EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Introduction to the EMA and how patients can be involved in EMA activities

Program EUpALS Scientific Webinar

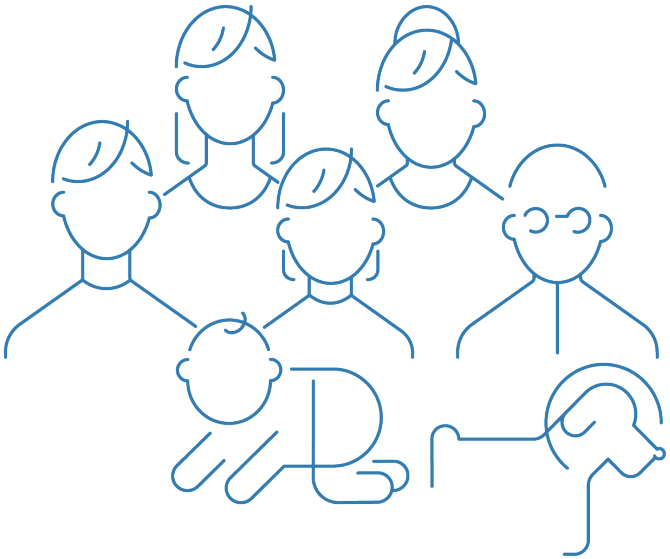
27 October 2021
Maria Mavris
Public and Stakeholders Engagement Department

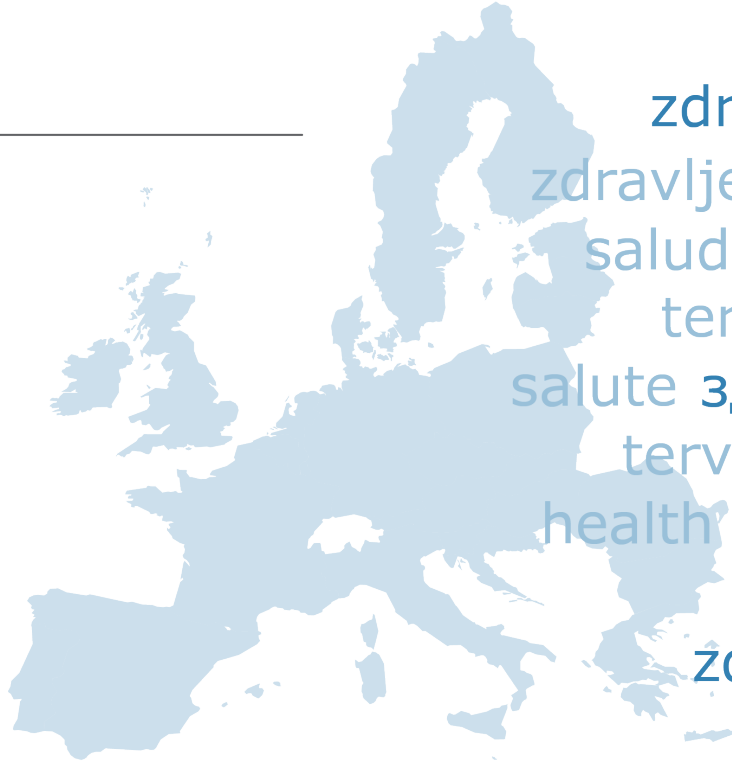
Outline

- What the European Medicines Agency (EMA) does
- Journey of patient involvement
- How EMA engages with patients
- Patient involvement in regulatory lifecycle
- Support and training by EMA
- Conclusions
- *Response to COVID-19* (if there is time)

EMA in the EU

Who do we work for?





zdrowie zdravie
zdravlje Gesundheit
salud υγεία saúde
tervist veselība
salute здраве saħħa
terveys sundhed
health hälsa sláinte
egészség’
zdravje zdraví
gezondheid
sveikata
santé sănătate

27 member states

21.5 % of global sales of medicines

24 official languages

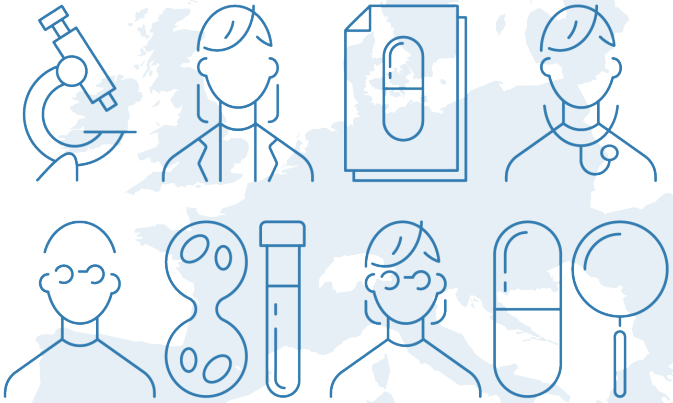
What we do

Protect human and animal health

- Facilitate development and access to medicines
- Evaluate applications for marketing authorisation
- Monitor the safety of medicines across their life cycle
- Provide reliable information on human and veterinary medicines to patients and healthcare professionals

Who we are

~4000 scientific experts from across Europe

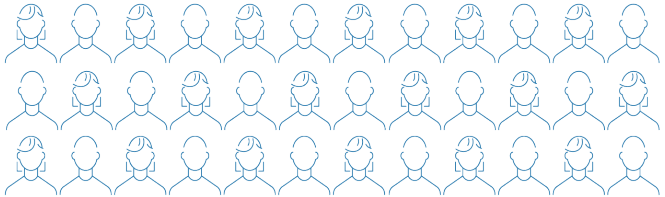


7 Scientific Committees

- CHMP
- CVMP
- COMP
- HMPC
- PDCO
- CAT
- PRAC

1 Management Board

- 27 Member States' representatives
- 4 Civil society representatives
- 2 European Commission representatives
- 2 European Parliament representatives

