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Rare Diseases Europe

Overview of Actions to Improve Access to Orphan Medicinal Products in Europe

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EURORDIS' Objective

To achieve the quickest access to as many safe, efficient and affordable medicines with a real therapeutic added value, for all rare disease patients in the European Union

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THE CONCEPTS

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Six Concepts

I. RD Treatments Evidence Generation is a Continuum

II. Regulators should adopt an official policy of flexibility and become Partners for Successful Development of Innovative Medicines

III. Focus on Effectiveness Beyond Quality, Safety and Efficacy

IV. Bridging the Gap between EU Centralised Regulatory Decision and National Decisions on Pricing & Reimbursement of EU 27 Member States

V. Enhancing the Dialogue between all Stakeholders all Along the Product Development & Life Cycle

VI. Financial sustainability for national healthcare system and societal acceptance

I. Evidence Generation: a Continuum !

RD treatments Evidence Generation is a continuum

- Marketing Authorisation is not anymore an on/off switch or a magic moment. Even less so for Orphan Medicines
- We need better and broader collection of relevant data all along the life cycle of the medicine on benefits as much as on risks:
  - Clinical trials
  - Compassionate use
  - Real life studies (actual heterogeneous population and real life constraints beyond clinical trials)
  - Off label use

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II. Regulators: Flexible & Partners

- Regulators are flexible - based on retrospective analysis of last 10 years experience of EMA and FDA - but they need to make it an "official policy" to:
- send the right message,
  - have better visibility, predictability, attractivity for drug developers
  - and better consistency of their scientific opinions
- Regulators need to change and have a supportive approach: Being a "Gate Keeper" is not good enough. Regulators should become "Partners for Successful Development of Innovative Medicines"
  - Conditional Approval
  - Even more intense roll-over process of Scientific Advice & Protocol Assistance before & after MA involving stakeholders
  - Next: Progressive / Adaptive Licencing

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III. Focus on Effectiveness

Focus on Effectiveness Beyond Quality, Safety and Efficacy

- Early dialogue between EMA, sponsors, medical experts, patient representatives on the Clinical Trial design to optimise resources allocation (number of patients, R&D investment, time of development) in a more proportionate manner to the expected level of evidence. This dialogue should take place as early as possible (ex: adaptive design in small population, de-link efficacy trials and safety trials, historical control)

- Anticipate more the demonstration of the therapeutic value (ex: registries, natural history, Good Clinical Practice Guideline on Diagnostic & Care, choice of comparator) and do it through Protocol Assistance (EMA) – Parallel to EUnetHTA?

- Key Success Factor: Interface and dialogue between regulators (EMA) and HTA (EUnetHTA) before and after MA

IV. Dialogue between EMA and HTA

Bridging the Gap between EU Centralised Regulatory Decision and National Pricing & Reimbursement Decisions.
A "must do" for Orphan Medicinal Products.

- HTA and Payers need to be involved in all procedural aspects at the EMA to be well informed about:
  - the reality of medical needs
  - the potential and reality of the product – what we know
  - the uncertainties – what we don't know
  - the pathway to generate additional evidence for well targeted patients and good medical practices – how to know

- Key Success factor: Building trust! An approach on pricing based on Value, means a common understanding of what is the Value of the medicine in question.

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V. Stakeholders Dialogue create Value

Enhancing the Dialogue between all Stakeholders all Along the Product Development & Life Cycle contributes to:

- Corporate Responsibility – unmet medical needs, improved patient access, certain degree of transparency on cost
- Shared-Value for all stakeholders – companies & shareholders, patients & physicians, payers & society
- Economic Sustainability & Public Perception

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VI. Financial Sustainability

Financial Sustainability for national healthcare systems and societal acceptance

- OMPs often more expensive than non OMPs due to:
  - Innovative technology involved
  - R&D costs + other costs divided by small number of patients
- However, high prices of some OMPs are not always justified
- High prices add to the discrepancy on access to OMPs in EU

→ EURORDIS and Stakeholders: Develop approach to reduce both cost of OMP per patient and budget impact for each OMP on the overall national healthcare budgets

