with other c4c partners. This workshop is open to all patients and patient representatives who are interested in finding out more about the life cycle of medicines and how to get involved within the [c4c project](#).

The 'train the trainers' workshop offers patients and patient representatives the opportunity to understand the different ways patients can get involved in the c4c project, and how patient organisations can support patients and parents involvement in paediatric clinical trials. To find out more about the work c4c is doing to involve patients [click here](#).

To attend this training workshop please complete the [application form here](#) by **15 June**.



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### EURORDIS COVID-19 Information Resource Centre!

With the fast-evolving situation surrounding COVID-19 in Europe and across the world, members of the rare disease community may be concerned about their health. [EURORDIS COVID-19 Information Resources Centre](#) is a collection of EURORDIS actions and communication around the COVID-19 pandemic. You can also find EURORDIS statements, sources of official information, and information/ activities organised in response to the pandemic that we have received through our network!

Please visit all the resources available via the [EURORDIS COVID-19 Information Resource Centre!](#)

THE 10<sup>th</sup> EUROPEAN CONFERENCE ON  
RARE DISEASES & ORPHAN PRODUCTS



ONLINE on 14-16 May **2020**

THE JOURNEY OF LIVING WITH  
a RARE DISEASE in

**2030**

**Did you miss it?**  
**Recordings available!**  
**Register today and**  
**one year to watch it!**

## Recordings of all ECRD 2020 sessions available for one year!

The *European Conference on Rare Diseases (ECRD)* took place online last 14 and 15 May 2020, with more than 1500 attendees. ECRD is recognised globally as the largest, patient-led rare disease event in which collaborative dialogue, learning and conversation takes place, forming the groundwork to shape future rare disease policies.

The ECRD2020 theme was “**The rare disease patient journey in 2030**” and *6 themes were running in parallel*:

- **Theme 1:** The future of diagnosis: new hopes, promises and challenges
- **Theme 2:** Our values, our rights, our future: shifting paradigms towards inclusion
- **Theme 3:** Share, Care, Cure: Transforming care for rare diseases by 2030
- **Theme 4:** When therapies meet the needs: enabling a patient centric approach to therapeutic development
- **Theme 5:** Achieving the triple As by 2030: Accessible, Available and Affordable Treatments for people living with a rare disease
- **Theme 6:** The digital health revolution: hype vs. reality

If you missed the event, it is still possible to [register for full access to all recordings](#). For the first time ever all registered participants will be able to **access all 29 conference sessions**, including inspiring speeches from 3 European Commissioners, 2 Health Ministers and 100+ expert speakers **up to one year after the conference until May 2021!** You can watch the guided virtual tour of the platform to see everything it can offer via [this link](#). If you have already attended the conference and you would like to watch it again, log in with the email address you registered to ECRD!



## IRDiRC Orphan Drug Development Guidebook is out!

The *International Rare Diseases Research Consortium (IRDiRC)* has created a **Guidebook** to facilitate drug development for rare diseases by organizing available tools into a standardized framework. Virginie Hivert, EURORDIS Therapeutic Development Director, together with other colleagues have been working over the past 2-3 years in this project, which is now published in the format of a *Commentary in Nature Reviews Drug Discovery*. Read it [here!](#)

The aim of this Guidebook is to provide all types of developers (including Patient Organisations involved in R&D) with tools and recommendations in order to navigate the complexity of the medicines development ecosystem. By enhancing the use of available tools, delays in development timelines can be avoided, risks and costs reduced, and patient and regulatory acceptability improved.

In the context of *ECRD 2020*, **Theme 4**, an explanatory webinar on the *IRDiRC Orphan Drug Development Guidebook* is now available, don't miss this opportunity and [register here!](#)

For more information, please see [IRDiRC website](#), and please you can find the paper [here!](#)