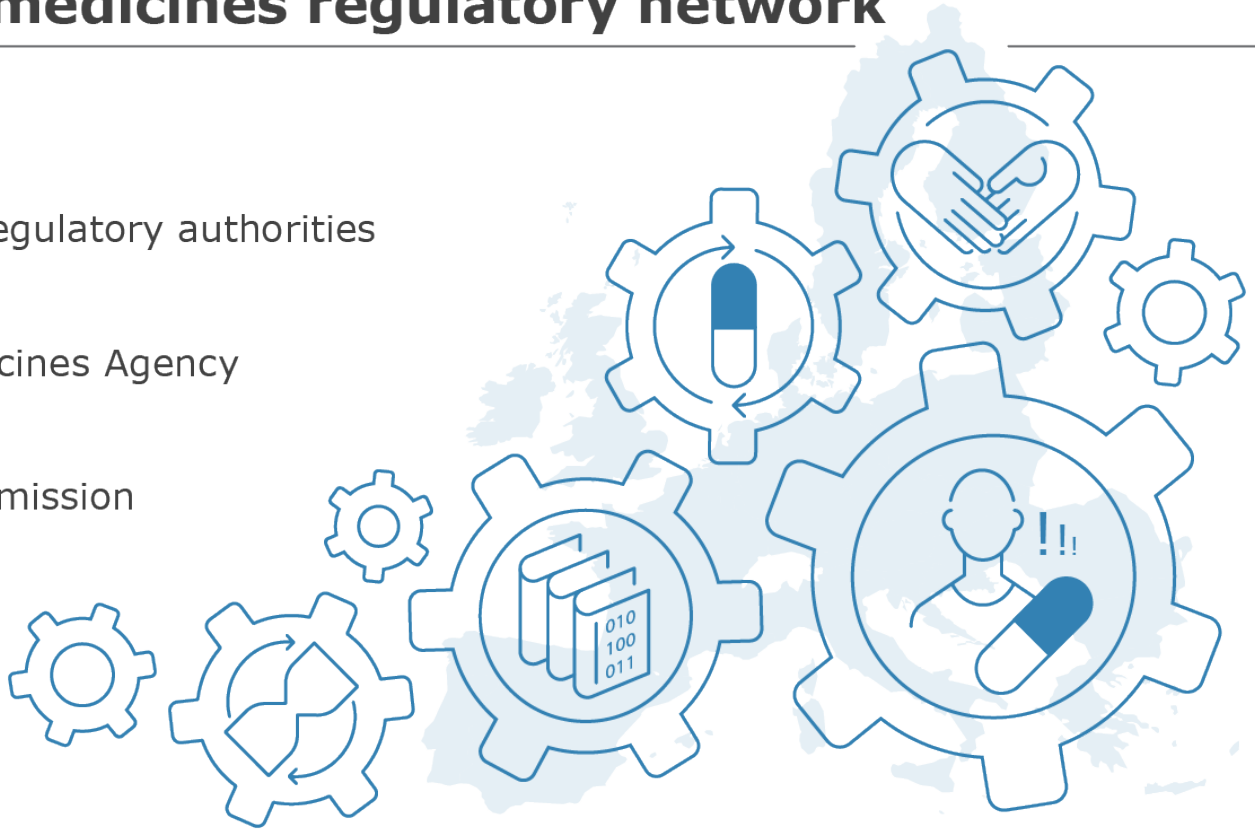


1995 EMA established

~800 staff members

The European medicines regulatory network

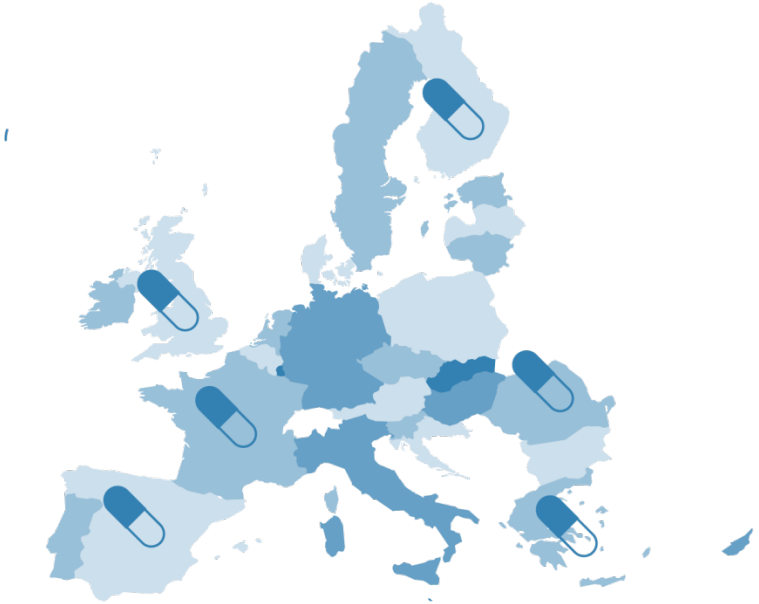
- ~50 national regulatory authorities
- European Medicines Agency
- European Commission



How are medicines approved?

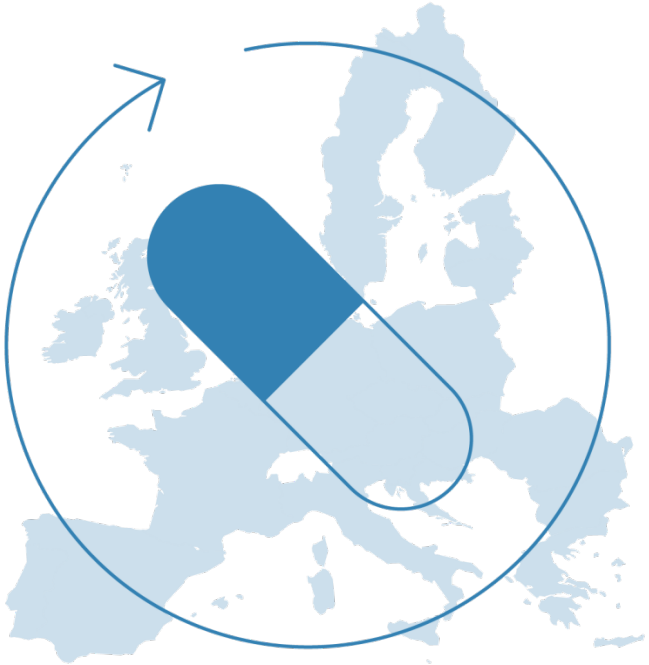
Different authorisation routes: one set of common rules

Centralised procedure (via EMA)



National procedures (via Member States)

Which medicines are approved through the centralised procedure?