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PROPOSALS

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EIGHT PROPOSALS

1. Early Dialogue & Horizon Scanning & De-Risking
2. Clinical Trials
3. Stronger FDA – EMA Collaboration
4. Clinical Added Value of Orphan Medicinal Products (CAVOMP) Information Flow
5. European Mechanisms of Coordinated Access to OMPs
6. Differential Pricing: a pilot with OMPs
7. Progressive/Adaptive Licensing / Step Wise Patients Access
8. National measures to be embedded in National Plans / Strategies on Rare Diseases in EU MS

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1. Early Dialogue / Scoping / De-Risking

- *EU Pharmaceutical Forum's Guiding Principles on OMPs recommends early dialogue*
- *Corporate Responsibility's Mechanism of Coordinated Access to OMPs recommends early dialogue*
- Early dialogue = a dialogue, at a very early stage of development, before orphan designation or protocol assistance, between 1 (or more companies) and all relevant stakeholders - EMA, HTA, Payers, Medical Experts, Patients -on a specific product (or on a specific rare disease) to discuss the potential to address an unmet medical need and the optimal research, regulatory, and health policy approach
- Next: at EMA and using Chattam House Rules?

2. Clinical Trials

EMA guidance:

- Guideline on Clinical Trial in Small Populations (design & statistical methods): need to be updated, strengthened, expanded
- Workshops & Points to Consider on Clinical Trials for Rare Diseases for which there is a cluster of designations
- Adaptive clinical trial design: more proactive promotion

EU Legislation:

- Ongoing revision of EU Directive on Clinical Trials toward an EU Regulation
- New amendments: European Expert Opinion and European procedure for Clinical Trials in Rare Diseases & OMPs

3. Stronger FDA – EMA Collaboration

Call for a Stronger FDA – EMA Collaboration:
Beyond Orphan Drugs Designation

- More Parallel Scientific Advice & Protocol Assistance
- Co-ordinated Guidelines / Points to Consider for Clinical Trials for specific Rare Diseases or group of diseases
- Sharing of File and Assessment at time of MA
- Mutual acceptance of data
- Coordination of Post-MA research plans

4. CAVOMP: Four Time Points

1. **Early dialogue**
2. **Compilation Report & evidence definition / Evidence Generation Plan**
3. **Follow-up of the evidence generation plan**
4. **Assessment of Relative Effectiveness**

- EUCERD Recommendation on CAVOMP adopted in October 2012 by 26 / EU27
- Pilots expected to start in 2014 (EMA and EUnetHTA)

