EURORDIS
THERAPEUTIC REPORT

May 2021

ISSUE 5

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

Supply of COVID-19 vaccines and other medicinal products

EURORDIS following an inquiry from member organisations on the availability of COVID-19 vaccines and other medicinal products has contacted the cabinet of Mr. Thierry Breton, European Commissioner for the Internal Market, to explain shortages of raw materials, ingredients and consumables used in the manufacturing of gene therapy treatments.

The Commission has long been aware of the industrial challenges to beat the COVID-19 pandemic. Consequently, in February 2021 it created a Task Force, composed of Member States representatives, Commission officials (including DG SANTE) and industry to address supply chain bottlenecks affecting COVID19 vaccine manufacturing and the production of other pharmaceutical products, including orphan medicines.

EURORDIS met with the European Commission, which assured that the EU is set to bounce back from the current crisis by September 2021 when the demand in the United States will be met, allowing for a smoother delivery to other world regions. EURORDIS will continue to inform the Task Force on products of special concern and to ensure that vaccines and medicines are made available and people living with a rare disease can receive the treatment they require in the near future.

For more information, please read the *EURORDIS communication*!

IMI-c4c: Supporting paediatric research

EURORDIS is a member of the project consortium *IMI - c4c (conect4children),* a European network that aims to facilitate the development of new drugs and other therapies for the entire paediatric population.

First c4c Workshop for Patient Organisations!

The c4c project held the *first workshop 'train the trainers' for patient organisations* with the following **objectives**:

- Building patients' capacity on the life cycle of medicines.
- Educate participants to support patients/parents involvement at the European level for paediatric clinical trials.
- Describe and demonstrate the different ways patients can be engaged within the c4c project.

This workshop was held online on the 16th and 17th of September 2020 with a total of **32 patients and patient representatives attended, with more than 20 diseases represented.**

During the 2 days' workshop, different topics such as patient involvement in the c4c project, ethics, clinical trials, the European regulatory system and how to engage with the European Medicines Agency were addressed. If you are interested in watching the recording, please find here the *slides and the videos by topics*!

Participants and speakers shared their experience and expertise in medicines development, and how to get involved in the c4c project! **Thank you all!**

Join the pool of expert patients for c4c

The voices of children, young people and their families are a pivotal part of the innovative approach of c4c project. It places **patients at the centre and will assign them an active role in the development of the different clinical trials that are going to be conducted during this project**. In order to guarantee patients' involvement in the project, c4c has setup a database to gather information on patients, caregivers, patient organisations and/or young person's advisory boards of rare/paediatric diseases.

Join the *c4c pool of expert patients* or spread the word among your members to participate in panels to review specific sections of a protocol, assessment of patient documentation, discussions on paediatric unmet needs in multi-stakeholder meetings and other activities! For more information, please see *c4c website!*

Pharmacovigilance Risk Assessment Committee (PRAC) May 2021

Minutes November 2020
Agenda May 2021
Meeting Highlights May 2021

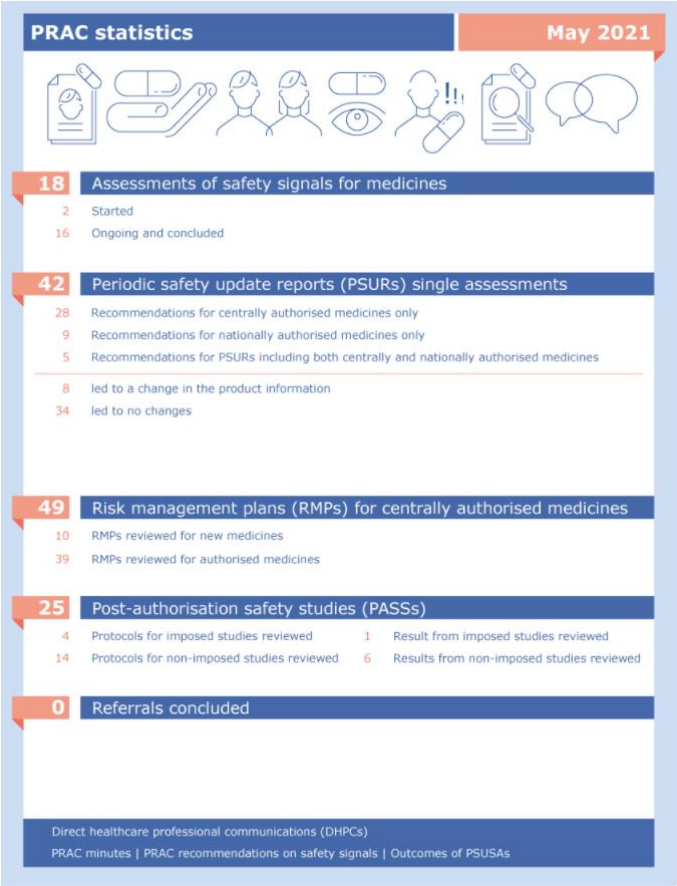
PRAC concludes review of unusual blood clots with Janssen's COVID-19 vaccine