## Pharmacovigilance Risk Assessment Committee (PRAC) April 2020

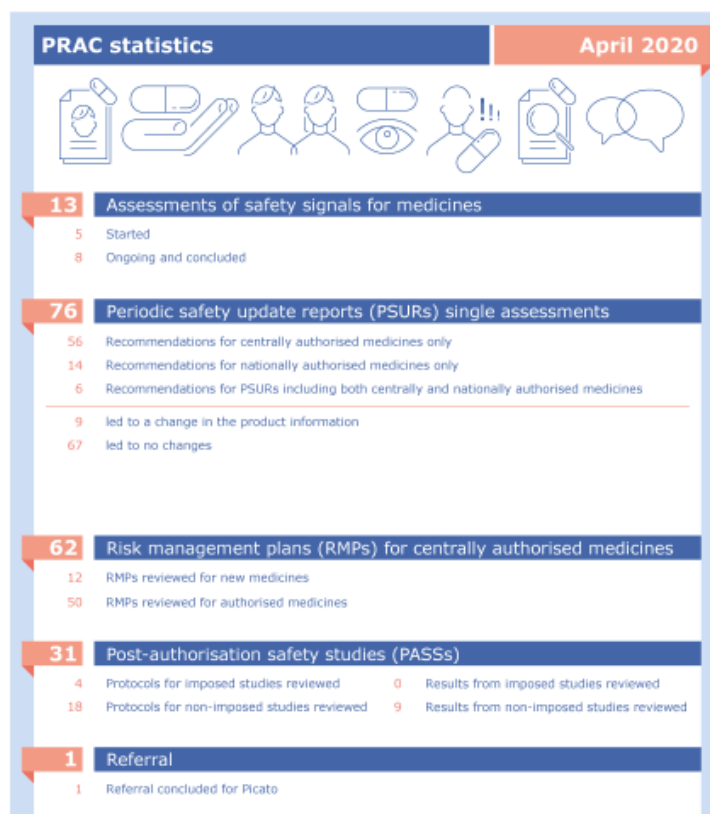
Minutes October 2019  
Agenda April 2020  
Meeting Highlights April 2020

### PRAC concludes Picato's risks are greater than its benefits

EMA's safety committee (PRAC) has confirmed that Picato (ingenol mebutate), a gel for treating the skin condition actinic keratosis, may increase the risk of skin cancer and concluded that the risks of the medicine outweigh its benefits.

The conclusions are based on a review of all available data on the risk of skin cancer in patients using Picato, including results of a study comparing Picato with imiquimod, another medicine for actinic keratosis. The study showed a higher occurrence of skin cancers, especially squamous cell carcinoma, in areas of skin treated with Picato than in areas treated with imiquimod. The marketing authorisation for Picato was withdrawn in February 2020.

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



**2289**  
Orphan  
designations



**213**  
Orphan designations  
included in authorised  
indication



**180**  
Authorised  
OMPs



**70**  
To be used in  
children



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

To date

**111**

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

21 May 2020

## ORPHAN MEDICINAL PRODUCTS AUTHORISED IN 2020

Medicinal Product	Marketing Authorisation Holder	Therapeutic Indication	Date of Marketing Authorisation
<b>Isturisa®</b> (osilodrostat)	Novartis Europharm Limited	Cushing Syndrome	09/01/2020
<b>Polivy®</b> (polatuzumab vedotin)	Roche Registration GmbH	Diffuse large B-cell lymphoma (DLBCL)	16/01/2020
<b>Givlaari®</b> (Givosiran)	Alnylam Netherlands B.V.	Acute hepatic porphyria	02/03/2020
<b>Trepulmix®</b> (Treprostinil)	SciPharm Sàrl	Chronic thromboembolic pulmonary hypertension (CTEPH)	03/04/2020

Please click also on the following links to see:

[Orphan medicinal products authorised during 2020](#)

[Orphan medicinal products authorised since 2000](#)

## CHMP Meeting Highlights April 2020

Minutes January 2020  
Agenda April 2020  
Meeting Highlights April 2020

In April, the CHMP recommended **8 medicines for approval, two orphan medicines**:

- [Daurismo](#) (glasdegib) for the treatment of acute myeloid leukaemia.
- [Reblozyl](#) (luspatercept) for the treatment of adults with transfusion-dependent anaemia associated with myelodysplastic syndromes or beta-thalassaemia.
- [Enerzair breezhaler](#), the first triple combination therapy for the treatment of asthma which includes an optional smart electronic sensor. Enerzair breezhaler consists of a fixed dose combination of three active substances (indacaterol / glycopyrronium / mometasone furoate) in capsules, to be administered using an inhaler. An optional digital sensor collects data on a patient's use and sends them to an app on a smart phone or another suitable device. [Zimbus Breezhaler](#) (indacaterol / glycopyrronium / mometasone furoate) which is a duplicate of Enerzair Breezhaler for the treatment of asthma.