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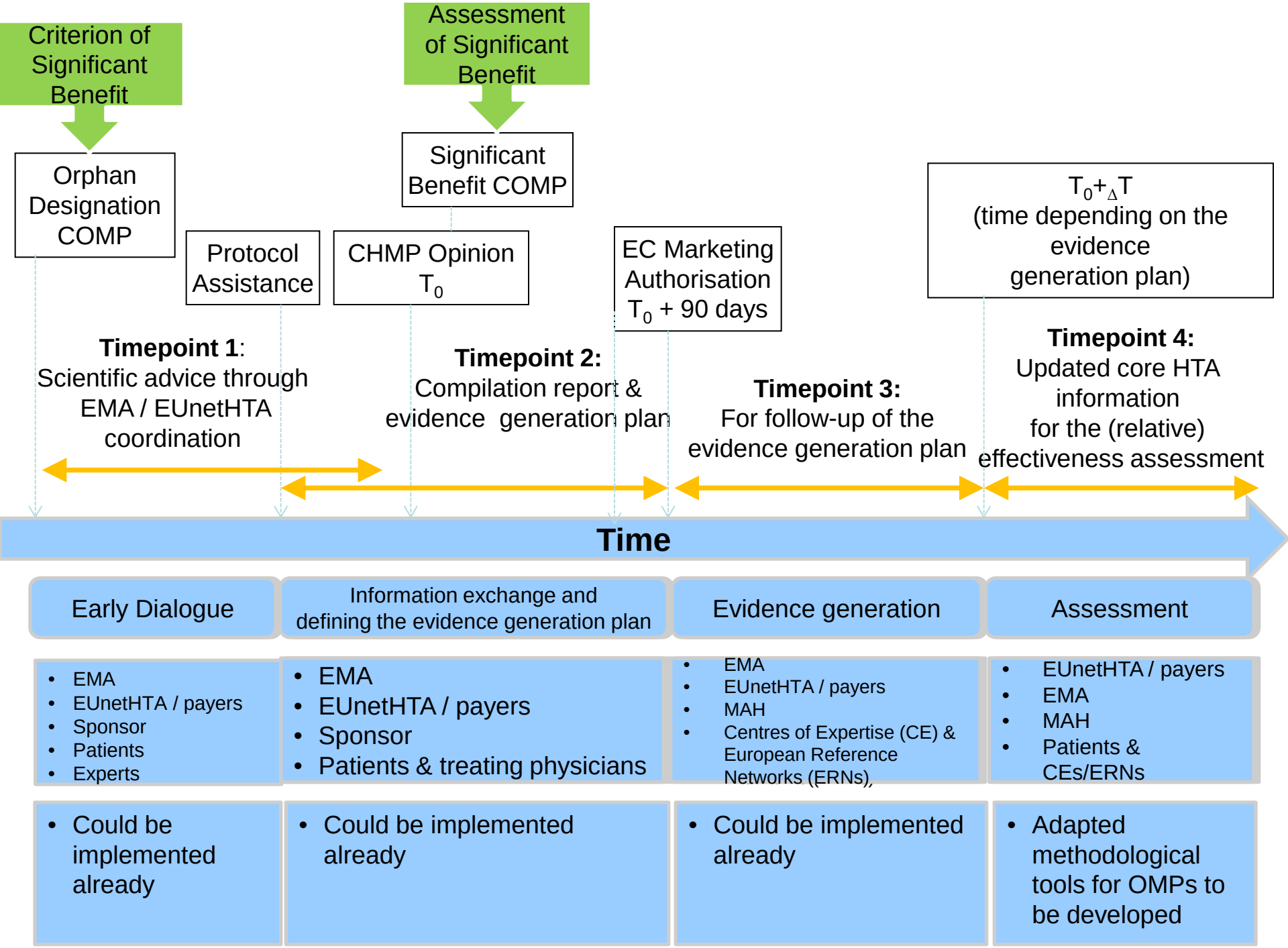
Criterion of Significant Benefit
Assessment of Significant Benefit
Orphan Designation COMP
Significant Benefit COMP
Protocol Assistance
CHMP Opinion T_0
EC Marketing Authorisation T_0 + 90 days
$T_0+_{\Delta}T$ (time depending on the evidence generation plan)
Timepoint 1: Scientific advice through EMA / EUnetHTA coordination
Timepoint 2: Compilation report & evidence generation plan
Timepoint 3: For follow-up of the evidence generation plan
Timepoint 4: Updated core HTA information for the (relative) effectiveness assessment
Time
Early Dialogue
Information exchange and defining the evidence generation plan
Evidence generation
Assessment
• EMA • EUnetHTA / payers • Sponsor • Patients • Experts
• EMA • EUnetHTA / payers • Sponsor • Patients & treating physicians
• EMA • EUnetHTA / payers • MAH • Centres of Expertise (CE) & European Reference Networks (ERNs)
• EUnetHTA / payers • EMA • MAH • Patients & CEs/ERNs
• Could be implemented already
• Could be implemented already
• Could be implemented already
• Adapted methodological tools for OMPs to be developed

5. MOCA

- A Mechanism for Coordinated Access to Orphan Medicinal Products at EU level – Volunteering Ms

- **Consensus**: A European Transparent Value Framework for a common assessment report based on multi-stakeholder dialogue (Authorities, MAH, experts, patients) and multi-criteria discussion with few first criteria: Rarity + Availability of alternative therapy + Relative Effectiveness/ Significant Benefit + Response rate + Robustness of data

- **Opportunity**: Price negotiation at European level based on Value (Common Assessment) + Volume (prevalence of therapeutic indication as defined in MA) + agreed Post-MA Research Activities

6. Differential Pricing

- Differential pricing is already a reality in today's OMP European market with variations of costs actually paid by MSs varying +/- 10% (without taking into account specific funding scheme with caps, rebate etc)

- Differential pricing for OMP can become a reality if limited to the scope of “authorised medicines” “unmet medical needs” + “High added value” and, associated with the negotiated / agreed price at European level (MOCA)

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7. Progressive Patients' Access (or Adaptive Licensing)