PRAC has now concluded its review of COVID-19 Vaccine Janssen and confirmed, as previously communicated, that **the benefits of the vaccine in preventing COVID-19 outweigh the risks of side effects.**

The Committee recommended further refinement of the warning about thrombosis (formation of blood clots in the vessels) with thrombocytopenia (low blood platelets) syndrome, which was listed previously in the product information for COVID-19 Vaccine Janssen.

The product information will now also include advice that patients who are diagnosed with thrombocytopenia within three weeks of vaccination should be actively investigated for signs of thrombosis. Similarly, patients who present with thromboembolism within three weeks of vaccination should be evaluated for thrombocytopenia. Lastly, thrombosis with thrombocytopenia syndrome will be added as an 'important identified risk' in the risk management plan for the vaccine.

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

235 Orphan designations included in authorised indication

202 Authorised OMPs

78 To be used in children

5 Removed from the market

67 Marketed, but no longer "orphans"

To date

130

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

21 June 2021

CHMP Meeting Highlights May 2021

Minutes May 2021
Agenda May 2021
Meeting Highlights May 2021

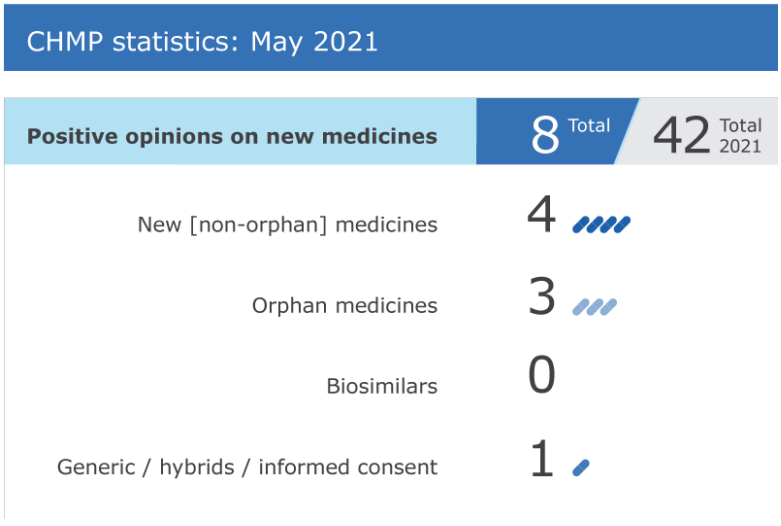
In May, the CHMP recommended **8 medicines for approval, 3 orphan medicines**:

- *Skysona* (elivaldogene autotemcel) for the treatment of early cerebral adrenoleukodystrophy (CALD) for patients without a matched sibling haematopoietic stem cell donor.
- Marketing authorisation under exceptional circumstances for *Bylvay* (odevixibat) for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older.
- *Imcivree* (setmelanotide) for the treatment of obesity and the control of hunger associated with genetic deficiencies of the melanocortin 4 receptor (MC4R) pathway.
- *Klisyri* (tirbanibulin mesylate) for the field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis.
- *Ozawade* (pitolisant) for the treatment of excessive daytime sleepiness in obstructive sleep apnea.
- *Ryeqo* (relugolix / estradiol / norethisterone acetate) for the treatment of symptoms of uterine fibroids in adult women of reproductive age.
- *Verquvo* (vericiguat) for the treatment of symptomatic chronic heart failure in adult patients with reduced ejection fraction.

