EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Challenges and Opportunities for Orphan Medicinal Products under the European Regulatory Framework

BioBridges 2018

Institute of Pharmacology, First Faculty of Medicine, Charles University Prague

Czech Republic

Presented by Bruno Sepodes
Chair of the Committee of Orphan Medicinal Products (COMP)

Human medicines

In 2017, EMA recommended 92 medicines for marketing authorisation. Of these, 35 had a new active substance, i.e. one which had never previously been authorised in EU.

Many of these medicines represent a significant improvement in their therapeutic areas; they include medicines for children, for rare diseases and advanced therapies.

Medicines for children:

Brineura for the treatment of a very rare, fatal neurodegenerative condition in children called neuronal ceroid lipofuscinosis type 2 (CLN2) disease. This is the first medicine approved in the EU for the treatment of CLN2.

Spinraza to treat spinal muscular atrophy (SMA), an inherited disease that affects the motor neurons and is usually diagnosed in the first year of life. This is the first medicine approved in the EU for the treatment of SMA.

Alkindi for the treatment of primary adrenal insufficiency, a rare hormonal disorder in infants, children and adolescents.

Crysvita for the treatment of X-linked hypophosphataemia (a genetic bone disorder leading to rickets and impaired growth) in children and adolescents with growing skeletons.

Advanced therapy medicinal products:

Spherox to treat adult patients who have symptomatic cartilage defects in the knee joint.

Alofisel for the treatment of complex perianal fistulas in patients with Crohn's disease. Perianal fistulas occur when an abnormal passageway develops between the rectum and the outside of the body.

Rare diseases:

Oxervate for the treatment of neurotrophic keratitis, a rare eye disease.

Qarziba (previously Dinutuximab beta Apeiron) for the treatment of high-risk neuroblastoma (a cancer of nerve cells).

Xermelo for the treatment of carcinoid syndrome (a rare cancer-related condition leading to diarrhoea and flushing).

What is a rare disease?

EU definition:

- Medical condition affecting **not more than** 5 in 10,000 persons in the European Community (close to 252,000 people)

US definition:

- The disease or condition for which the drug is intended affects fewer than 200,000 people in the US (close to 6.4 in 10,000)

What is different about rare diseases?

- Diseases are usually **poorly** or **incompletely understood**

  Generally, the lower the prevalence, the less well we tend to understand them

- **Small populations**

  Limited opportunity for study and replication

- Highly **heterogeneous** group of disorders

  Some references point to *~6000-7000 different diseases*

  Often high phenotypic diversity within individual disorders

- Usually little **precedent** for **drug development** within individual disorders

- Development often requires **more** (and more careful) **planning** than non-Orphan

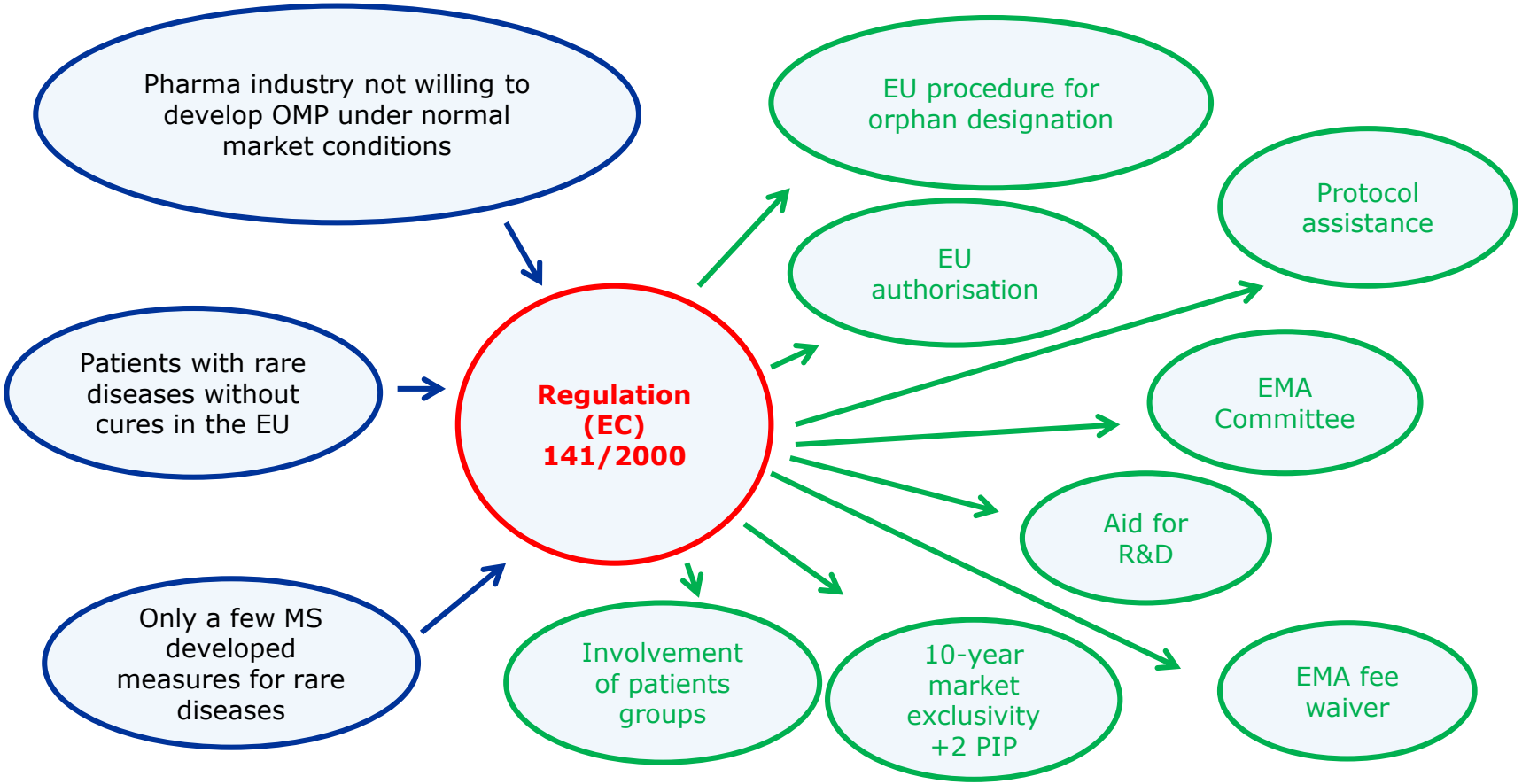
  Need a solid scientific base upon which to build an overall program

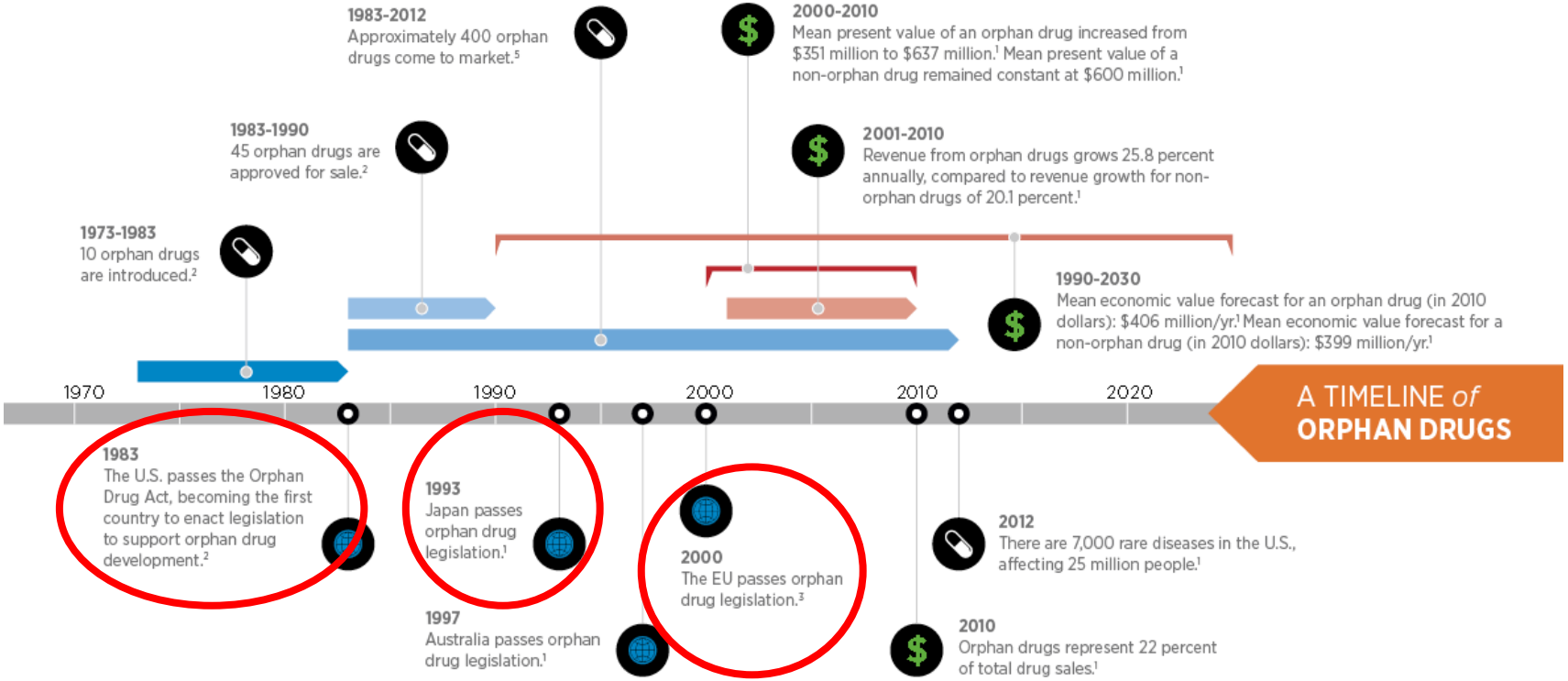
How did we get from

Oliver Twist … to the orphans everyone wants to adopt?