- For diseases which are severe, with no alternative therapies or non-satisfactory therapies
- Within current regulatory framework:
  - Conditional Approval
  - Progressive enlargement of targeted population treated based on hospital prescription & inclusion criteria
  - Collection of real life data within post-MA research activities (safety, efficacy, effectiveness) including new pharmacovigilance legislation, risk management plan…
- Within the new framework of healthcare organisation for rare diseases in EU with Centres of Expertise, European Reference Networks and Registries

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7. Adaptive Licensing: Pros

- Generation of real life data: an essential point for rare diseases as patients have a high heterogeneity
- Earlier patients access for the population targeted by the new therapeutic intervention beyond patients included in the clinical trials
  - Important for patients with no alternative therapy or no satisfactory treatments or limited treatment options
  - Important for hospital doctors who can become partners in clinical research development and elaborate better clinical practices
- Transfer of a significant part of research & development costs from sponsors/shareholders to healthcare payers/society thanks to earlier marketing authorisation and reimbursement
  - Important for SMEs to de-risk their investment and enable them to carry out studies generating the required level of evidence
  - Important for payers who gets lower price – lower Value and lower R&D Costs – and higher control on post-MA evidence generation

7. Adaptive Licensing: Cons

- Feasibility of limiting prescriptions to the targeted population? Yes, all OMPs for severe diseases are prescribed by hospital physicians
- Feasibility of carrying out the required clinical studies/ research activities after marketing authorisation? Yes, with careful planning of post-marketing research activities and rolling on protocol assistance
- Feasibility of withdrawing a conditional marketing authorisations? Yes, we need to educate EU & NCA as well as patients & clinicians
- Unwillingness of health authorities to pay for this? Yes, a risk to address. Arguments: Adaptive Licencing will bring down the prices; Conditional Pricing; Market Entry Agreement; Pricing scheme can include risk sharing and pay back
- Feasibility of revising the price or conditional pricing? Yes, based on evidence generated and real therapeutic value with proposed CAVOMP and MOCA; HTA & Payers can be partners in this policy

7. A Pragmatic Approach

- Today: Pilot Adaptive Licencing within current regulatory framework using Conditional Approval
- Limit "Adaptive licensing" to diseases that are severe, with no alternative therapies or non-satisfactory therapies (use same criteria as Compassionate Use)
- Limit "Adaptive Licensing" to prescription medicines restricted to hospitals: better understanding of trade-off between evidence generation and access + higher chances of collecting robust data rapidly; link to centres of expertise and registries with data reported by physicians along with patients reported outcomes
- Link "Adaptive Licensing" with compulsory Scientific Advice & Protocol Assistance from pre-clinical, phase I, II: continuum of dialogue with a "rolling-on" dialogue between sponsors and regulators on the research plan to generate the level evidence expected. Stop earlier when candidate to failure. Speed up access when promising

Key Success Factors

- A clear commitment within CHMP and among assessors – the national medicine agencies
- A clear commitment from HTA & Payers to accept Conditional Approval / Adaptive Licencing
- A clear commitment from EMA & CHMP to engage HTA & Payers in the dialogue at time of Protocol Assistance and review of MA
- Tomorrow: Integrate this « step wise patient access » into new EU Pharmaceutical legislation based on experience gained

CONCLUSIONS

Conclusions

At Minimum:

- Within the development of the National Strategy / Plan on Rare Diseases, encourage your Member State to embed in their strategy/ plan:
  - **The CAVOMP process**
  - **The MOCA process**

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Conclusions

- **A new policy** to support innovation, address unmet medical needs and improve patients access is possible based on proposals well identified.

- De-risking investment, reducing R&D growing costs, promoting a new economic model, more sustainable and more predictable both for payers and companies is possible.

- Development of medicines can be fostered based on a more robust collection of data coordinated at EU level all along the life cycle, on dialogue with all stakeholders, on collaboration between EMA & HTA & Payers.

Conclusions

- **We need more Europe not less**. More gathering of expertise. More streamlined processes. And a comprehensive approach to product development, approval, life cycle and good clinical practices.

- **We need a common understanding and clarity** across European Commission & European Parliament & EMA & EUnetHTA as well as across NCAs in MSs and companies in industry.

- **Robust decision making can be ensured**. We need decision makers to be less risk advert. There is no innovative medicine without risk.

THANK YOU

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