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THE NEW PARADIGMS OF RARE DISEASES TREATMENT DEVELOPMENT & ACCESS IN EUROPE

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THE NEW PARADIGMS

- Part I: in European Rare Diseases Policy
- Part II: in Treating Rare Disease Patients in Europe
- Part III: in Improving Access to Rare Diseases Treatments
- Part IV: in International Collaboration in Rare Diseases
- Conclusion: Expected actions
PART I

The new Paradigm in European Rare Diseases Policy:

From Regulations & Policy Framework to Implementation and Sustainability: Technical Guidance and Budget
OUR STRATEGIC VISION
AND STRUCTURED APPROACH

• **Integrated**: articulating national and EU levels

• **Comprehensive**: from research, drug development & access, health care provision, information, patient empowerment (so much more than orphan drugs or rare disease therapies, but also research and health care for rare diseases at large)

• **Long term**: until 2020 trying to build-in sustainability

• Driven by **patient advocacy**

• Developed through **partnership of all stakeholders**, intended to create value perceived by these stakeholders

• **Guided by** Regulations & Directives (laws), Recommendations & Communications (policies), Road Maps & Programmes & Guiding Principles & Expert Recommendations (technical guidance) and European Committees
2000 - 2011: BUILDING THE EU REGULATORY WITH AN INTERNATIONAL PERSPECTIVE

• EU Regulation on Orphan Medicinal Products
  ▪ Adopted in 1999, implemented since 2000
  ▪ Creation of the Committee for Orphan Medicinal Products (COMP) at the European Medicines Agency (including 3 patients’ representatives for the first time)
  ▪ Commission Communication on Orphan Medicinal Products, 2003

• EU Regulation on Medicinal Products for Paediatric Use
  ▪ Adopted in 2006, implemented since 2007
  ▪ Creation of the Paediatric Committee (PDCO) at the European Medicines Agency (including 3 patients’ representatives and their alternates)

• EU Regulation on Advanced Therapies
  ▪ Adopted in 2007, implemented since 2009
  ▪ Creation of the Committee for Advanced Therapies (CAT) at the European Medicines Agency (including 2 patients’ representatives and their alternates)
2000 - 2011: BUILDING AN EU POLICY ENVIRONMENT WITH AN INTERNATIONAL PERSPECTIVE

• **Communication from the European Commission** to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions: “Rare Diseases, Europe’s challenge” - 11 November, 2008

• **Council Recommendation on an Action in the field of Rare Disease** - 9 June, 2009
  - Creation of the European Union Committee of Experts on Rare Diseases (EUCERD) in November 2009; includes 4 EURORDIS patient representatives and their alternates & 4 industry representatives and their alternates
  - Recommendation to implement national plans or strategies for rare diseases in all EU Member States by the end of 2013
CURRENT PRIORITIES IN EU POLICY ENVIRONMENT WITH AN INTERNATIONAL PERSPECTIVE

  ▪ Rare Diseases: reinforced as a top priority
  ▪ Legal base for European Reference Networks of Rare Diseases
  ▪ Mobility of expertise and of patients across EU
  ▪ Strengthen EU cooperation on HTA
  
  => All these points have a direct impact on Access

• Optimal implementation of EU Pharmaceutical Regulations – including for orphan products - & EU Rare Diseases policy

• 3rd EU Public Health Programme (2014 – 2020) “Health for Growth”

• 8th EU Programme for Research and Innovation (2014 – 2020) “Horizon 2020”

→ Sustainability of the policy environment
UPCOMING POLICY EXPERT GUIDANCE
(WITH AN INTERNATIONAL PERSPECTIVE)

• EUCERD Recommendation on Quality Criteria for Centers of Expertise on Rare Diseases (adopted in October 2011)

• EUCERD Recommendation on Quality Criteria for European Reference Networks on Rare Diseases (November 2012 ?)

• EUCERD Recommendation on Improving Access through Clinical Added Value of Orphan Drugs (CAVOD) (June 2012)

• EUCERD Recommendation on Patient Registries (January 2013?)