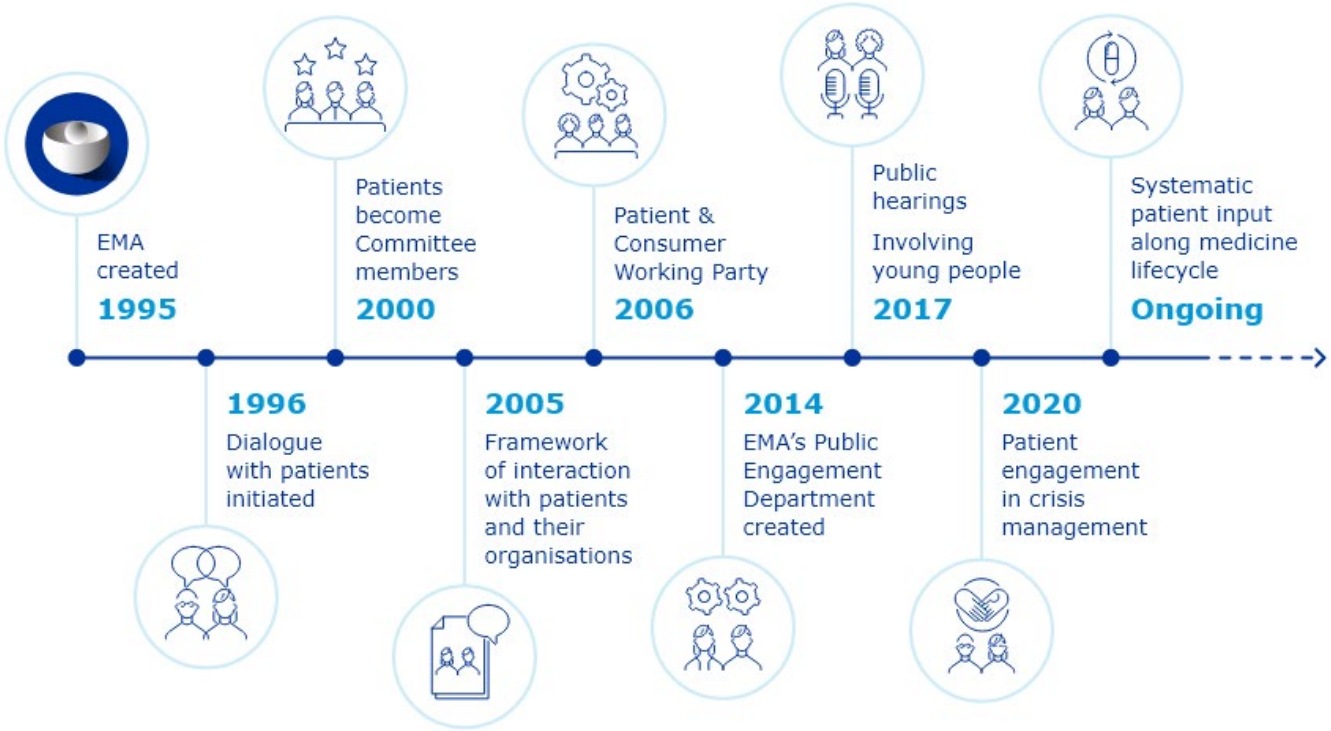


- Human medicines containing new active substances for the treatment of HIV/AIDS cancer, diabetes, neurodegenerative diseases, auto-immune, and other immune dysfunctions, and viral diseases
- Medicines derived from biotechnology processes, such as genetic engineering
- Advanced therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines
- Officially designated 'orphan medicines' (medicines used for rare human diseases)
- Veterinary medicines for use as growth or yield enhancers

What EMA is not responsible for

- Authorisation of clinical trials
- Pricing or availability of medicines
- Advertising of medicines
- Patents on medicines
- Homoeopathic medicines
- Food supplements and cosmetics
- Develop treatment guidelines or provide medical advice

Interaction with patients and consumers: a progressive journey…



EMA scientific committees and Management Board

7 Scientific Committees

1 Management Board

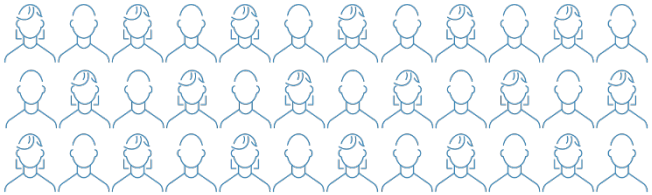
- CHMP
- CVMP
- COMP
- HMPC
- PDCO
- CAT
- PRAC

27 Member States' representatives

4 Civil society representatives

2 European Commission representatives

2 European Parliament representatives



~800 staff members

Representing their *community*

Management Board
EMA Scientific Committee Members

Patient membership

Working parties –PCWP and HCPWP

Patients and Consumers Working Party (PCWP)

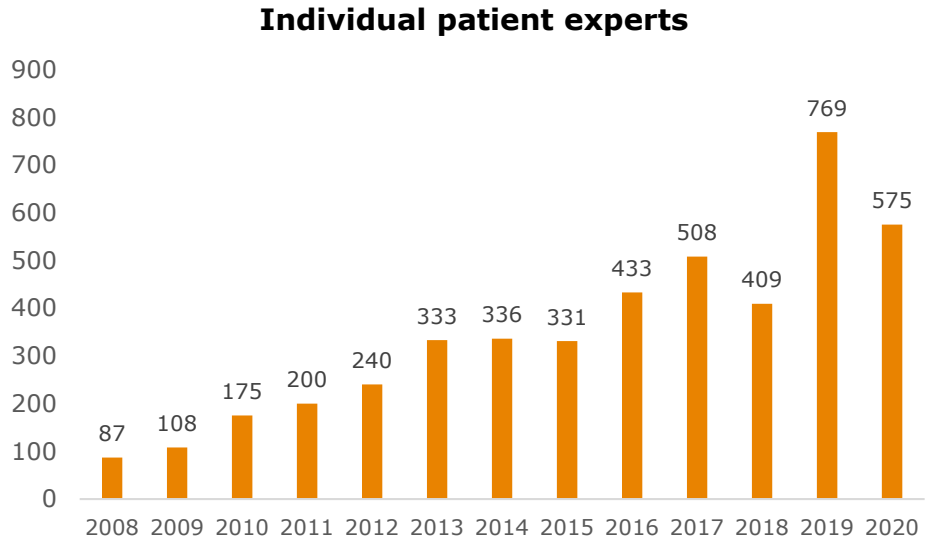
Healthcare professional working party (HCPWP)

- Act as filter and generator of activities at EMA
  - Workshops
  - Information sessions
  - Training
  - Topic groups

