

HCPWP meeting: COMP feedback September 2018

Dr Daniel O'Connor (UK COMP representative)
On behalf of the COMP



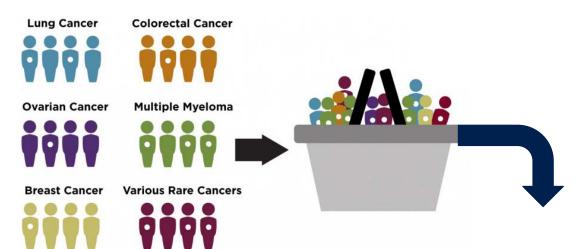






Importance of a valid orphan condition

- Orphan designation starts with the condition without it COMP cannot evaluate any of the other criteria
 - ➤ A condition is understood as any deviation from the normal structure or function of the body, as manifested by a characteristic set of signs and symptoms (typically a recognised distinct disease or a syndrome)
 - The condition is a critical first component needs to be rare!
- COMP asks details on the aetiology, specific characteristics, histopathology, clinical characteristics, classification, diagnosis and symptoms



Novel Trial Designs

- Increasingly drug development programmes are supported by novel clinical trial designs
- E.g. basket study which relies on extrapolation of evidence = challenges for orphan criteria

Therapeutic indication: treatment of unresectable or metastatic solid tumours with X mutation in patients who require systemic therapy

Traditional rare orphan conditions which may also express molecular marker

Orphan designation

Rare molecular defined subset of common tumours

? May meet the orphan designation criteria

Common molecular defined subset of common tumours

Unlikely to meet orphan designation

Image source: https://www.mskcc.org/blog/clinical-trial-shows-promise-basket-studies-drugs

Flexibility in the FDA approach to orphan drug development

Nina L. Hunter, Gayatri R. Rao and Rachel E. Sherman

Scientific advances, in combination with government incentives and commercial opportunity, have fuelled strong investment in orphan drugs, resulting in many innovative therapies.

- FDA: will need to take advances in genomics and precision medicine into account as it considers what constitutes an orphan 'disease or condition'
 - Whether a disease should be defined in a tissue specific or tissue agnostic manner?
 - Current scientific understanding may support the designation and approval of certain drugs across multiple rare tumour types
 - As more targeted therapies are developed, more drugs may qualify for orphan designation based on orphan subsets
 - how a disease is defined and whether a valid orphan subset exists may need to be refined
- **EU:** 'subsetting' a condition with the use of biomarkers will not be acceptable unless the sponsor provides solid scientific evidence that the activity of the product would not be shown on the larger population

COMP paper on defining the orphan condition

- Discusses challenging areas when delineating an orphan condition
- Four main sections:
 - Symptoms of a disease
 - Subsetting severity/ stages and biomarkers
 - latrogenic and adverse reactions to a medicinal product
 - Treatment modalities
- Provides an at-a-glance chart of available guidance

COMMENT

Defining orphan conditions in the context of the European orphan regulation: challenges and evolution

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The definition and acceptability of an orphan condition is pivotal for the assessment of European orphan medicinal product designation applications, and consequently the eligibility for incentives. Here, based on the experiences of the Committee for Orphan Medicinal Products, we discuss how to define orphan conditions in the context of the European regulatory framework.

 Explains COMP decisions in the context of the EU orphan drug regulation and provides some discussion points to help future sponsors

EC activities

- Regulation (EC) No 847/2000
 provides a definition of 'similar
 medicinal products' for the
 purposes of the application of the
 incentives provided under the
 Regulation
- Due to major developments in the field of biological medicines and technical progress including advanced therapy medicinal products (ATMPs), the definitions required adaption
- Two new documents released by the EC in May 2018 to reflect changing science

EN

II

(Non-legislative acts)

REGULATIONS

COMMISSION REGULATION (EU) 2018/781

of 29 May 2018

amending Regulation (EC) No 847/2000 as regards the definition of the concept 'similar medicinal product'

(Text with EEA relevance)

QUESTIONS AND ANSWERS RELATED TO THE ASSESSMENT OF SIMILARITY FOR ADVANCED THERAPY MEDICINAL PRODUCTS ("ATMPS") IN THE CONTEXT OF THE ORPHAN LEGISLATION.

