EURORDIS
RARE DISEASES EUROPE

EURORDIS
THERAPEUTIC REPORT

March 2021

ISSUE 3

UPDATE ON THERAPEUTIC DEVELOPMENT AND PATIENT INVOLVEMENT IN EMA ACTIVITIES

GENERAL NEWS

EMA third public stakeholder meeting on COVID-19

Last 26th March the EMA organised the 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* was broadcasted live, please see the *agenda* , the *presentations* and the *recording here*.

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!*

For more information, please check the *EMA COVID-19 section* with the latest updates.

IN THIS ISSUE

EURORDIS calls for a global and equitable access to COVID-19 vaccines

EURORDIS and its members call on European and global leaders to urgently take steps towards equitable access to COVID-19 vaccines to save lives globally and locally, protecting first those at high risk, in particular people with comorbidities, including people living with about 30 different rare diseases, as recommended by *European Reference Networks experts.*

EURORDIS calls for **immediate actions** to ensure a more equitable access to COVID-19 vaccines:

- Include people with rare diseases and their carers, as an at-risk population from COVID-19, on the national priority vaccination lists;
- Implement the recommendations by the *24 European Reference Networks* on priorities and contraindications for COVID-19 vaccination of people with rare diseases;
- Involve patient organisations in decision-making and activities at the policy and programme level to ensure an ethical and transparent process to patients and the population;
- COVID-19 vaccine production to be increased;
- Contributions to the COVAX / GAVI should be increased by the EU and high-income countries across the globe.

EURORDIS strongly supports the *WHO Vaccine Equity Declaration* and calls for equitable distribution of vaccines against the coronavirus globally.

For more information, please read the *press release here*, and check the *EURORDIS COVID-19 Information Resource Centre*.

*Check here all the **events** that took place **worldwide** on the **Rare Disease Day 2021**!*

Rare 2030 Recommendations

Rare 2030 was a foresight study which gathered the input of a large group of patients, practitioners and key opinion leaders to propose policy recommendations that would lead us to improve policy and a better future for people living with a rare disease in Europe. For more information on the Rare 2030 project in which EURORDIS was a partner, see *here*.

The Rare 2030 *"Recommendations: The future of rare diseases starts today"* presents the conclusions of the Rare 2030 Foresight Study, initiated by the European Parliament and co-funded by the European Commission Pilot Project and Preparatory Actions Programme.

This two-year study with over 250 experts from across the rare disease community, has resulted in **eight overarching recommendations** to ensure that the future of 30 million people living with a rare disease is not left to luck or chance. These recommendations cover diagnosis, treatment, care, research, data and European and national infrastructures sets out the roadmap for the next decade of rare disease policies, and the need for a new European policy framework for rare diseases to:

- Guide the implementation of national plans for rare diseases with the same measurable objectives.
- Bring together a refreshed concerted strategy across research, digital, healthcare, social welfare complementing existing legislations
- Encourage continued investment in the field of rare diseases at both the European and national levels to ensure we do not lose momentum.

For more information, please read the *full report here* and watch the *Rare 2030 Final Policy Conference recording here*.

Rare 2030
Foresight in Rare Disease Policy

Pharmacovigilance Risk Assessment Committee (PRAC) March 2021

Minutes November 2020
Agenda March 2021
Meeting Highlights March 2021

Review of thalassaemia medicine Zynteglo started

EMA's human safety committee (*PRAC*) began a safety review of the medicine Zynteglo, a gene therapy authorised to treat the rare blood condition beta thalassaemia.

The review follows a case of acute myeloid leukaemia, a cancer of the blood, in a patient treated with a related investigational medicine, bb1111. This medicine uses the same modified virus (known as a viral vector) as Zynteglo, to deliver a gene into body cells. So far, no cases of leukaemia have been reported with Zynteglo itself.

The company responsible for developing both medicines has paused supply of Zynteglo while the evidence is examined.

For more information, please see *EMA website*.

Update on COVID-19 Vaccine AstraZeneca

The PRAC is reviewing all cases of thromboembolic events, and other conditions related to blood clots, reported post-vaccination with Vaxzevria (previously COVID-19 Vaccine AstraZeneca).

There is currently no indication that vaccination has caused these conditions, which are not listed as side effects with this vaccine. The position of the PRAC is that the **COVID-19 AstraZeneca vaccine's benefits continue to outweigh its risks and the vaccine can continue to be administered** while investigation of cases of thromboembolic events is ongoing.

Following the *assessment of a safety signal regarding cases of anaphylaxis (s*evere allergic reactions) with Vaxzevria, PRAC has recommended an update to the product information to include anaphylaxis and hypersensitivity (allergic reactions) as side effects, with an unknown frequency, and to update the existing warning to reflect that cases of anaphylaxis have been reported.