The CHMP recommended granting marketing authorisations for one generic medicine.

The CHMP also recommended **17 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 May 2021
Meeting Report May 2021

COMP May 2021 meeting update

During the May plenary, the COMP adopted **14 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:

- Essential thrombocythaemia, Imago Biosciences B.V.
- Pulmonary arterial hypertension, MDC RegAffairs GmbH
- Cystinuria, Consorcio Centro de Investigación Biomédica en Red, M.P.
- Nasopharyngeal cancer, BeiGene Ireland Limited
- Mantle cell lymphoma, Eli Lilly Nederland B.V.
- Methylmalonic acidaemia, Parexel International (Irl) Limited
- Friedreich's ataxia, Novartis Gene Therapies EU Limited
- Neuronal ceroid lipofuscinosis, Real Regulatory Limited
- Preeclampsia, Corion Biotech S.r.l.
- Glioma, Sapience Therapeutics Limited
- Primary IgA nephropathy, Otsuka Pharmaceutical Netherlands B.V.
- Achondroplasia, Genzyme Europe B.V.
- Bronchopulmonary dysplasia, Laboratoire Aguettant
- Retinopathy of prematurity, Worphmed S.r.l.

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

- *Enspryng* (satralizumab) for treatment of neuromyelitis optica spectrum disorders, Roche Registration GmbH
- *Koselugo* (selumetinib) for treatment of neurofibromatosis type 1, AstraZeneca AB

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.*

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

Please click also on the following links to see:

Orphan medicinal products authorised during 2021

Orphan medicinal products authorised since 2000

PDCO April&May meeting to be updated next issue

Minutes March 2021
Agenda March 2021
Meeting Report March 2021

PDCO March 2021 meeting update

In March, the PDCO adopted **4 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.

- RAAV8 viral vector encoding the human UGT1A1 transgene (rAAV8-hUGT1A1), from GENETHON, for the treatment of Crigler-Najjar syndrome;
- Vedolizumab, from Takeda Pharma A/S, for the treatment of pouchitis;
- Pegfilgrastim, from Accord Healthcare S.L.U., for the prevention of chemotherapy-induced febrile neutropenia and treatment of chemotherapy-induced neutropenia;
- Respiratory syncytial virus stabilised prefusion f subunit vaccine (RSVpreF), from Pfizer Europe MA EEIG, for the prevention of lower respiratory tract disease caused by respiratory syncytial virus via maternal immunization.

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 May meeting to be updated next issue

Minutes February 2021
Agenda April 2021
Meeting Report April 2021

CAT April 2021 meeting update

In April the Committee for Advanced Therapies (CAT) finalised **5 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 **somatic cell therapy medicinal products:**

- Autologous antigen-specific cytotoxic T-lymphocytes, intended for the treatment of cancer patients that are overexpressing the specific antigen;
- Autologous dendritic cells activated against tumour peptides, intended for the treatment of cancer patients;
- Autologous M1-polarized macrophages, intended for the treatment of cancer patients;
- Autologous Cytotoxic Natural Killer cells, intended for the treatment of cancer patients;
- Autologous plasma cells producing monoclonal antibodies against specific tumour antigen, intended for the treatment of cancer patients.

CAT heard a detailed feedback of the teleconferences that took place between CAT members and colleagues from the European Commission, DG Santé on the revision of the EU legislation on blood, tissues and cells (BTC). Following this feedback CAT discussed the potential impact of this revision on ATMPs, borderline products and CAT participation to the workshops that will be organised by the European Commission in the frame of the BTC revision.

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). EMA's new Executive Director, Emer Cooke, introduced the meeting that 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 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

Co-funded by the Health Programme of the European Union

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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.

Co-funded by the Health Programme of the European Union

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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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