• EUCERD Recommendation on Good Practice Guidelines for Diagnostic & Care

• EUCERD Recommendation on Quality Testing

• EUCERD Recommendation on Population Screening
PART II

The new Paradigm
To Treat Rare Diseases Patients in Europe:

Innovation in Healthcare Provision
RARE DISEASE TREATMENT GOES BEYOND ORPHAN DRUGS

• Bringing an orphan drug or rare disease therapy to patients goes far beyond providing a medicine, it is about treating a person living with a rare disease in a holistic approach and long term view on a chronic debilitating life threatening disease

  ▪ Access to quality information (on the disease, the diagnosis, the care, the medicines, the social and support services)
  ▪ Access to the actual diagnosis
  ▪ Access to Experts or Centers of Expertise, possibly networked into national / European / international Networks on Rare Diseases offering multidisciplinary approach
  ▪ Use of Good Clinical Practices Guidelines for Diagnosis & Care
  ▪ Data collection systems to monitor the rare disease population as well as the individual patient
  ▪ Access to Patients’ support, therapeutic education, social services
CENTRES OF EXPERTISE: QUALITY CRITERIA (EUCERD Recommendation’s main points)

- “CEs bring together, or coordinate, within the specialised healthcare sector multidisciplinary competences/skills, including paramedical skills and social services, in order to serve the specific medical, rehabilitation and palliative needs of rare diseases patients.” (EUCERD Recommendations)

- Linked with specialised laboratories and patient organisations
- **Produce/adhere to Good Clinical Practice for Diagnosis & Care**
- Assure quality of care
- Contribution to state-of-the-art research
- **Participation in data collection**
- **Participation in clinical trials if applicable**
- Links with other CoEs at national and EU levels
- **Integrated in a European Reference Network for Rare Diseases**
All rare disease patients should be covered by at least one ERN. No patients should be left outside.

Support a limited number of ERNs, 20 to 30.

Each ERN covering a broad range of diseases (progressively), clusters of RDs, gathered by therapeutic areas.

ERNs should structure expertise & patients’ healthcare pathways.

ERNs should share common tools and methodologies (in particular: data collection for registries, methodology to produce good practice guidelines for diagnosis and access, clinical trials in small populations, observational studies, research on treatment protocols etc).

With high level of inter-operability amongst ERNs.

With high level of flexibility (experts, geographic outreach).
RARE DISEASE REGISTRIES: GROWING CONSENSUS

• A high priority: natural history, protocol research, clinical trials…
• Rare disease registries rather than product registries
• Core to Centres of Expertise and European Reference Networks
• Progressive coverage of more rare diseases (toward all)
• Minimum common data set and standard operating procedure
• Data collection by HCP and by Patients Self-Registration
• Inter-operability
• Link disease registries and biological resources
• Public-private partnership
• Active involvement of Patients (governance, access & use of data)
• Common policy of public funding sources (e.g. EUCERD, IRDiRC)
STANDARD OF DIAGNOSIS & CARE

- Good Clinical Practices Guidelines for Diagnosis & Care will improve and raise quality of care across Europe
- Produced by the European Reference Networks for Rare Diseases
- Improved thanks to increased collection of data from registries, clinical trials, protocol clinical research
- Link to assessment of quality, safety and efficacy of medicines for rare diseases as well as progressively their relative effectiveness assessment
- Link to access & reimbursement of off-label use in some countries
PART III

The new Paradigm in Improving Access to Rare Disease Treatment to all patients in Europe:

New concepts and better practices to increase approval and access to life saving medicines
RARE DISEASE TREATMENTS EVIDENCE GENERATION IS A CONTINUUM!

- Marketing Authorisation is not anymore an on/off switch
- Better and broader collection of relevant data

Data collected all along the life cycle of the medicine on risks as well as on benefits:
clinical trials, compassionate use, real life studies (actual heterogeneous population and real life constraints beyond clinical trials), off label use
Regulators are flexible (Based on last years experience of EMA and FDA) but need to say it clearly, so have better visibility, predictability, attractivity and better consistency of scientific opinions

Regulators need to have a supportive approach: Being a Gate Keeper is not good enough + Regulators should be Partners for Successful developments

- Conditional Approval and MA under Exceptional Circumstances
- Need for an intense roll-over process of Scientific Advice & Protocol Assistance before and after MA
- Future: Progressive Approval / Adaptive Licencing
FOCUS ON EFFECTIVENESS
BEYOND QUALITY, SAFETY AND EFFICACY

• Early dialogue between regulators (EMA), sponsors, medical experts, patient representatives to adapt Clinical Trial designs, as early as possible (ex: methodology in small population, de-link efficacy trials and safety trials, historical control)