Representing their *organisations*

Working Party (PCWP or HCPWP)
EMA consultations
Workshops

Involvement in EMA medicine-specific activities

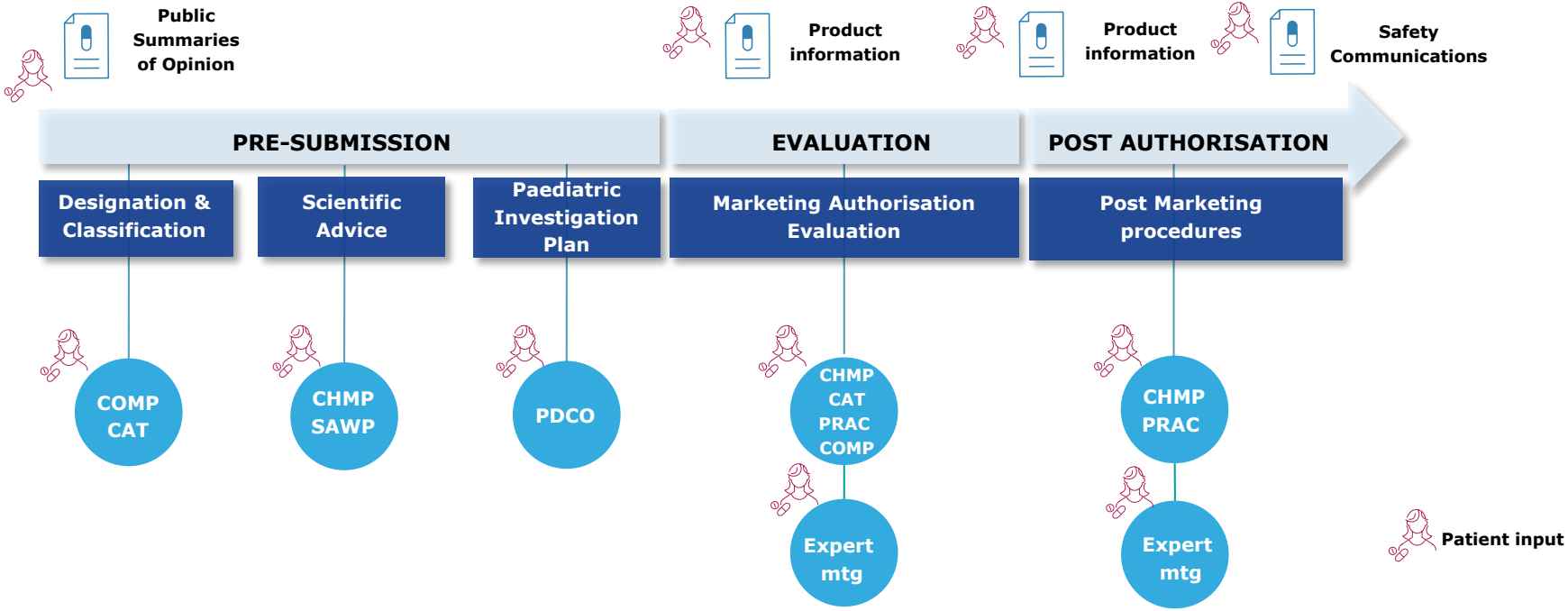


Individual experts

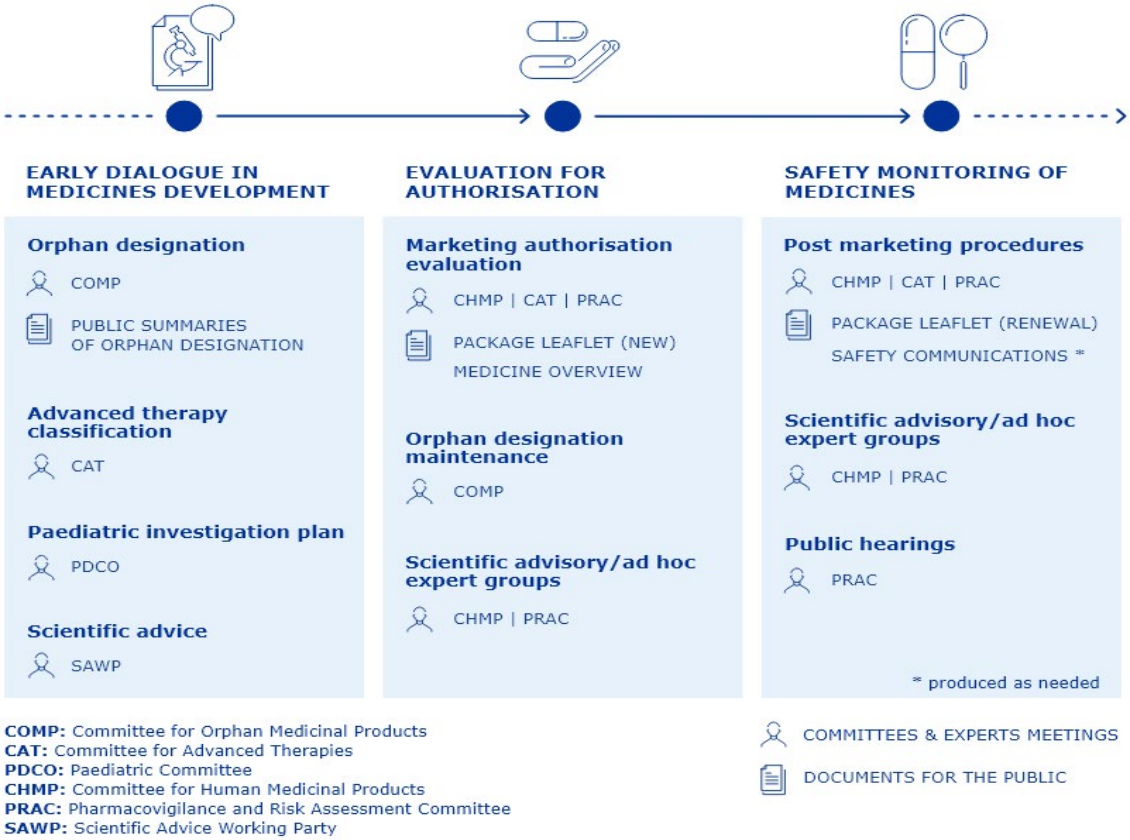
Scientific Advice / Protocol Assistance Procedures
Scientific Advisory/ad hoc expert Groups
Scientific Committee consultations
Review of documents

Register as
Patient expert

Where are patients involved?



Where are patients involved?



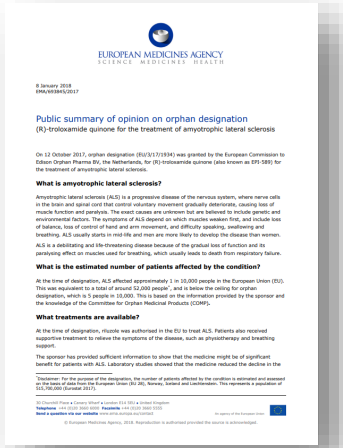
Where are patients involved? Rare disease committee

Public Summaries of Opinion

PRE-SUBMISSION

Designation & Classification

COMP
CAT



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 January 2018
EMA/693845/2017

Public summary of opinion on orphan designation
(R)-troloxamide quinone for the treatment of amyotrophic lateral sclerosis

On 12 October 2017, orphan designation (EU/3/17/1934) was granted by the European Commission to Edison Orphan Pharma BV, the Netherlands, for (R)-troloxamide quinone (also known as EPI-589) for the treatment of amyotrophic lateral sclerosis.

What is amyotrophic lateral sclerosis?

Amyotrophic lateral sclerosis (ALS) is a progressive disease of the nervous system, where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis. The exact causes are unknown but are believed to include genetic and environmental factors. The symptoms of ALS depend on which muscles weaken first, and include loss of balance, loss of control of hand and arm movement, and difficulty speaking, swallowing and breathing. ALS usually starts in mid-life and men are more likely to develop the disease than women.

ALS is a debilitating and life-threatening disease because of the gradual loss of function and its paralysing effect on muscles used for breathing, which usually leads to death from respiratory failure.

What is the estimated number of patients affected by the condition?

At the time of designation, ALS affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 people[1], and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, riluzole was authorised in the EU to treat ALS. Patients also received supportive treatment to relieve the symptoms of the disease, such as physiotherapy and breathing support.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALS. Laboratory studies showed that the medicine reduced the decline in the

[1]Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 515,700,000 (Eurostat 2017).

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An agency of the European Union

Committee for Orphan Medicinal Products (COMP)

- ALS is a rare disease
- Prevalence of 1/10000 people in EU

Patient involvement

- Members of committee
- Can be invited to committee meeting
- Surveys can be used to answer committee questions

As ALS is a rare disease, obtaining Orphan Designation is crucial for a potential ALS medicine to start the regulatory pathway at EMA

- What is the time gain that an Orphan Designated Medicine can make as compared to a medicinal product that follows the regular pathway?

