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Support for development of orphan medicines EMA event 30 Nov 2020

Stakeholders' perspective on the value of orphan designation

SME perspective

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on behalf of EUCOPE

About 30 Million people living in the EU suffer from a rare disease - ODD a precondition for a MA of a OMP

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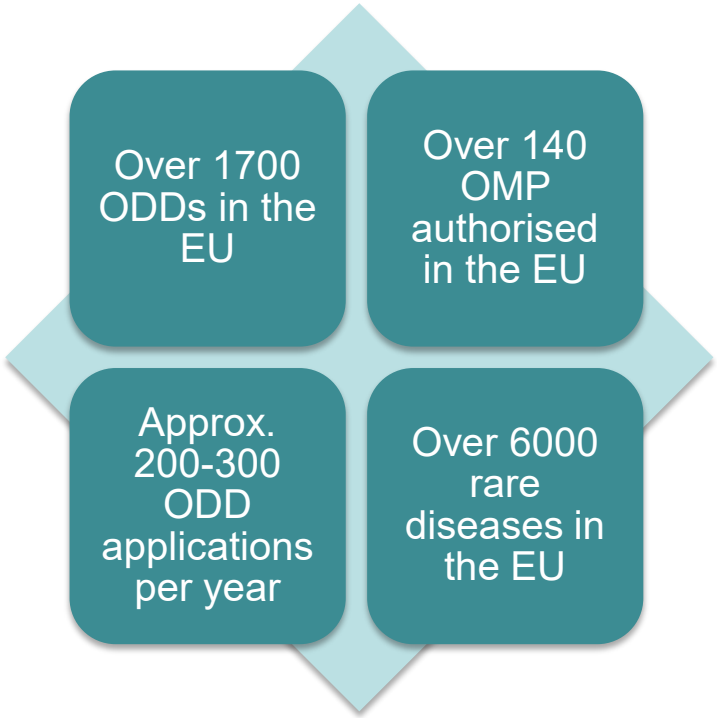
Orphan Drug Designation (ODD) - Orphan Medicinal Product (OMP)



Large number of ODDs leads to increased number of OMPs:

- Is this enough?
- What could be realistically expected in the last 20 years?

ODD - Orphan Drug Designation, OMP – Orphan Medicial Product, MA – Marketing Authorisation

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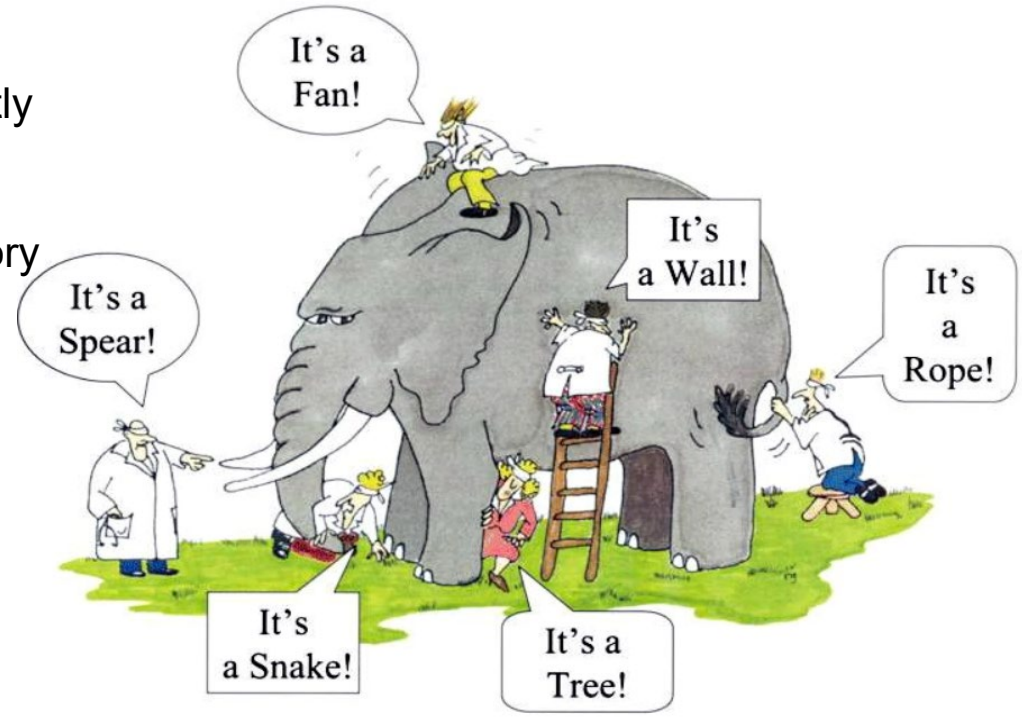
Rare Disease often highly heterogenous in clinical manifestations