2000

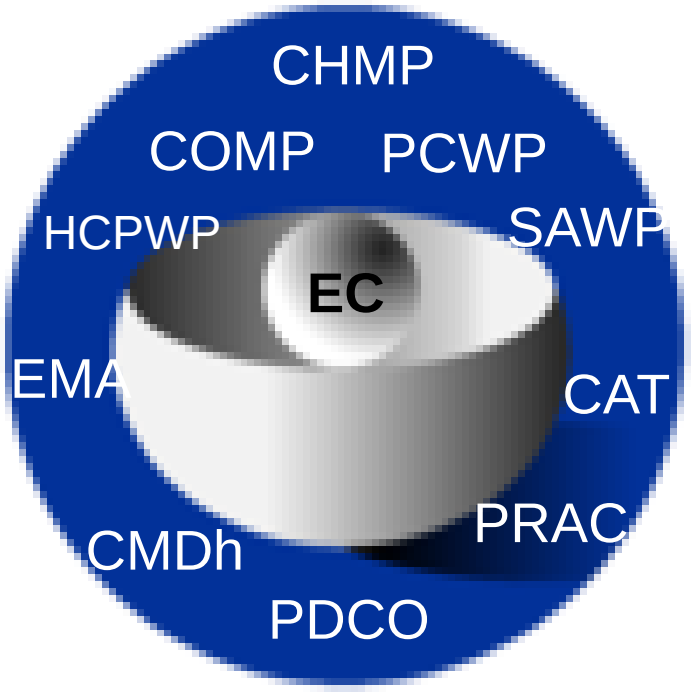
2018


Pharma industry not willing to develop OMP under normal market conditions
Patients with rare diseases without cures in the EU
Only a few MS developed measures for rare diseases
Regulation (EC) 141/2000
EU procedure for orphan designation
EU authorisation
Protocol assistance
EMA Committee
Aid for R&D
EMA fee waiver
10-year market exclusivity +2 PIP
Involvement of patients groups



Source: PAMPLIN, College of Business Magazine, Virginia Tech, 2013

Team players



Elosulfase alfa

MS Type IV A
Morquio A syndrome

Active substance	Recombinant human N-acetylgalactosamine-6-sulfatase
Medicine Name	Vimizim
Disease/condition	Treatment of mucopolysaccharidosis, type IVA (Morquio A syndrome)
Date of decision	24/07/2009
Outcome	Positive
Orphan decision number	EU/3/09/657

1

COMP
Orphan designation

2

PDCO
PIP Decision

Overview | Decision

Invented name	Vimizim (elosulfase alfa)
Active substance	Recombinant human N-acetylgalactosamine-6-sulfatase (BMN110)
Decision number	P/0055/2015
PIP number	EMEA-000973-PIP01-10-M03
Pharmaceutical form(s)	Concentrate for solution for infusion
Condition(s)/indication(s)	Treatment of mucopolysaccharidosis, type (Morquio-A syndrome)
Route(s) of administration	Intravenous use

3

CHMP
B/R assessment

Vimizim
elosulfase alfa

About | Authorisation details | Product information | Assessment history

Next tab »

This is a summary of the European public assessment report (EPAR) for Vimizim. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Vimizim.

For practical information about using Vimizim, patients should read the package leaflet or contact their doctor or pharmacist.

Expand all items in this list

- What is Vimizim and what is it used for?
- How is Vimizim used?
- How does Vimizim work?
- What benefits of Vimizim have been shown in studies?
- …are the risks associated with Vimizim?
- …izim approved?
- …re being taken to ensure the safe and effective use of …izim

EU/3/09/657

Orphan designation | Key facts | Review of designation

During its meeting of 11 to 12 March 2014, the Committee for Orphan Medicinal Products (COMP) reviewed the designation EU/3/09/657 for Vimizim (elosulfase alfa, previously known as recombinant human N-acetylgalactosamine-6-sulfatase) as an orphan medicinal product for the treatment of mucopolysaccharidosis, type IVA (Morquio A syndrome). The COMP assessed whether, at the time of marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the condition, and the existence of other satisfactory methods of treatment. The COMP recommended that the orphan designation of the medicine be maintained[1].

[1]The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after authorisation, the EU cannot accept another application for a marketing authorisation, or grant a marketing authorisation, or accept an application to extend an existing marketing authorisation for a similar medicinal product with a comparable therapeutic indication for the same indication, unless the second medicinal product is safer, more effective or otherwise clinically superior to the first medicinal product.

Expand all items in this list

- Life-threatening or long-term debilitating nature of the condition
- Prevalence of the condition
- Existence of other satisfactory methods of treatment
- Conclusions

Name	Language
Recommendation for maintenance of orphan designation at the time of marketing authorisation: Vimizim (elosulfase alfa) treatment of muco…	

	First published	Last updated
English	…/06/2014	

…shed	Last updated

4

COMP
Review of designation

The Committee of Orphan Medicinal Products

- 1 elected Chair
- 1 elected Vice chair
- 1 Member per MS (28)
- 3 Patients Reps
- 3 Members by EC on proposal from EMA
- 1 Member for Norway, 1 for Iceland

Current EMA/COMP activities in the orphan landscape
COMP mission and responsibilities

Give **opinions** on **designation** and orphan drug status **maintenance**

Actively contribute to ***Protocol Assistance*** for ***Significant Benefit***

Advise the **European Commission** on establishment and development of a **policy** on orphan medicinal products

Assist on **guidelines**

Assist the European Commission in **international liaison**

Main characteristics orphan designation

- Applications for **treatment**, **prevention** or **diagnosis** of rare diseases
- Procedure **free of charge**
- Designation can be requested at **any stage** of development before the application for MAA is made
- Sponsor can be either company or individual [Established in the EEA (EU, Ice, Liech, Nor)]
- European Commission decision gives **access to incentives** such as protocol assistance and centralised procedure
- Designated products are entered into the Community Register of OMPs by the EC

Incentives after Initial Orphan Designation

Economic / marketing

- Fee reduction / exemption

Product development

- Protocol assistance
- Benefits for SMEs

Community marketing authorisation

- Centralised procedure and Conditional Licencing

National incentives (EC inventory)

Designation criteria

RARITY (prevalence) / NO RETURN OF INVESTMENT (Art 3.1 (a) of 141/2000)

- Medical condition affecting not more than 5 in 10,000 in the Community (around 250,000 people)
- Without incentives it is unlikely that the marketing of the product would generate sufficient return to justify the necessary investment

SERIOUSNESS

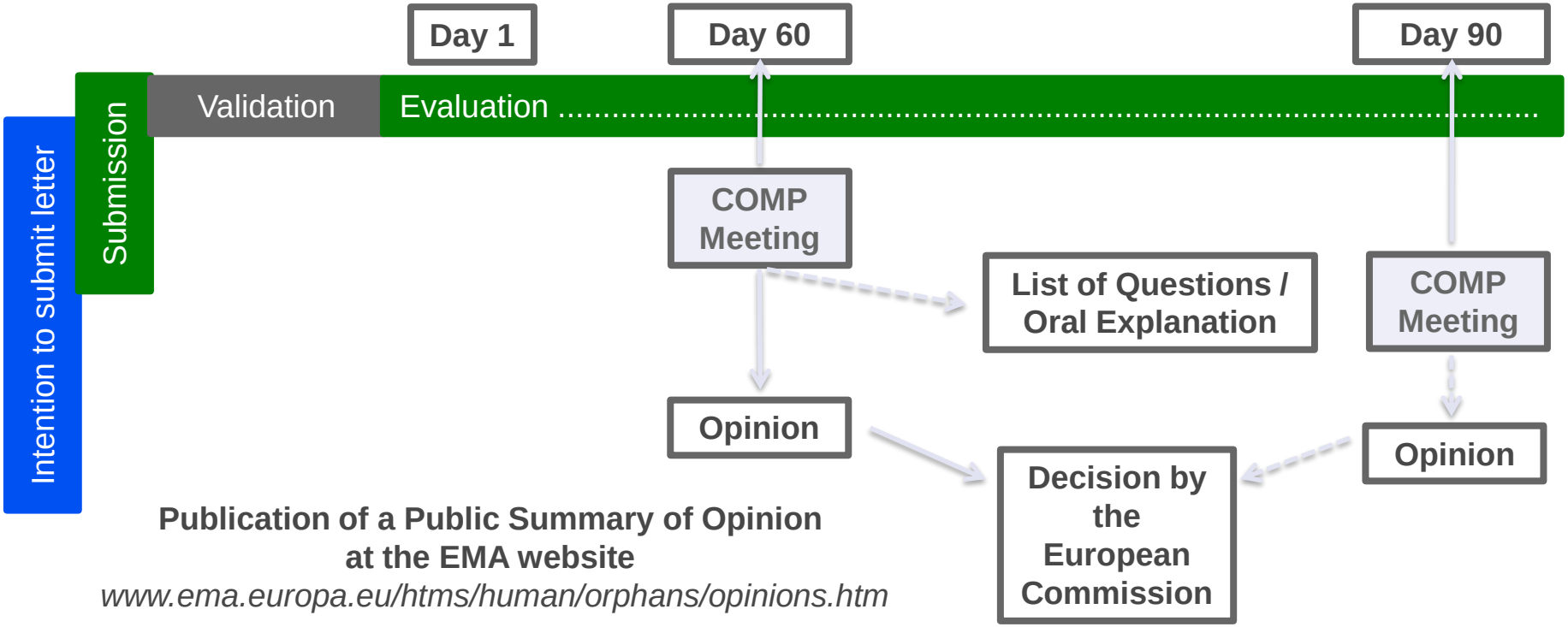
- Life–threatening or chronically debilitating