Union Register of medicinal products - European Commission

EU #	Product	Indication	Sponsor	Designation date
EU/3/21/2470	Pridopidine hydrochloride	Treatment of amyotrophic lateral sclerosis	Prilenia Therapeutics B.V.	19 Jul 2021
EU/3/21/2436	Trehalose	Treatment of amyotrophic lateral sclerosis	FGK Representative Service GmbH	20 May 2021
EU/3/21/2426	Ganglioside GM1	Treatment of amyotrophic lateral sclerosis	3R Pharma Consulting GmbH	13 Apr 2021
EU/3/20/2395	Celecoxib, ciprofloxacin	Treatment of amyotrophic lateral sclerosis	Morrison & Foerster	06 Jan 2021
EU/3/20/2358	L-pyroglutamyl-L-asparaginyl-L-prolyl-D-tyrosyl-D-tryptophan amide	Treatment of amyotrophic lateral sclerosis	Neuropath Therapeutics Limited	13 Nov 2020
EU/3/20/2318	Dextran sulfate low molecular weight	Treatment of amyotrophic lateral sclerosis	TikoMed AB	21 Aug 2020
EU/3/20/2284	Sodium phenylbutyrate, tauroursodeoxycholic acid	Treatment of amyotrophic lateral sclerosis	Drug Development and Regulation S.L.	04 Jun 2020
EU/3/20/2256	Reldesemtiv	Treatment of amyotrophic lateral sclerosis	Pharma Gateway AB	28 Feb 2020
EU/3/19/2231	H-Leu-Pro-Pro-Leu-Pro-Tyr-Pro-OH	Treatment of amyotrophic lateral sclerosis	AdRes EU B.V.	16 Dec 2019
EU/3/19/2232	Lactobacillus plantarum	Treatment of amyotrophic lateral sclerosis	MDC RegAffairs GmbH	16 Dec 2019
EU/3/19/2155	Human culture expanded autologous mesenchymal stromal cells	Treatment of amyotrophic lateral sclerosis	IQVIA RDS Ireland Limited	24 Apr 2019
EU/3/18/2017	Ambroxol hydrochloride	Treatment of amyotrophic lateral sclerosis	Spedding Research Solutions SAS	25 May 2018
EU/3/18/2008	Adeno-associated viral vector serotype 9 encoding miRNA against human superoxide dismutase 1	Treatment of amyotrophic lateral sclerosis	Stolmár & Partner Patentanwälte PartG mbB	16 Apr 2018
EU/3/17/1934	(R)-troloxamide quinone	Treatment of amyotrophic lateral sclerosis	PTC Therapeutics International Limited	08 Nov 2017
EU/3/17/1894	Recombinant human antibody directed against misfolded human superoxide dismutase 1	Treatment of amyotrophic lateral sclerosis	Granzer Regulatory Consulting & Services	17 Jul 2017
EU/3/17/1844	Tauroursodeoxycholic acid	Treatment of amyotrophic lateral sclerosis	Bruschettini s.r.l.	27 Feb 2017
EU/3/16/1801	Ibudilast	Treatment of amyotrophic lateral sclerosis	Medicinova Europe GmbH	12 Dec 2016
EU/3/16/1722	Masitinib mesilate	Treatment of amyotrophic lateral sclerosis	AB Science	29 Aug 2016

https://ec.europa.eu/health/documents/community-register/html/reg_od_act.htm?sort=a

You showed that over the recent 5 years EMA positively adviced Orphan Designation for 3 to 4 potential ALS medicines per year. By this the pipeline of ALS medicines under clinical development in Europe has never been so full.

- However, are you aware of any application to obtain Orphan Designation for a potential ALS medicine that was not designated? If so, what was the main reason?

- Do patients in the COMP often have to convince other members about the importance for a potential ALS medicine to obtain Orphan Designation?

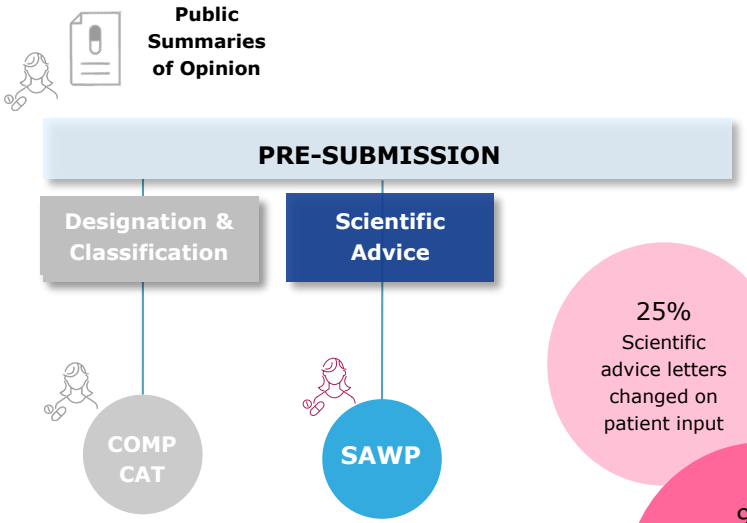
Orphan criteria for designation

1. That the **product** is intended for the **diagnosis, prevention or treatment** of a **life-threatening or chronically debilitating condition** not affecting more than **five in ten thousand persons** in the European Community

2. That the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition and is unlikely that the marketing of the medicinal product in the Community would generate sufficient **return to justify the necessary investment**

3. There **exists no satisfactory method** of diagnosis, prevention or treatment of the condition that has been authorised in the European Community

Where are patients involved? Scientific Advice/ Protocol Assistance



25% Scientific advice letters changed on patient input

90% Patients agree with medicine development plans in scientific advice

Scientific Advice Working Party (SAWP)

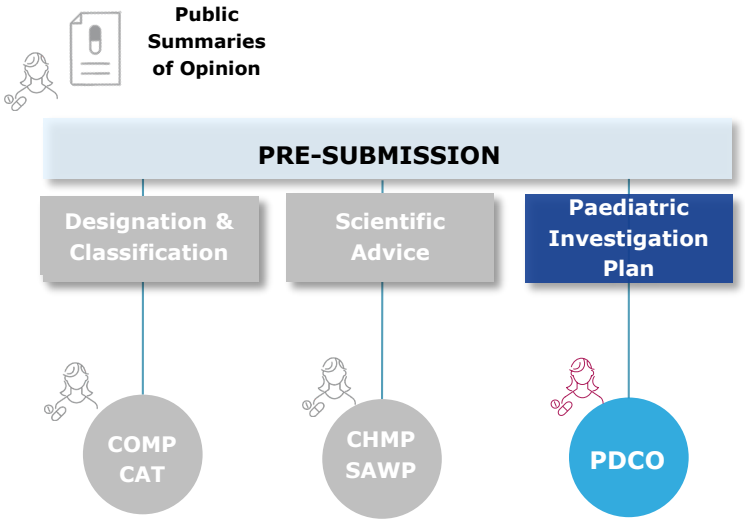
Areas where patients can contribute to development plan

- Patient population
- Endpoints
- Comparator medicines
- Quality of life
- Feasibility of trials
- Living with a disease/condition and implications