• Anticipate more the therapeutic value demonstration (ex: registries, natural history, Good Clinical Practice Guideline on Diagnostic & Care) in Protocol Assistance (EMA)

• Early dialogue between regulators (EMA) and HTA (EUnetHTA) to adapt Post MA Research Plan
TWO INNOVATIVE APPROACHES TO IMPROVE ACCESS TO ORPHAN PRODUCTS

• Coordinated approach at EU level

  ➢ **CAVOD:** a process to generate better evidence at time of MA and for post-MA research activities to assess the Clinical Added Value of Orphan Drugs (real life value, not clinical trial value) and the actual place of the product within the therapeutic strategy of the disease

  ➢ **MOCA:** Mechanism of Coordinated Access to Orphan Drugs between EU Member States, based on value, volume, access, generation of knowledge
PART IV

The new Paradigm of International Collaboration in Rare Diseases:

From Good Intentions to Joint Actions
ORPHAN DRUGS: RELEVANCE OF DEBATING INTERNATIONAL DEVELOPMENT & MARKETS

• Rarity of the diseases calls for an international approach to experts and to small patients population
• Companies act global for their drug R&D and commercialization
• Investors think global to assess their risks and potential return on investment
• The Potential Orphan Drug Market is global (the market of the targeted patient population affected by the conditions)

• But the Real Orphan Drug Markets (reimbursement) are local (country or sub-division of countries, not global, not regional)
• And Regulators are regulated regionally (e.g. EU, US) and act regionally
EURORDIS – NORD: A STRATEGIC PARTNERSHIP

• The common Voice of 60 million Patients
• People living with rare diseases are facing many challenges in common which could be better addressed on an international basis
• The common Vision that bringing together the rare disease patient communities from the USA and Europe would catalyse transatlantic collaboration of all stakeholders – patient groups, healthcare professionals, researchers, health industry, regulators, policy makers
• Strategic Partnership signed up in 2009
• Concrete achievements: Rare Disease Day, RareConnect, cycle of US / European / Transatlantic conferences, dialogue with industry and regulators
• Coordination of positions in regulatory framework and policy
• Launch of Rare Disease International Network and promote Rare Diseases as an International Public Health Priority: “Low Prevalence but High Impact”
GROWINGLY STRUCTURED NETWORKS, MOST WITH AN INTERNATIONAL PERSPECTIVE

- ORPHANET (1998)
- IRDiRC: International Rare Diseases Research Consortium (2011)
- Clinical Research Networks (e.g. ECRIN 2006)
- Common Methodologies on Good Practice Guidelines: Rare-BestPractices project (2012-2014)
- European Reference Networks for Rare Diseases (pilots since 2008 - expansion from 2014)
- Collaboration between EMA & FDA on orphan designation (2000; 2007)
- EMA dialogue with EUnetHTA + Patients & Experts (> 2010)
- EFPIA & PHARMA & IFPMA?
THE INTERNATIONAL RARE DISEASE RESEARCH CONSORTIUM (IRDiRC)

• Launch: April 2011

• A mechanism to catalyse collaboration on RD research on a global scale

• Two main objectives by the year 2020:
  • deliver 200 new therapies for rare diseases
  • diagnose most rare diseases by the year 2020

• Governance:
  • Executive Committee: members committed to invest 10 M EUR: Funding agencies from Member States, industry, not for profit bodies supporting RD research, as well as patient umbrella groups
  • 3 Scientific Committees: Diagnostics, Therapies, and Interdisciplinary

• 23 committed Research Funding Agencies from Europe, North America, Australia and Japan
CALL FOR A STRONGER FDA – EMA COLLABORATION: BEYOND ORPHAN DRUGS DESIGNATION

- Parallel Scientific Advice & Protocol Assistance
- Guidelines for methodology of clinical trials per disease or relevant group of diseases
- Sharing of File and Assessment at time of MA
- Mutual acceptance of data
- Coordination of Post-MA research plans
CONCLUSION: EXPECTED ACTIONS

- EC and EMA commit to optimal and full implementation of the Orphan Drug Regulation
- Recognise the continuum of evidence generation in orphan products and encourage collaboration between EMA and EUnetHTA in orphan products
- Make EMA flexibility practice an official policy to promote more on rare disease treatment development and approval
- Take a big new step in EMA-FDA collaboration
- EC, Member States, industry commit to improve patient access to orphan products with innovative approaches so to guarantee long term sustainability
THANK YOU