ALTERNATIVE METHODS AUTHORISED (Art 3.1(b)of 141/2000)

- If satisfactory method exist the sponsor should establish that the product will be of **significant benefit**

EXCLUSIVE for EU

The designation process in the EU



Publication of a Public Summary of Opinion at the EMA website

www.ema.europa.eu/htms/human/orphans/opinions.htm

Areas of growing interest and trends in OMP development

Eye diseases: e.g. Retinitis pigmentosa, Non-infectious uveitis, Leber's congenital amaurosis, Choroideremia, Stargardt's disease

Skin diseases: e.g. Epidermolysis bullosa, Congenital ichthyosis, Dyskeratosis congenita, Pemphigus;

Genetic a/o Metabolic disorders – continuing and rising

Conditions in prematurely born infants (e.g. Bronchopulmonary dysplasia, Respiratory Distress Syndrome, Retinopathy of prematurity)

Tropical diseases: Malaria, Leishmaniasis

'**The first orphan designation sparks the interest'** – clusters of applications for e.g. pulmonary arterial hypertension, hemophilias (A and B), amyloidosis, epidermolysis bullosa, Fragile X syndrome

New types of therapies - Gene therapies / Stem cell therapies (mesenchymal etc.), cancer 'vaccines'

Oncology: glioma, pancreatic cancer and ovarian cancer

Drug Repurposing and orphan drugs

- *'De-risking'* therapeutic development
- Aprox. 20% of Orphan Drugs
- CNS diseases with high potential
- Reduced development costs (1/20)
- Time to market is reduced
- Safety profile in general well-known
- Manufacturing process in place
- PK / PD known in humans

- Medical plausibility needs to be established
- PK / PD particularities relevant for the new orphan condition need to be fully substantiated
- SB needs to be demonstrated (when applicable)
- Bibliographic data needs to be fully suportive of the claims
- New data might still need to be generated

COMP responsibilities

"Dreamworks"

COMP

CHMP

Idea

Hypothesis

Assumption or viable hypothesis

Proof / Evidence

“Maintenance of Orphan Status” is not an easy walk

Philippe Petit high-wire walk between the Twin Towers of the World Trade Center (7th of August of 1974)

Review of the orphan criteria at the time of MAA

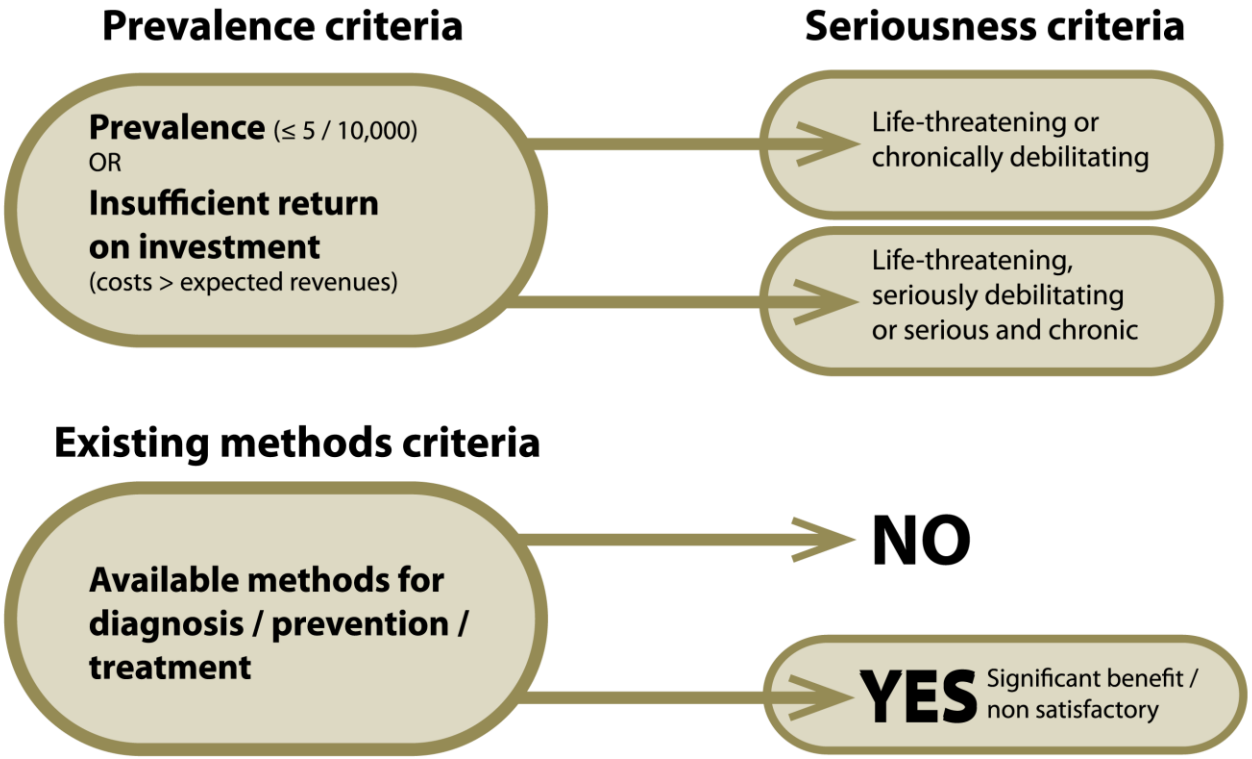
- At the time of submission for MAA, the sponsor is requested to submit a report on the maintenance of ODD criteria.
- Guidance on the submission of this report in the pre-submission mtg for MAA.
- The COMP re-evaluates the criteria based on data generated by the sponsor (not assumption) in parallel to the MA assessment, if doubt the sponsor will be invited for an oral hearing.
- The opinion by the COMP on if the product should be removed or not from the Community Register

Maintenance Designation Criteria

- Key criteria that must be met:
  - Confirm that the condition/disease is a distinct medical entity.
  - Confirm that the prevalence calculation which meets the criteria of being below 5 in 10,000
  - Where there are authorised medicines the sponsor will need to confirm that their product offers a significant benefit over authorised medicinal products in Europe

Incentives After MAA and Review of ODD

- Reduced Licencing fees for SMEs.
- 10-year market exclusivity protection against
  - similar products (structure/mechanism of action)
  - same indication
- 2yr extension if PIP has been complied with specific per indication.