Patient involvement

- ALS patient representatives invited to participate in several procedures

Where are patients involved? Medicines for Children



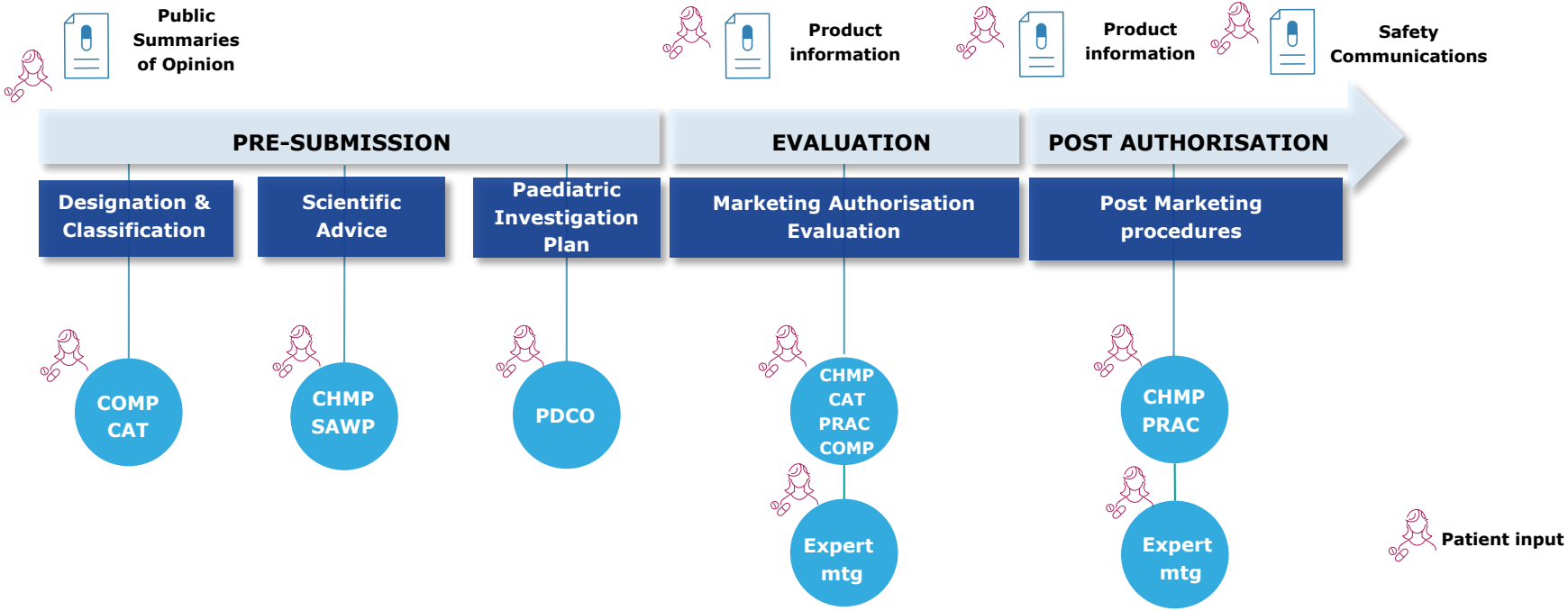
Paediatric Committee (PDCO)

- Assess content of paediatric investigation plans (PIPs)
- Determine studies that companies must perform in children when developing a medicine.
- Assess applications for full/ partial waiver or deferral

Patient involvement

- Members of committee
- Can be invited to committee meeting
- Surveys can be used to answer committee questions

Where are patients involved?



Where are patients involved? Marketing authorisation

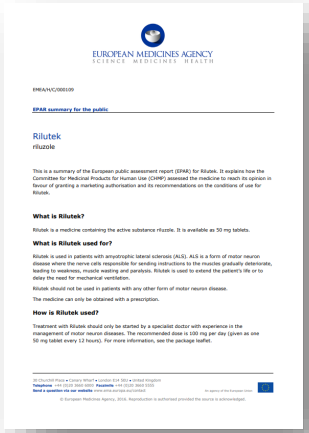
Product information

EVALUATION

Marketing Authorisation Evaluation

CHMP
CAT
PRAC
COMP

Expert mtg


EUROPEAN MEDICINES AGENCY
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EMEA/H/C/000109

EPAR summary for the public

Rilutek
riluzole

This is a summary of the European public assessment report (EPAR) for Rilutek. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Rilutek.

What is Rilutek?

Rilutek is a medicine containing the active substance riluzole. It is available as 50 mg tablets.

What is Rilutek used for?

Rilutek is used in patients with amyotrophic lateral sclerosis (ALS). ALS is a form of motor neuron disease where the nerve cells responsible for sending instructions to the muscles gradually deteriorate, leading to weakness, muscle wasting and paralysis. Rilutek is used to extend the patient's life or to delay the need for mechanical ventilation.

Rilutek should not be used in patients with any other form of motor neuron disease.

The medicine can only be obtained with a prescription.

How is Rilutek used?

Treatment with Rilutek should only be started by a specialist doctor with experience in the management of motor neuron diseases. The recommended dose is 100 mg per day (given as one 50 mg tablet every 12 hours). For more information, see the package leaflet.

Link to full EPAR

Committee for Human Medicinal Products (CHMP)

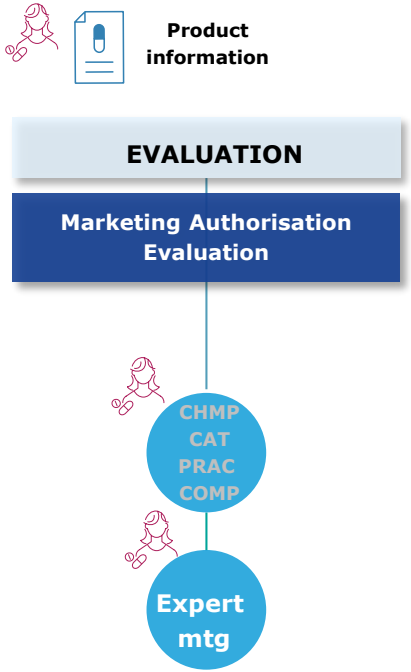
- Plays a vital role in the authorisation of medicines in the EU
- Conducts the initial assessment of EU-wide marketing authorisation applications
- Additional monitoring - labelled with a black inverted triangle (▼)

Patient involvement

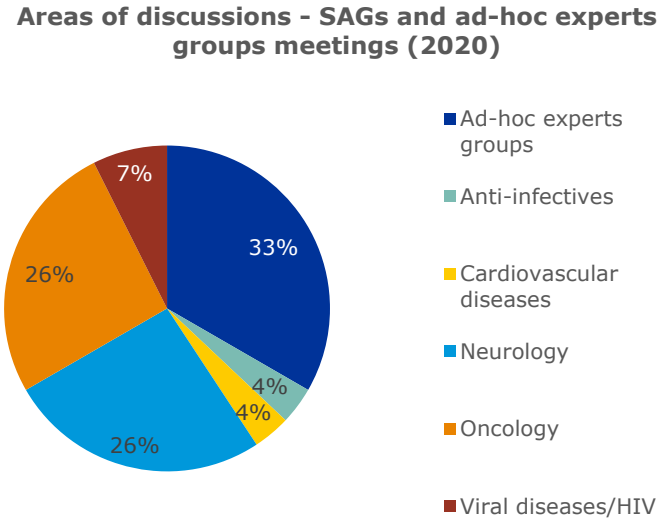
- Can be invited to committee meeting
- Can be invited to expert meeting (SAG/ad hoc)
- Pilot on early involvement in assessment
- Surveys can be used to answer committee questions

Scientific Advisory Groups (SAGs)/ ad hoc expert groups

EMA's scientific committees can consult additional experts, patients and healthcare professionals to enrich their scientific assessment of medicines. These external parties may be involved in SAGs or ad-hoc expert groups.



42 patients were involved in SAG meetings in 2020



Where are patients involved?