The CHMP recommended the **suspension of all ranitidine medicines** in the EU due to the presence of low levels of an impurity called N-nitrosodimethylamine (NDMA). Ranitidine medicines are used for reducing levels of stomach acid in patients with conditions such as heartburn and stomach ulcers. NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on animal studies.

**Nine recommendations on extensions of therapeutic indication were also granted.**

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

For further information on the work of the CHMP for this 2020, see the [work plan](#).

CHMP statistics: April 2020		
Positive opinions on new medicines	8 Total	33 Total 2020
New [non-orphan] medicines	2 //	
Orphan medicines	2 //	
Biosimilars	1 /	
Generic / hybrids / informed consent	3 ///	



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 April 2020 meeting update

During the April plenary, the COMP adopted **12 positive opinions** on the designation of medicines as orphan medicinal products to the European Commission (EC). For further information, please see the [meeting report](#).

For further information on the work of the COMP for this 2020, see the [work plan](#).

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

- Multiple myeloma, FGK Representative Service GmbH
- Marginal zone lymphoma, Nordic Nanovector ASA
- Retinal detachment, Helio Vision Germany GmbH
- Paroxysmal nocturnal haemoglobinuria, Novartis Europharm Limited
- Hepatocellular carcinoma, Medivir AB
- Canavan disease, Raremoon Consulting Limited
- Soft tissue sarcoma, Adaptimmune Limited
- Neonatal encephalopathy, Clinipace GmbH
- Non-traumatic aneurysmal subarachnoid haemorrhage, Qanatpharma GmbH
- Immune thrombocytopenia, Clinical Network Services (NL) B.V.
- Amyotrophic lateral sclerosis, Drug Development and Regulation S.L.
- Duchenne muscular dystrophy, Medpace Finland Oy.

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

**PDCO April 2020 meeting to be updated in the next issue**

Minutes November 2019  
Agenda March 2020  
Meeting Report March 2020

## PDCO March 2020 meeting update

In March, the PDCO adopted **7 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.

- Livoletide, from Millendo Therapeutics SAS, for the treatment of PraderWilli syndrome
- Cyclophosphamide, from Accord Healthcare S.L.U., for the treatment of all malignant neoplasms
- Imatinib, Accord Healthcare S.L.U., for the treatment of acute lymphoblastic leukaemia and treatment of chronic myeloid leukaemia
- Idasanutlin, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)
- Spesolimab, from Boehringer Ingelheim International GmbH, for the prevention of generalised pustular psoriasis and treatment of generalised pustular psoriasis
- Difelikefalin, from Vifor Fresenius Medical Care Renal Pharma France, for the treatment of chronic kidney disease associated pruritus
- Ibrexafungerp, from SCYNEXIS, Inc., for the prevention of recurrent vulvovaginal candidiasis and for the treatment of vulvovaginal candidiasis

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](#).



## CAT April 2020 meeting update

Minutes March 2020  
Agenda April 2020  
Meeting Report April 2020

In April the Committee for Advanced Therapies (CAT) finalised **2 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](#).

For further information on the work of the CAT for this 2020, see the [work plan](#).

The following product was classified as **gene therapy medicinal product**:

- Autologous CD34+ cells genetically modified with a lentiviral vector expressing IL2RG gene, intended for the treatment of X-linked severe combined immunodeficiency.

The following products were classified as advanced therapy medicinal products. *CAT was unable to consider if these products meet the definition of somatic cell therapy or tissue engineering product due to shortcomings in the information provided regarding the claimed mode of action:*

- Allogeneic viable Wharton's jelly derived mesenchymal stem cells, intended for the treatment of adrenomyeloneuropathy.

For more information, see also the [EMA news release](#).



# 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 first 2020 meeting

Last 3&4 March took place the [first meeting of 2020](#) which has 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 these two days meeting at the European Medicines Agency's (EMA) it was discussed:

- strategies for future activities, including the Regulatory Science Strategy and the Network Strategy to 2025
- review of ICH guidelines for clinical trials and GCP
- big data taskforce recommendations addressing aspects related with data sharing and data protection
- feedback from the various scientific committees
- update on Electronic product information (ePI) activities
- CIOMS guidelines on patient involvement
- shortages

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

## PCWP and HCPWP 2019-2022 Work Plan



Adapted from EMA's [work plan 2019 - 2022](#)

## 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.