- Rare Diseases often not well described in literature
- Scientific knowledge not sufficiently available
- Sometimes wrong scientific knowledge regarding natural history
- Heterogenous clinical manifestations
- Every rare disease different



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Orphan Drug Development

- Recognition of rare disease through ODD
- Very challenging diseases, often high heterogeneity

- Specific Rare Disease Development Program
  - Smaller, shorter, less studies? Innovative design?
  - Single arm studies?
  - Feasibility to conduct?
  - Real World Evidence (Registry & Data)
  - Key to involve the patient systematically into the development particularly for rare diseases (PRO development)
  - Important to involve HTA bodies

  - For Approval consider:
    Conditional Authorisation or Exceptional Circumstances

ODD - Orphan Drug Designation, PRO – Patient Reported Outcome, HTA – Health Technology Assessment

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What is the Value of an Orphan Designation?

The Orphan Drug Designation (ODD) of strong value:

- As pre- condition for development of orphan medicinal products
  - To address unmet medical need
  - For patients with debilitating or life-threatening diseases
  - EU harmonised approach for orphan disease
- Incentives during Development/Orphan Medicinal Products (OMP)
  - Reduced Fees for Centralised Scientific Advice (called Protocol Assistance) (minus 75%)
    - For paediatric advice (minus 100%)
  - MAA filing costs (minus 10%)
  - Inspection Fees (pre-authorisation) (minus 100 %)
  - **10 years of market exclusivity**

ODD - Orphan Drug Designation, OMP – Orphan Medicial Product, MAA - Marketing Authorisation Application

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What is the Value particularly for SME?

- SMEs benefit from even further reduction of costs for OMPs
  - Centralised Scientific Advice (called Protocol Assistance) (minus 100%)
  - MAA Submission (minus 100%)
  - Inspection Fees (pre-authorisation) (minus 100 %)
    - Inspection (post-authorisation) (minus 90%)
- SME office
  - As additional resource
  - Can help support/guide the SME
- Why should an SME consult EU regulators during development?
  - Challenging rare diseases
  - Discussion of development program at Protocol Assistance (significant benefit)
  - High value for development program
  - Ability to anticipate requirements for MAA

SME – Small & medium sized enterprise, OMP- Orphan Medicinal Product, MAA – Marketing Authorisation Application

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Challenges and room for improvement within the legal framework

- Increased requirements for ODDs (incl. significant benefit)
- Align various EMA committees on one development package
  - Few studies and patients to satisfy all stakeholders requirements
  - Specific patient expertise for committees and SAWP
- Global alignment regarding paediatric requirements for OMPs
- Global alignment for ODD
- Research incentives
- Innovative Drug Device Combination
- Improved involvement of specific patient expertise (regulators/HTA)
- HTA – additional requirements due to different mandates

ODD – Orphan Drug Designation, OMP- Orphan Medicinal Product, HTA – Health Technology Asessment, SAWP- Scientific Advice Working Party

Challenges for orphan and ultra orphan diseases for HTA

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Heterogeneous disease manifestation, often < 100 patients in the EU

<u>Comparative, randomized clinical study</u>

- For ultra-rare diseases often no comparator
- Standard of Care often diverse due to high heterogeneity in disease manifestation
- Many single arm studies - move towards agreement across stakeholders (regulators/HTAs) – value of RWE as acceptable methodologies for indirect comparisons

<u>Patient population</u>

- Extremely small

<u>Robust clinical outcome as primary endpoint</u>

- Very heterogenous patient population due to variable disease manifestation and progression
- No clinically robust primary endpoint for whole population, due to variable disease manifestations - instead various potential endpoints, per subset of patients.
- Patient Relevant Outcomes (incl. PRO) move toward acceptability
- Biomarker instead of robust clinical outcome endpoint, which is often not possible

HTA – Health Technology Asessment, RWE-Real World Evidence, PRO – Patient Reported Outcomes

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How to foster development of medicines in rare diseases ?

- Keep concept of Orphan Drug Development
- Provide a stable and positive environment for sustainability
- Further incentivise research and development
  - Address the knowledge gap (incl. patient involvement)
  - Lead collaboration within European Reference Networks (ERNs) to concrete actions for research and development through support (€)
  - Increase value of Real World Evidence (RWE) also for regulatory decision making and beyond
- Support integrated pathway for orphan drug device combination products
- Support HTA understanding of Orphan Medicinal Product specific requirements (patients and disease)

ERN – European Reference Network, RWE – Real World Evidence, HTA – Health Technology Asessment