Prevalence criteria
Seriousness criteria
Prevalence (≤ 5 / 10,000)
OR
Insufficient return on investment
(costs > expected revenues)
Life-threatening or chronically debilitating
Life-threatening, seriously debilitating or serious and chronic
Existing methods criteria
Available methods for diagnosis / prevention / treatment
NO
YES
Significant benefit / non satisfactory

Significant benefit in the context of the orphan regulation **is ADDED VALUE to patients**

http://www.eurordis.org/news/eurordis-photo-contest-2015-and-winners-are

The orphan status of a product in Europe **is not easy to maintain** …

Orphan Designation

"Assumptions of potential benefit(s) should be plausible"

Market Authorisation

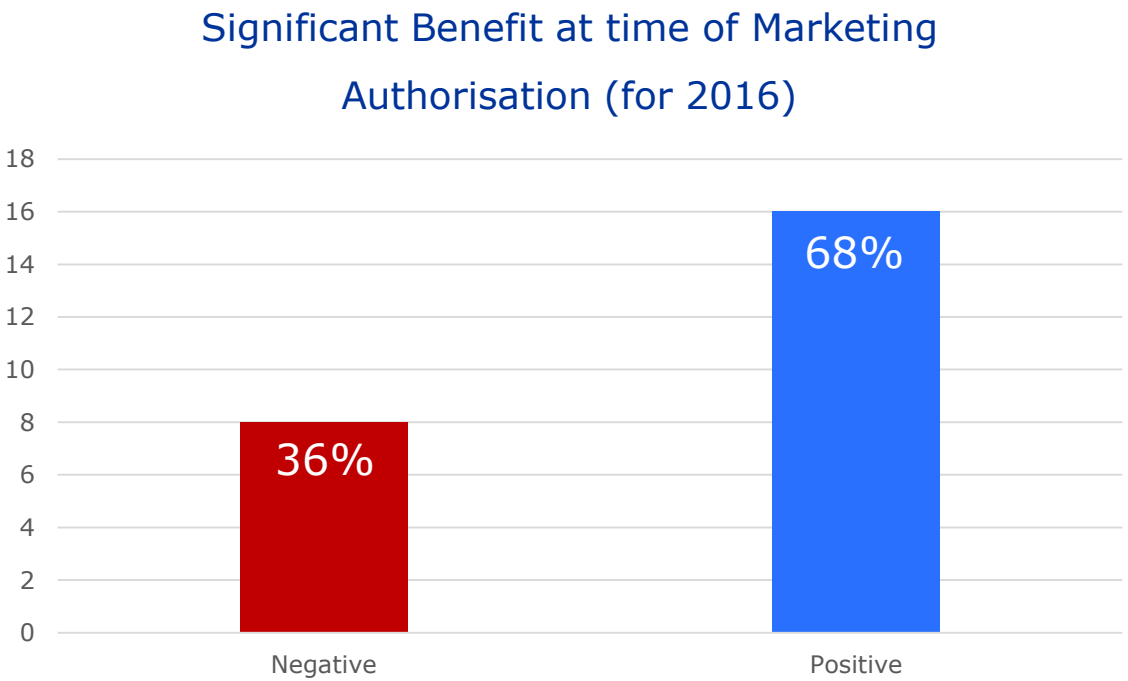
"demonstration of significant benefit over currently authorised methods in order to maintain orphan status"

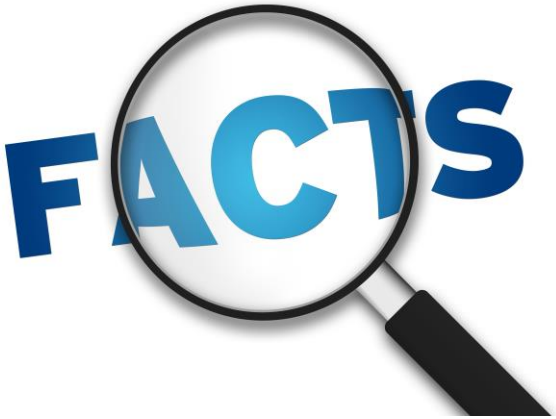
The COMP will require a higher level of data/evidence for the orphan status at the time of Market Authorisation.

It's very easy to be different, but very difficult to be better.

Jonathan Ive

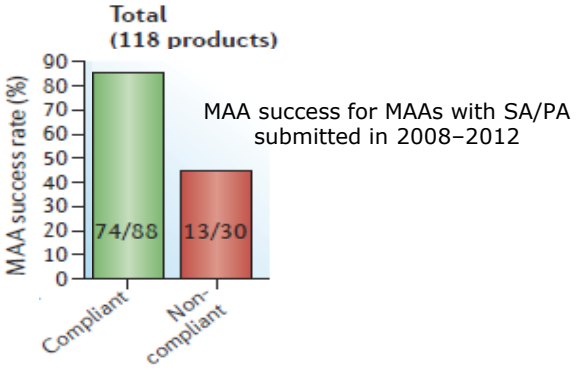
The orphan status of a product in Europe **is not easy to maintain** …



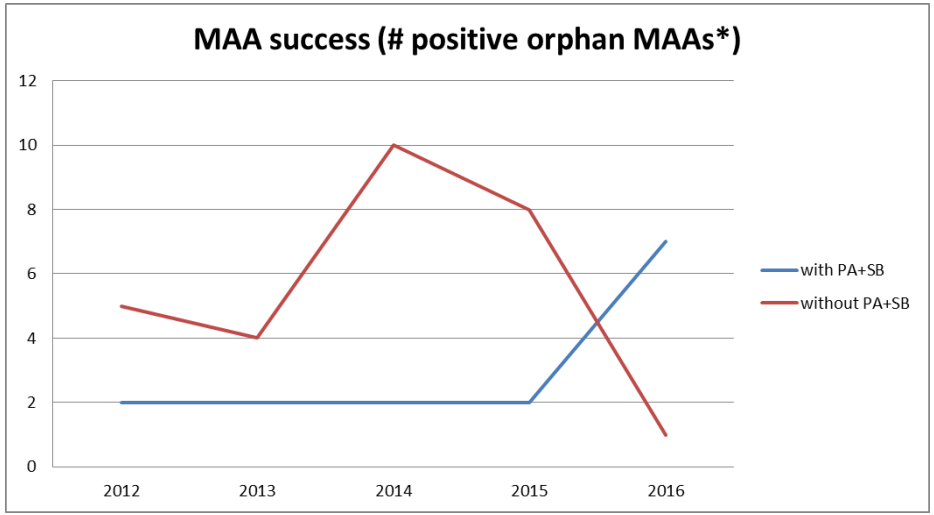


Orphan environment after 16 years of EU legislation

- Rising importance in PA+SB for marketing success
- Stark rise of appeal procedures on COMP SB assessment in 2016/2017



Hofer et al., *Nat Rev Drug Discov*. 2015



* Only orphan marketing authorisations with SB criterion

[adapted from Matthias Hofer, 2017]

How Applicants *[used to]* see us at the time of Marketing Authorisation

The orphan status of a product in Europe **is not meant to last forever**.

Art 8 (2):

This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the medicinal product concerned, that the criteria laid down in Article 3 are no longer met, *inter alia*, where it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity. To that end, a Member State shall inform the Agency that the criterion on the basis of which market exclusivity was granted may not be met and the Agency shall then initiate the procedure laid down in Article 5. The sponsor shall provide the Agency with the information necessary for that purpose.

Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation (EMA/COMP/15893/2009 Final)

At the time of initial Orphan Designation (OD):

Sound pharmacological concept to support the assumption

Compelling evidence in relevant preclinical models

Unconvincing preliminary clinical data

Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation (EMA/COMP/15893/2009 Final)

*'…the COMP will evaluate whether there is a high probability for the patients to **experience** a clinically relevant benefit… it has to be concrete and based on the data contained in the application for marketing authorisation and the arguments presented by the sponsor'*

Communication from the Commission on Regulation (EC) No 141/2000 on orphan medicinal products (2003/C178/02)

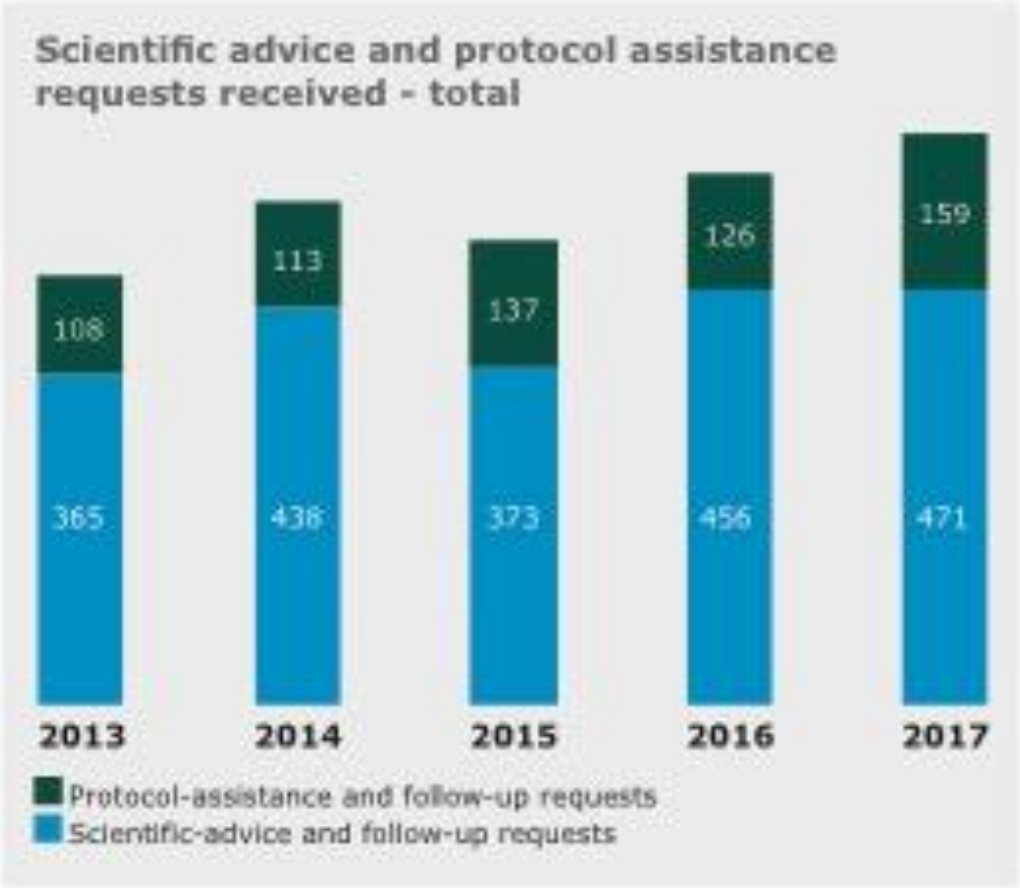
Replaced by:

Commission Notice on the application of Articles 3,5 and 7 of regulation (EC) No 141/2000 on Orphan Medicinal Products (2016/C424/03)

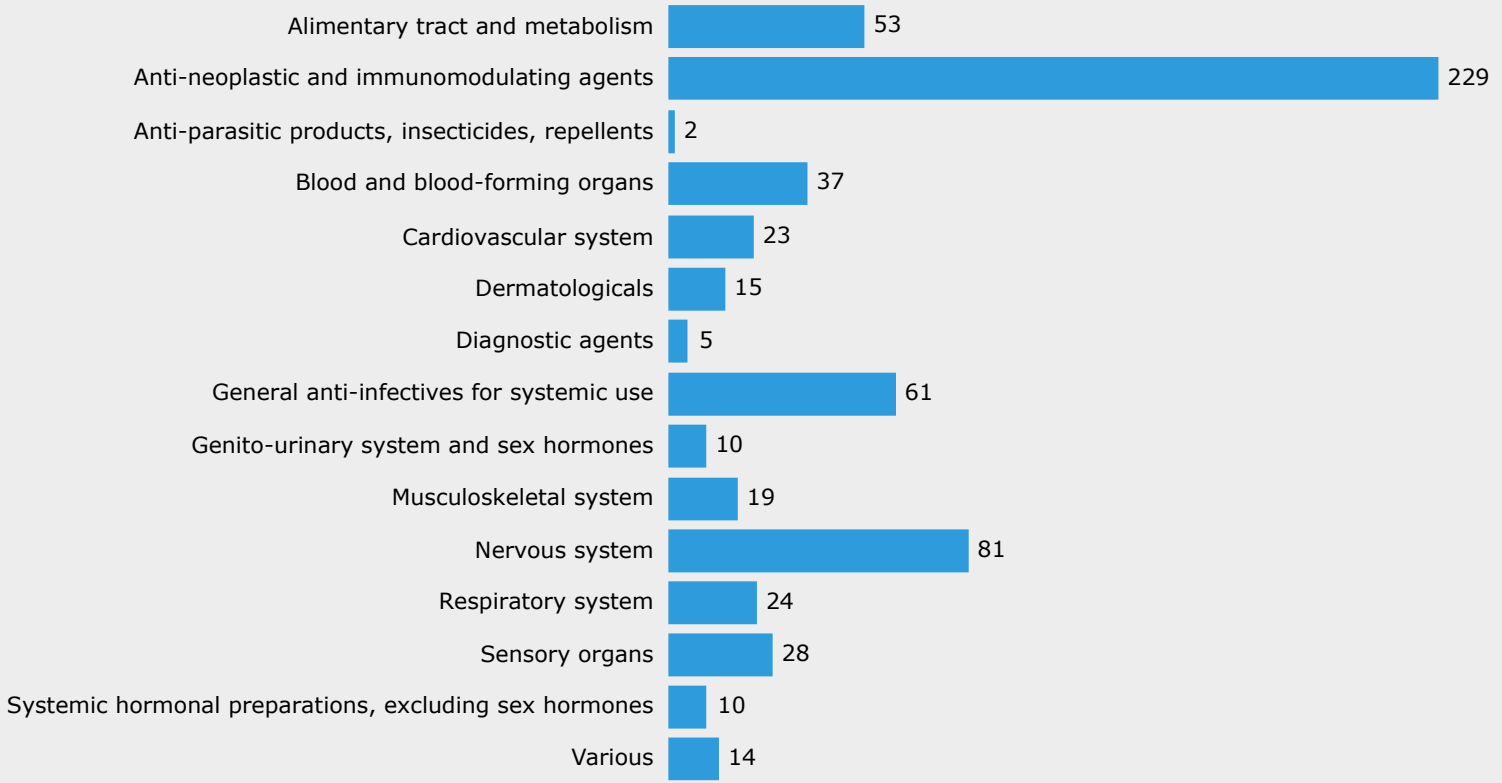
"Significant benefit' is defined in Article 3(2) of Regulation (EC) No 847/2000 as '*a clinically relevant advantage or a major contribution to patient care*'. The purpose of the legislation is to encourage and reward innovative treatments. These require investment in research and in the development of potential improved medicinal products that can bring meaningful advantages for patients. It is clear from Article 3(1)(b) of Regulation (EC) No 141/2000 and the spirit underlying the system it establishes, that the criteria for a finding of significant benefit are strict."

Commission Notice on the application of Articles 3,5 and 7 of regulation (EC) No 141/2000 on Orphan Medicinal Products

"Protocol assistance is recommended to ensure an appropriate clinical development …can also include guidance to demonstrate significant benefit…"

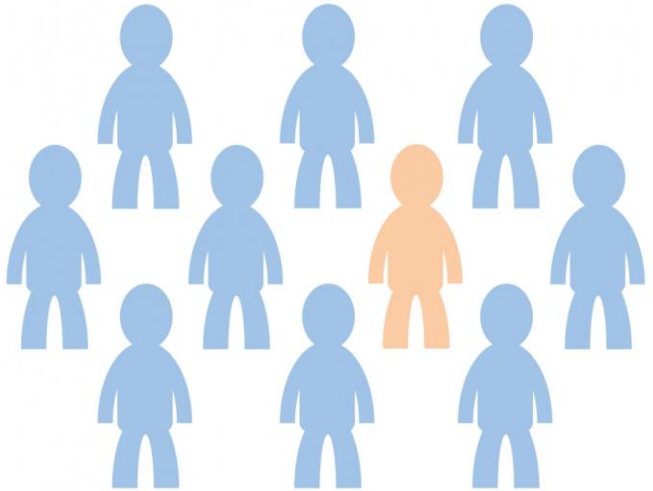

Scientific advice and protocol assistance requests received - total
108
365
113
438
137
373
126
456
159
471
2013
2014
2015
2016
2017
Protocol-assistance and follow-up requests
Scientific-advice and follow-up requests

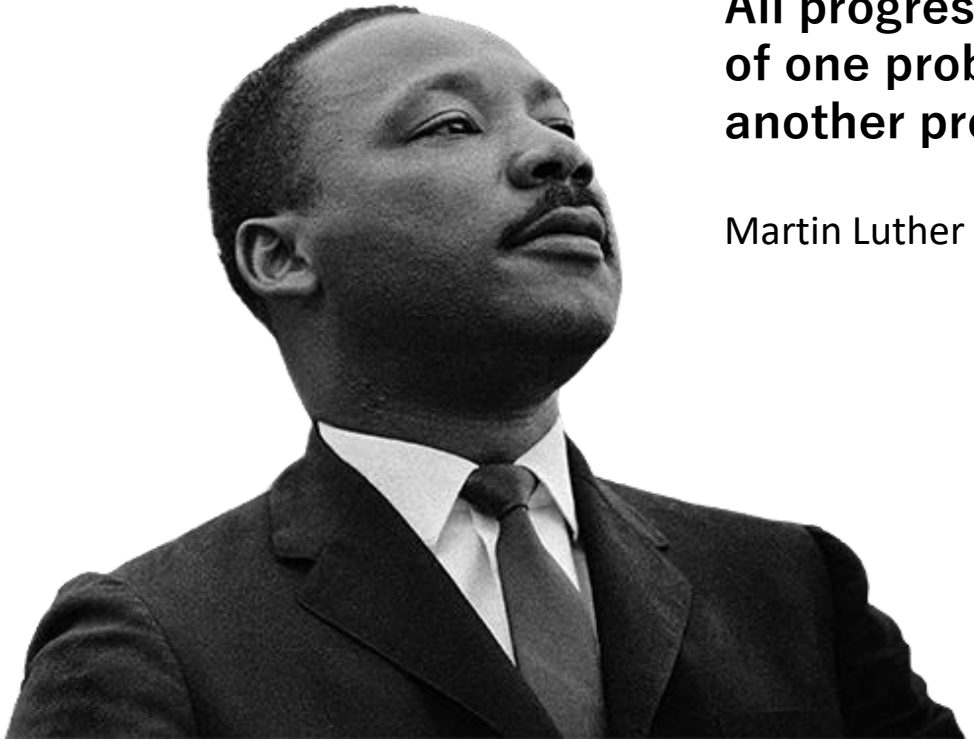
Scientific advice requests by therapeutic area (2017)



Commission Notice on the application of Articles 3,5 and 7 of regulation (EC) No 141/2000 on Orphan Medicinal Products