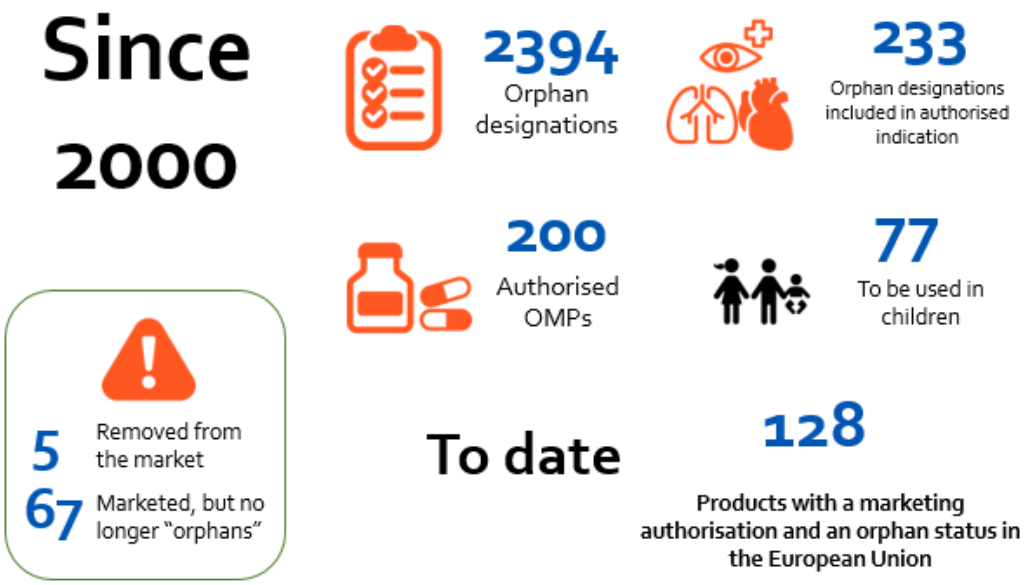
For more information, see *EMA's update.*

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



22 April 2021

CHMP Meeting Highlights March 2021

Minutes January 2021
Agenda March 2021
Meeting Highlights March 2021

In March, the CHMP recommended **5 medicines for approval, 1 hybrid orphan medicine**:

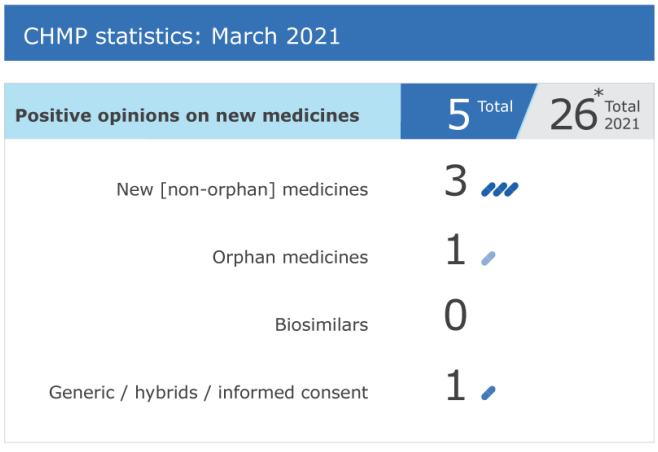
- Hybrid medicine Efmody (*hydrocortisone*) for the treatment of congenital adrenal hyperplasia (CAH) in patients aged 12 years and over. Hybrid applications rely in part on the results of pre-clinical tests and clinical trials of an already authorised reference product and in part on new data.
- Copiktra (*duvelisib*) for the treatment of adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) or refractory follicular lymphoma (FL).
- Ponvory (ponesimod) for the treatment of active relapsing forms of multiple sclerosis.
- Drovelis and its duplicate Lydisilka, both containing the active substances estetrol and drospirenone, received positive opinions from the Committee for use as oral contraceptives.

The CHMP also recommended six 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.*



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 January 2021
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Meeting Report March 2021

COMP March 2021 meeting update

During the March plenary, the COMP adopted **3 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:

- Multiple myeloma, Roche Registration GmbH;
- Cutaneous T-cell lymphoma, Almirall S.A.;
- Amyotrophic lateral sclerosis, 3R Pharma Consulting GmbH.

Re-assessment of orphan designation at time of marketing authorisation

When a designated orphan medicinal product receives a positive opinion for marketing authorisation from EMA's Committee for Medicinal Products for Human Use (CHMP), the COMP has the responsibility to review whether or not the medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation. The COMP adopted **1 positive opinion at time of CHMP opinion**:

- *Epidyolex* (cannabidiol) for treatment of tuberous sclerosis, GW Pharma (International) B.V.

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
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 March meeting to be updated next issue

PDCO February 2021 meeting update

Minutes January 2021
Agenda February 2021
Meeting Report February 2021

In January, 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.

- Ritlecitinib, from Pfizer Europe MA EEIG, for the treatment of alopecia areata;
- Surufatinib, from Hutchison MediPharma Ltd, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours and myeloid neoplasms) and treatment of malignant neoplasms of haematopoietic and lymphoid tissue;
- Pioglitazone (hydrochloride) / Spironolactone / metformin (hydrochloride), from Katholieke Universiteit Leuven (KUL) Research & Development, for the treatment of polycystic ovary syndrome;
- Zilucoplan, from UCB Pharma SA, for the treatment of myasthenia gravis;
- Adeno-associated virus, serotype 9 (AAV9)-based non-replicating, self-complementary recombinant vector containing an expression cassette for the human ASPA transgene (scAAV9-CB6-hASPAopt), from Aspa Therapeutics, Inc., for the treatment of Canavan disease;
- Chikungunya Virus Virus-Like Particle Vaccine, from Emergent Netherlands B.V., for the chikungunya disease;
- Dupilumab, from Sanofi-Aventis recherche & développement, for the treatment of chronic spontaneous urticaria;
- Hydroxypropyl-β-cyclodextrin, from Cyclo Therapeutics Inc, for the treatment of Niemann Pick disease type C;
- Ruxolitinib (phosphate), from Incyte Biosciences Distribution B.V., for the treatment of vitiligo;
- Sepofarsen, from ProQR Therapeutics, for the treatment of Leber congenital amaurosis;
- Severe acute respiratory syndrome coronavirus 2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS)/matrix-M1 adjuvant, from Novavax, Inc., 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.*

CAT March meeting to be updated next issue

Minutes January 2021
Agenda March 2021
Meeting Report February 2021

CAT February 2021 meeting update

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 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.

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