FREQUENTLY ASKED QUESTIONS

Version 1

EMA activities

- An overview of the EU's orphan designation programme provided in a infographic →
- Questions and answers document addresses some common misunderstandings

28 February 2018 EMA/551338/2017

Rare diseases, orphan medicines

Getting the facts straight

EMA is eager for European citizens with rare diseases to have access to specific and effimedicines. The European Union's orphan legislation has been designed to help overcom hurdles these medicines face to get on the market.

Broadly speaking, the orphan legislation foresees giving orphan designation for substant be used for treating, preventing or diagnosing a rare and serious condition. Orphan deshelp the medicine's developer advance the medicine to the stage where it can be authoron the market. Formal approval (marketing authorisation) is needed before a medicine marketed.

Misunderstandings often arise about orphan medicines and how orphan designation is $\boldsymbol{\varsigma}$ following questions and answers address some common ones.

EMA

Orphan medicines in the EU—leaving no patient behind

thating offertive translates that a patient with one of the 6,000 near discusses our be very Offert. The Fifty explore designation programme encourages the decemperant of residence in this time material.

leaded deladed last

1 in 17 people in the EU has a rare disease

Amond 30 relitor people in the SU are thely to suffer from a debitating rare disease. The represents a huge unrest medical need and a significant jubble health challenge.

"This is beand to be extinuous 25 without patients with view otherwise and of a population of \$1.5 million in the \$1.5.

6000 rare diseases

When is a disease a rare disease?

A disease is coincidered rare of fewer than 5 to 10,000 people. Have 5, Very few medicines are evaluate for these lare observed. One of the research is that companies she has filling to recover the development coal for medicines for such small numbers of people.

Development of medicines for rare diseases

The BL offers transform to encourage companies to research and develop medicine for one disease. Dut of the transaction of the disease. To notice these transforms, companies ion apply for applies designation for their medicine, provided certain others.

Criteria for orphan designation

- The medians must treet, present, or dispose a disease which is the threatening or disposably debtacking, or it is underly that the medians will generate sufficient returns to justify the transformati messes for its development.
- The cleaner must not affect more than 2 in 10,000 people econor the EU
- No substaction method of diagnosis, prevention or treatment exists, or if such a method attenty exists, the medicine must be of digithout additional benefit to those affected by the condition.

Incentives.

Outing an original medicine's research and development, the company can benefit from incentives such as scientific advice on study protocols, vertices he reductions and access to EU grants.

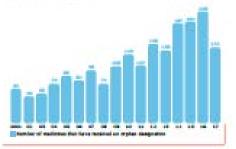
Orphan-designated meditines that eventually make it to the market, and for which it can be demonstrated that they market the criteria for the designation, are granted 10 years of market.

1900 medicines with orphan designation

EMA's Committee for Orphan Medicines

The Committee for Organia Healthrad Frieductic (CDFF) is to change of reviewing applications for organize designation.

If a medicine makes it is the merbelling exthorization stage, the COMP will means it again to direct whether the orderts are diff met and the upstern designation can be mentioned for the authorizant medicine.



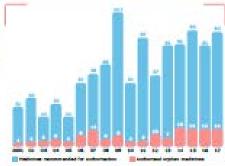
Orphan designation is not an authorisation

Not all contracting of all resolutions and the contracting author entire application stage. These that is, we excluded the first a Convention to Positions Position in Proceedings (COPP) using the assess which softly and off-timely standards that apply to all resolutions producted by PAA.

140 orphan medicines authorised in the EU

How orphan medicines reach patients

Once an orphan medicine is authorized by the Surspann Commission, it can be manifeld to all SU Herniter Balles. However, evaluating and reinforcement are subject to review by the reterent reduced authorities.







Thank you

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