Decisions on the most relevant endpoints, including those capturing patients' views should stem from discussion and collaboration not only between regulators and industry, but also with **academia** and **patients** that have to work together to generate the data and work towards validation of new outcome measures to be used for regulatory purposes



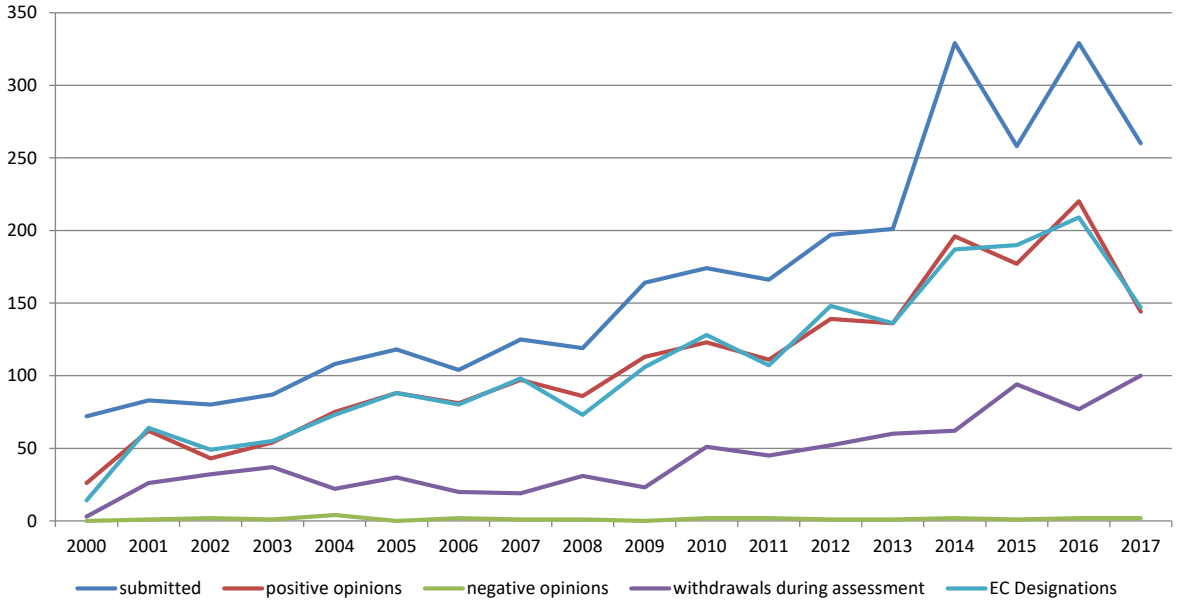


All progress is precarious, and the solution of one problem bring us face to face with another problem.

Martin Luther King

The changing world of Orphan Designations

Applications for orphan medicinal product designation



IRDiRC
INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

Objective 2020: 200 new therapies

Since 2000

2069 Orphan designations

166 Orphan designations included in authorised indication

151 Authorised OMPs

61 To be used in children

4 Removed from the market

45 Marketed, but no longer "orphans"

To date

106

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

06 September 2018

Translation of regulatory experience to guidance

The scientific and regulatory experience from designations, protocol assistance and marketing authorisations gives us valuable information to identify bottle necks and research needs

Analysing the reasons why there continue to be **gaps in the development of orphan medicines**

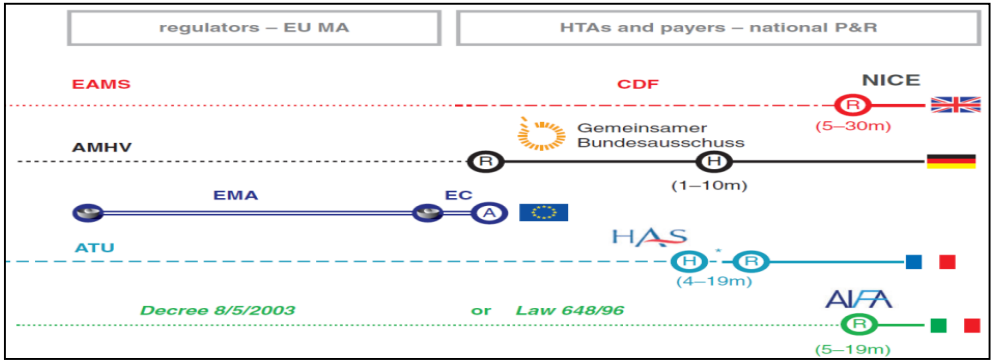
- negative outcome of a Marketing Authorisation assessment procedure
- withdrawn and negative applications for designation
- rare diseases where we see no or very little development

To be used to reduce the gaps for the benefit of the public health

> Regulators, HTA bodies and payers – we all perform an important task in one way or the other as gatekeepers for medicines to the healthcare systems in the EU. But we also have an increasingly important role as enablers of medicine development. Our cooperation can help medicine developers to address some of the inefficiencies in the current system of clinical research so that they become better at generating the evidence each of us needs for good decision-making.

Guido Rasi
EMA Executive Director

Reality check: from EU regulatory approval to national HTA/P&R decisions for orphan oncology products

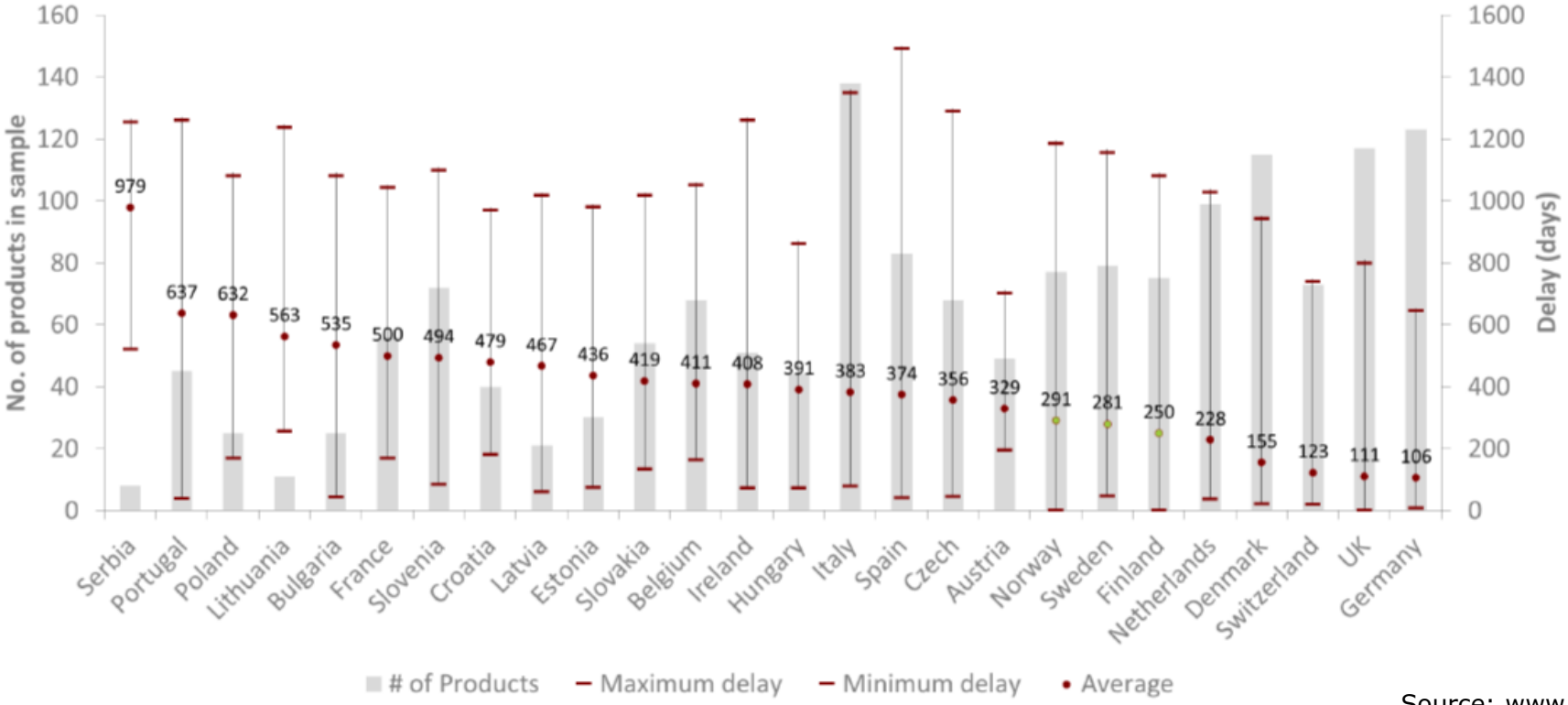


Orphan medicine	Indication	EU MA Approval	Time for HTA/P&R after MA (month)			
bosutinib (Bosulif)	chronic myeloid leukaemia	03/2013	7	7	11	18
cabozantinib (Cometriq)*	medullary thyroid cancer	03/2014	n/a	10	8	n/a

*first in class; MA = marketing authorisation; P&R = price and reimbursement cut-off: 15 September 2015