Committee for Orphan Medicinal Products (COMP)

- Reviews orphan criteria prior to marketing authorisation

Pharmacovigilance and Risk Assessment Committee (PRAC)

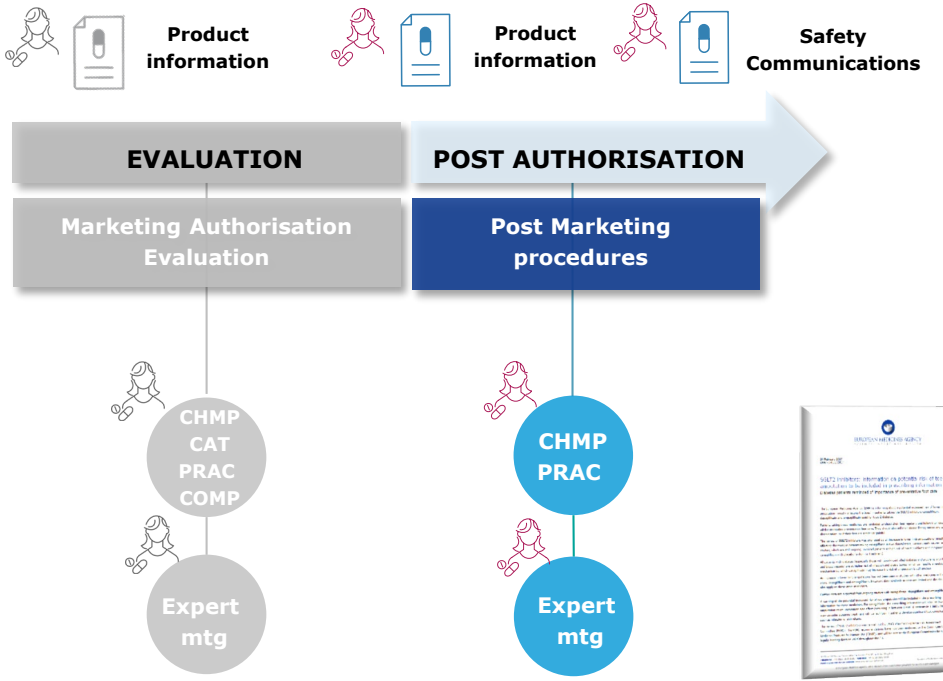
Evaluates Risk Management Plan (RMP) submitted with marketing authorisation application:

- Any possible (known or potential) safety concerns
- How risks will be managed and monitored once the medicine is authorised
- What information is intended to be gathered from follow-up studies after authorisation

Patient involvement

- Can be invited to COMP meeting on orphan maintenance
- Review of documents for public
  - Medicines overview
  - Package leaflet

Where are patients involved? Safety committee



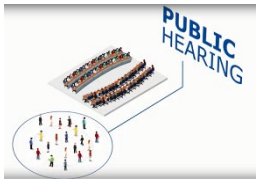
Stakeholder meetings

- With patients and healthcare professionals
- Valproate; Retinoids; Methotrexate

Public hearings at PRAC

2017: Valproate containing medicines;

2018: Quinolones and fluoroquinolones



Review of safety communications

Challenges

- Finding suitable patients (e.g. language barrier, availability)
- Ensuring comprehensive, tailored training to facilitate and enhance participation
- Provide a clear definition of patients role in the different activities / committees to manage expectations from all angles
- Managing potential conflicts of interest
- Representativeness
- Measuring the value / impact of patients

How to address the challenges

- **Who** to interact with?
  - Creating a diverse group of stakeholders to consult
  - Criteria for organisations
  - Individual experts
- **How** to interact?
  - Methodologies for engaging stakeholders
  - Support and training
  - Develop appropriate content and ensure targeted communication
- **Transparency**
- **Monitoring** and **reporting**

Who to interact with?

Eligible organisations

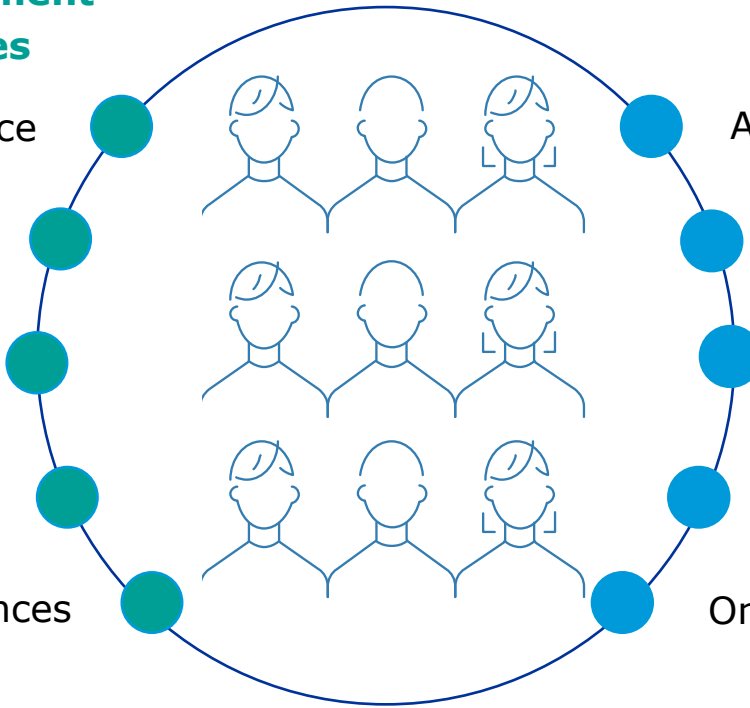
International/European organisations – EMA stakeholders database

Organisation representatives	Individual Experts
EMA 'eligibility' criteria	**Declaration / assessment of Interests**
Transparent on the funding of the organisation ▶ Legitimacy ▶ Mission/activities ▶ Representation ▶ Structure ▶ Accountability ▶ Transparency	**Confidentiality undertaking** Identification through European network of registered organisations and EMA database of individuals

How to interact?

Flexible engagement methodologies

- Face to face
- In writing
- Committee meetings
- Surveys
- Patient preferences



Appropriate support and training

- Annual training day
- Info-sheets
- Videos
- Webpages
- One-to-one personalised support

Transparency

- Declarations of Interest – publication of declarations and CVs of individual experts
- Eligibility criteria for organisations and publication of funding
- Publication of agendas, minutes, highlights of committees
- Civil society members in committees
- Proactive publication of clinical trial data
- Public Hearings

As you showed, engagement of EMA with patients is based upon a **delicate balance between trust and transparency**, where EMA publishes reports of meetings as open as possible, but also expects confidentiality from patients they engage with.

- Has EMA advice for the ALS patients that engage with them, who feel huge (social media) pressure from their fellow-patients to get additional information and to speed up clinical development of potential ALS medicines?

- Can EMA - to a certain extent - understand that such fellow-patients unjustly think that ‘too little, too slow’ is happening in clinical development of an ALS medicine?

Monitoring and measuring

- Description of patient/HCP input into EMA activities
- Proposals for improvements included in next work-plan
- Annual report to EMA Management Board

Annual reports with summaries of feedback

25%
Scientific advice letters changed on patient input

50%
Changes by patients included in published documents

90%
Patients agree with medicine development plans in scientific advice

Some conclusions

- Engaging with patients:
  - Brings **everyday aspects** of living with a disease **into scientific discussions**
  - Helps **bridge the gap** between clinical trial data and real world data
  - Increases **transparency, awareness and understanding: TRUST**
- Engage in a **stepwise approach; learn together** what format works best;
  - **Define roles** - manage expectations
  - Ensure engagement is **mutually beneficial**

Everyone has a role to play to ensure engagement happens

Engaging with patients leads to **more meaningful outcomes** for everyone!