Martinalbo et al., Early access to cancer drugs in the EU. *Ann Oncol* 27: 96–105, 2016

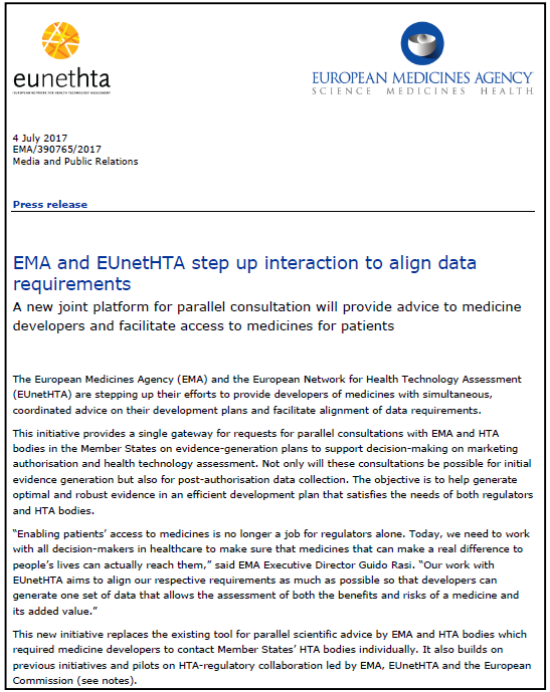
Differences in Time to Market Entry across EU countries



Source: www.efpia.eu

Synergy through alignment of evidence generation

- Experience shows that parallel scientific advice can **help to align regulatory and HTA views** on evidence needs
- There is close collaboration between EMA and EUnetHTA to **continuously optimise the processes** to facilitate such dialogue
- Whilst the focus so far has been on **evidence** needed **for market entry**, more engagement is needed on **post-licensing evidence generation**, which is particularly relevant for orphan medicines



eunethta

EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

4 July 2017
EMA/390765/2017
Media and Public Relations

Press release

EMA and EUnetHTA step up interaction to align data requirements

A new joint platform for parallel consultation will provide advice to medicine developers and facilitate access to medicines for patients

The European Medicines Agency (EMA) and the European Network for Health Technology Assessment (EUnetHTA) are stepping up their efforts to provide developers of medicines with simultaneous, coordinated advice on their development plans and facilitate alignment of data requirements.

This initiative provides a single gateway for requests for parallel consultations with EMA and HTA bodies in the Member States on evidence-generation plans to support decision-making on marketing authorisation and health technology assessment. Not only will these consultations be possible for initial evidence generation but also for post-authorisation data collection. The objective is to help generate optimal and robust evidence in an efficient development plan that satisfies the needs of both regulators and HTA bodies.

"Enabling patients' access to medicines is no longer a job for regulators alone. Today, we need to work with all decision-makers in healthcare to make sure that medicines that can make a real difference to people's lives can actually reach them," said EMA Executive Director Guido Rasi. "Our work with EUnetHTA aims to align our respective requirements as much as possible so that developers can generate one set of data that allows the assessment of both the benefits and risks of a medicine and its added value."

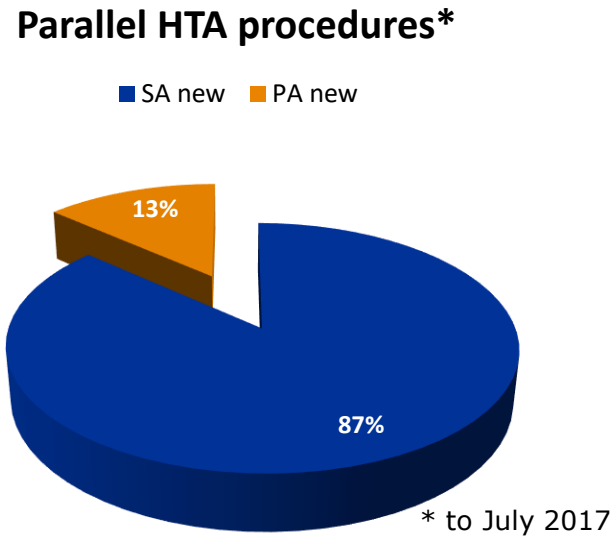
This new initiative replaces the existing tool for parallel scientific advice by EMA and HTA bodies which required medicine developers to contact Member States' HTA bodies individually. It also builds on previous initiatives and pilots on HTA-regulatory collaboration led by EMA, EUnetHTA and the European Commission (see notes).

Parallel regulatory/HTA advice for orphan medicines

Since the inception of parallel regulatory/HTA advice in 2010, there have been:

- 15 protocol assistance procedures on development of orphan medicines*
- 4 of these also covered questions related to the demonstration of significant benefit

* includes 2 follow-up requests



Opportunities to stimulate such discussions on development plan for orphan medicines.

[adapted from Michael Berntgen 2017]

Beyond the scientific/clinical debate on data and requirements

An orphan product in the US is also orphan in the EU

Significant benefit equals benefit risk

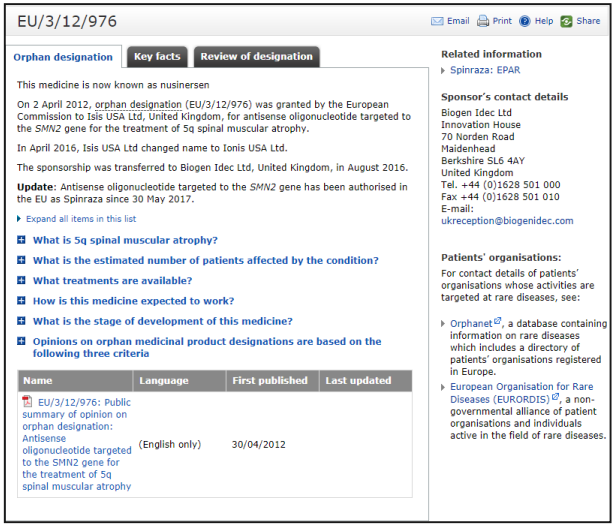
Personalised medicine means every disease can be orphan

Acknowledges the positive impact of Regulation (EC) No 141/2000 on the development of orphan medicines, which has enabled a number of innovative products for patients deprived of treatment to be placed on the market; notes the concerns surrounding the possible incorrect application of orphan medicinal products designation criteria and the possible effect of this on the growing number of orphan medicines authorisations;

EP report Options for improving access to medicines, March 2017

Currently published documents:

Public Summary of Opinion (PSO)



EU/3/12/976

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Orphan designation | Key facts | Review of designation

This medicine is now known as nusinersen

On 2 April 2012, orphan designation (EU/3/12/976) was granted by the European Commission to Isis USA Ltd, United Kingdom, for antisense oligonucleotide targeted to the *SMN2* gene for the treatment of 5q spinal muscular atrophy.

In April 2016, Isis USA Ltd changed name to Ionis USA Ltd.

The sponsorship was transferred to Biogen Idec Ltd, United Kingdom, in August 2016.

Update: Antisense oligonucleotide targeted to the *SMN2* gene has been authorised in the EU as Spinraza since 30 May 2017.

Expand all items in this list

- What is 5q spinal muscular atrophy?
- What is the estimated number of patients affected by the condition?
- What treatments are available?
- How is this medicine expected to work?
- What is the stage of development of this medicine?
- Opinions on orphan medicinal product designations are based on the following three criteria

Name	Language	First published	Last updated
EU/3/12/976: Public summary of opinion on orphan designation: Antisense oligonucleotide targeted to the SMN2 gene for the treatment of 5q spinal muscular atrophy	(English only)	30/04/2012	

Related information

Spinraza: EPAR

Sponsor's contact details

Biogen Idec Ltd
Innovation House
70 Norden Road
Maidenhead
Berkshire SL6 4AY
United Kingdom
Tel. +44 (0)1628 501 000
Fax +44 (0)1628 501 010
E-mail:
ukreception@biogenidec.com

Patients' organisations:

For contact details of patients' organisations whose activities are targeted at rare diseases, see:

Orphanet, a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.

European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Recommendation for maintenance of OD at the time of MA

EU/3/12/976

Orphan designation | Key facts | Review of designation

On 25 April 2017, the Committee for Orphan Medicinal Products (COMP) concluded its review of the designation EU/3/12/976 for Spinraza (nusinersen, previously known as antisense oligonucleotide targeted to the SMN2 gene) as an orphan medicinal product for the treatment of 5q spinal muscular atrophy. The COMP assessed whether, at the time of marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the condition, and the existence of other methods of treatment. The COMP recommended that the orphan designation of the medicine be maintained[1].