Any questions?

Further information

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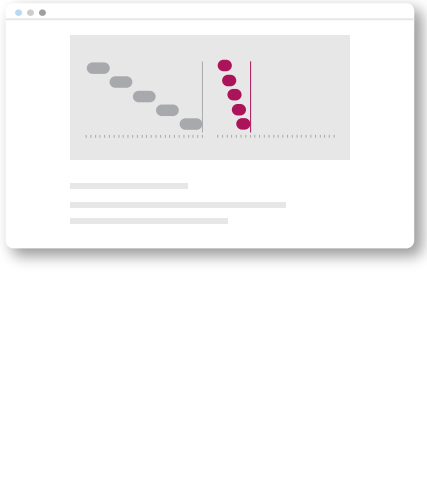
COVID-19: current situation and approach

- Key challenge is to develop and approve *safe* and *effective* medicines as quickly as possible
- COVID-19 vaccines and treatments must be rigorously tested and meet the same high standards of safety, efficacy and quality as any other medicine.
- EMA is expediting its processes supporting the development & approval of treatments and vaccines COVID-19 EMA pandemic Task Force is a main tool for EMA and the EU medicines regulatory network to enable quick and coordinated regulatory actions.
- International collaboration via ICMRA, WHO, FDA.
- EMA publishes and disseminates key information for patients and healthcare professionals.

Stakeholder engagement: critical for crisis management

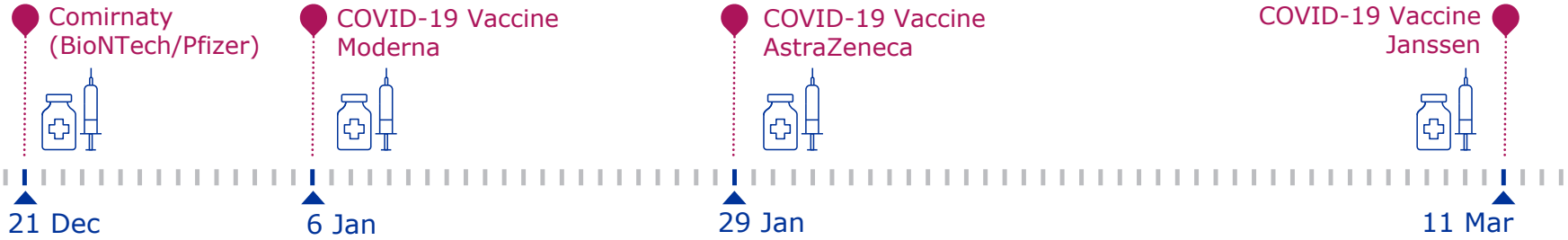
- Engagement with patients and healthcare professionals is vital; involvement in discussions, user-testing and document review are critical elements
- EMA can engage rapidly via established network of patients and healthcare professionals
- Pool of COVID ‘patients’ registered at EMA
- Active dissemination of EMA COVID-19 communications is key to increase their effectiveness and ensure EMA is a trusted and regular source of reliable information for patients and healthcare professionals (and help dispel ‘false news’)



COVID-19 vaccines approved in the EU

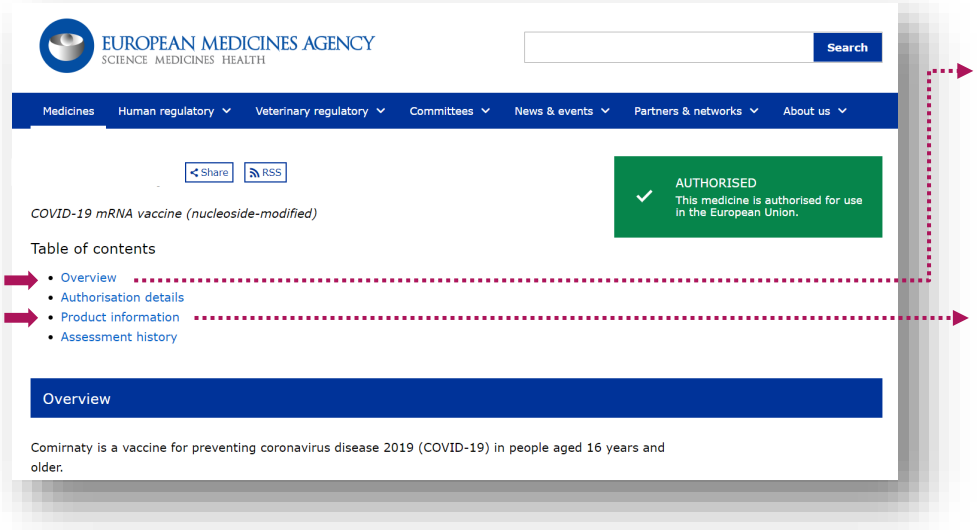
4 vaccines **authorised in the EU**

- **Comirnaty and Moderna** vaccines contain a molecule called **messenger RNA (mRNA)** with instructions for producing the spike protein from SARS-CoV-2, the virus that causes COVID-19
- The **AstraZeneca and Janssen** vaccine use a **non-replicating adenovirus** as a carrier that has been modified to produce the spike protein from SARS-CoV-2.
- The vaccines do not contain the SARS-CoV-2 virus causing COVID-19 itself and **cannot cause the disease.**



More information about the COVID-19 vaccines

- Comirnaty
- COVID-19 Vaccine Moderna
- COVID-19 Vaccine AstraZeneca
- COVID-19 vaccine Janssen



COVID-19: key facts

- **Medicine overview** addressing questions and answers in lay language; available in all EU languages
- Risk management plan (RMP)

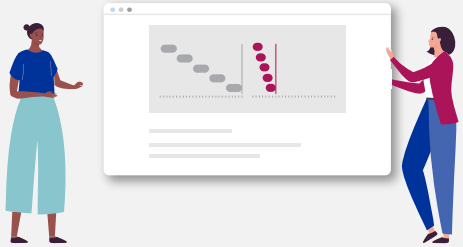
- Recommendations and precautions to be followed by
  - healthcare professionals (summary of product characteristics) and
  - patients (**package leaflet**)

  for the safe and effective use of each approved vaccine; available in all EU languages

EMA public meetings

11 December 2020

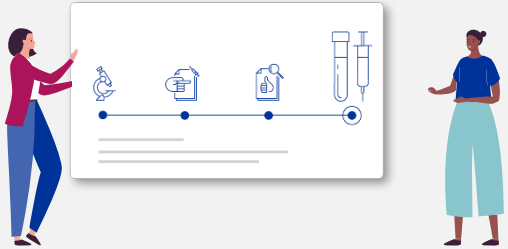
BROADCAST LIVE



Inform the public and stakeholders about EU regulatory process for approval of COVID-19 vaccines and EMA's role in their development, evaluation and approval

8 January 2021

BROADCAST LIVE



Explain the basis for the approval and use of new vaccines, how their safety will be monitored and their roll-out at national level

26 March 2021

BROADCAST LIVE

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

Listen to the public and stakeholder groups on their needs, expectations and any concerns, so that these can be considered in the relevant regulatory processes.