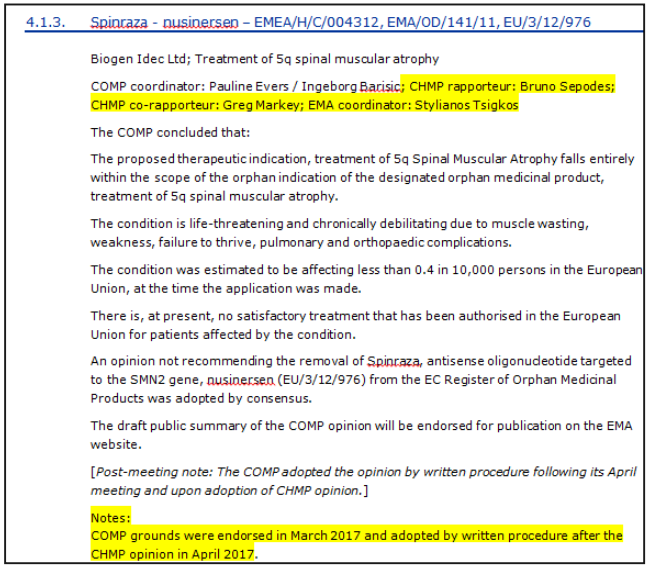
[1]The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after its authorisation similar products with the same therapeutic indication cannot be placed on the market.

Expand all items in this list

- Life-threatening or long-term debilitating nature of the condition
- Prevalence of the condition
- Existence of other methods of treatment
- Conclusions

Name	Language	First published	Last updated
Recommendation for maintenance of orphan designation at the time of marketing authorisation: Spinraza (nusinersen) for the treatment of 5q spinal muscular atrophy	(English only)	21/06/2017	

COMP minutes



4.1.3. Spinraza - nusinersen – EMEA/H/C/004312, EMA/OD/141/11, EU/3/12/976

Biogen Idec Ltd; Treatment of 5q spinal muscular atrophy

COMP coordinator: Pauline Evers / Ingeborg Barisic; CHMP rapporteur: Bruno Sepodes; CHMP co-rapporteur: Greg Markey; EMA coordinator: Stylianos Tsigkos

The COMP concluded that:

The proposed therapeutic indication, treatment of 5q Spinal Muscular Atrophy falls entirely within the scope of the orphan indication of the designated orphan medicinal product, treatment of 5q spinal muscular atrophy.

The condition is life-threatening and chronically debilitating due to muscle wasting, weakness, failure to thrive, pulmonary and orthopaedic complications.

The condition was estimated to be affecting less than 0.4 in 10,000 persons in the European Union, at the time the application was made.

There is, at present, no satisfactory treatment that has been authorised in the European Union for patients affected by the condition.

An opinion not recommending the removal of Spinraza, antisense oligonucleotide targeted to the SMN2 gene, nusinersen (EU/3/12/976) from the EC Register of Orphan Medicinal Products was adopted by consensus.

The draft public summary of the COMP opinion will be endorsed for publication on the EMA website.

[*Post-meeting note: The COMP adopted the opinion by written procedure following its April meeting and upon adoption of CHMP opinion.*]

Notes:
COMP grounds were endorsed in March 2017 and adopted by written procedure after the CHMP opinion in April 2017.

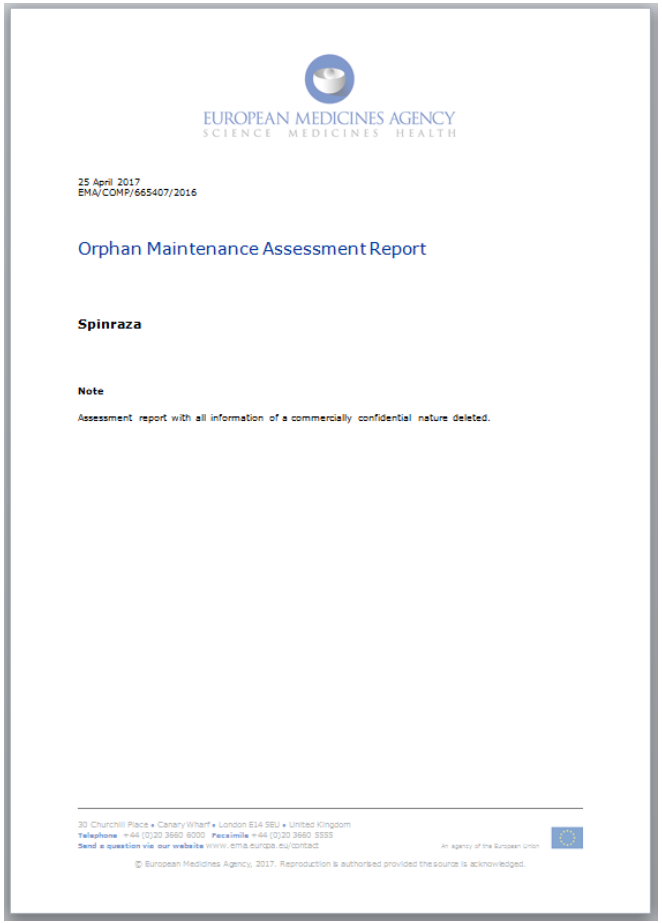
OMAR

Orphan

Maintenance

Assessment

Report



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 April 2017
EMA/COMP/665407/2016

Orphan Maintenance Assessment Report

Spinraza

Note

Assessment report with all information of a commercially confidential nature deleted.

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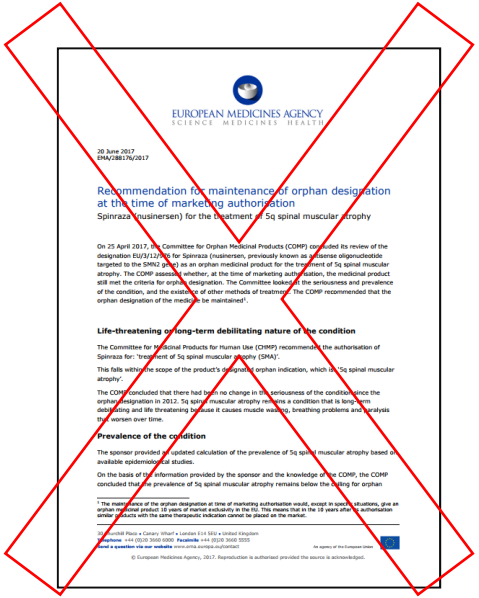

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 June 2017
EMA/288176/2017

Recommendation for maintenance of orphan designation at the time of marketing authorisation
Spinraza (nusinersen) for the treatment of 5q spinal muscular atrophy

On 25 April 2017, the Committee for Orphan Medicinal Products (COMP) concluded its review of the designation EU/3/12/976 for Spinraza (nusinersen, previously known as ISIS-SMN-Rx) a antisense oligonucleotide targeted to the SMN2 gene) as an orphan medicinal product for the treatment of 5q spinal muscular atrophy. The COMP assessed whether, at the time of marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the condition, and the existence of other methods of treatment. The COMP recommended that the orphan designation of the medicine be maintained[1].

Life-threatening or long-term debilitating nature of the condition

The Committee for Medicinal Products for Human Use (CHMP) recommended the authorisation of Spinraza for: 'treatment of 5q spinal muscular atrophy (SMA)'.

This falls within the scope of the product's designated orphan indication, which is '5q spinal muscular atrophy'.

The COMP concluded that there had been no change in the seriousness of the condition since the orphan designation in 2012. 5q spinal muscular atrophy remains a condition that is long-term debilitating and life threatening because it causes muscle wasting, breathing problems and paralysis that worsen over time.

Prevalence of the condition

The sponsor provided an updated calculation of the prevalence of 5q spinal muscular atrophy based on available epidemiological studies.

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of 5q spinal muscular atrophy remains below the ceiling for orphan

[1] The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after the authorisation similar products with the same therapeutic indication cannot be placed on the market.

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Where?

Spinraza

nusinersen

About | Authorisation details | Product information | Assessment history

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Changes since initial authorisation of medicine

Name	Language	First published	Last updated

Initial marketing-authorisation documents

Name	Language	First published	Last updated
Spinraza : EPAR - Public assessment report	(English only)	21/06/2017	
CHMP summary of positive opinion for Spinraza	(English only)	21/04/2017	

Spinraza: OMAR – Orphan Maintenance Assessment report

Spinraza

nusinersen

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Next tab »

This is a summary of the European public assessment report (EPAR) for Spinraza. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Spinraza.

For practical information about using Spinraza, patients should read the package leaflet or contact their doctor or pharmacist.

Expand all items in this list

- What is Spinraza and what is it used for?
- How is Spinraza used?
- How does Spinraza work?
- What benefits of Spinraza have been shown in studies?
- What are the risks associated with Spinraza?
- Why is Spinraza approved?
- What measures are being taken to ensure the safe and effective use of Spinraza?
- Other information about Spinraza

+ what is the orphan status?

Facilitating patient access through collaboration

The dialogue on evidence generation plans and the exchange on assessment outcomes are **two crucial pillars** to enable later patient access to orphan medicines

There are **specific topics and concepts** where regulators and down-stream decision makers can benefit from increased mutual understanding, also involving payers

Engagement and communication is crucial to ensure that healthcare systems are prepared for the needs of patients with rare diseases

Indiana Jones and the Raiders of the Lost Ark (1981)

Indiana Jones and the Raiders of the Lost Ark (1981)

End scene from Indiana Jones and the Raiders of the Lost Ark (1981)

Thank you for your attention

Further information

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