Relation between pharmaceuticals regulatory framework and timely access of patients to medicines: Reflection on difficulties and opportunities

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2015: a landmark for the EU pharmaceutical legislation (1/3)

1965: 50 years since first Community rules on medicinal products. **Directive 65/65/EEC**

- **prevent a recurrence of the thalidomide disaster**
- **safeguard public health by not allowing medicinal products ever again to be marketed without prior authorisation.**

- **1995: 20 years since:**
  - **The establishment of the EMEA**
  - **new European procedures : centralised procedure and mutual recognition procedure**

2015: a landmark for the EU pharmaceutical legislation (2/3)

- **2005: 10 years** since most provisions of the 2004 review of the Directive and Regulation took effect:
  - **New rules for approval of generics (8+2 yrs data exclusivity)**
  - **Scope of centralised procedure**
  - **Quicker approval process**
  - **Stricter pharmacovigilance**
  - **Increased transparency**
  - **Compassionate use**
  - **Support of SMEs**
- In addition legislation on **orphans** and **paediatrics**

2015: a landmark for the EU pharmaceutical legislation (3/3)

- Furthermore:

- In 2008 Strategic Commission communication on "**Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector"**

- And new legislation **on falsified medicines (2011)** and reinforced **pharmacovigilance (2010, 2012)**

Earlier Access to innovative Medicines

- Since the 1965 first pharmaceutical law a lot has been achieved:
  - **rigorous evaluation of safety, quality, and efficacy of medicines**
  - **Streamlined and efficient procedures for the evaluation and authorisation of medicines and post-authorisation monitoring**
  - **Incentives (market and data exclusivity, orphan and paediatric medicines) to encourage innovation**
  - **flexibilities (conditional MA, exceptional circumstances, accelerated assessment) for faster approval of medicines**
- Still one issue continues to be raised: **Earlier access to innovative medicines for patients**

Earlier Access to innovative Medicines

Several discussion fora and proposals have emerged the last years, including:

- **Council conclusions on the "Reflection process on modern, responsive and sustainable health systems" and Reflection process under the Council Working Party on Public Health at Senior Level (SLWP) : Subgroup on cost-effectiveness of medicines-**Coordinator: The Netherlands; Members: Belgium, Cyprus, Greece, Poland, Spain, European Commission
- **EMA: Adaptive licensing initiative**
- **The Innovative Medicines Initiative (IMI):** Medicines Adaptive Pathways to Patients (MAPP)
- **International developments on adaptive approaches to authorisation of medicines**

Council conclusions from December 2013 on the "Reflection process on modern, responsive and sustainable health systems"

- Council Conclusions encourage the Commission and MS to "*continue reflection, on a voluntary basis, on aspects that may have an impact on* ***availability, accessibility****, prices, costs,* ***patient safety and innovation of pharmaceuticals*** *and medical devices and, where relevant, on systems that facilitate access, while fully respecting areas of Member States' competence*"

Council Working Party on Public Health at Senior Level (SLWP)

- Reflection Process on modern, responsive and sustainable health systems: **Cost effective use of medicines**

- **One of the subjects considered*:***
  - *Can **time to market be shortened** without damaging the safety of pharmaceuticals?*
- **Recommendation of SG: To further explore the area of regulation and market access for pharmaceuticals**

- **At the SLWP meeting of 18 February 2014 it was considered that discussion on this topic could be continued at the Pharmaceutical Committee**

EMA-adaptive licensing pilot

- **EMA Road map to 2015**
  - **[…] a key issue for regulators will be whether a more 'staggered' approval' (or progressive licensing) concept should be envisaged for situations not covered by conditional marketing authorisations […]**

- "**Adaptive licensing** is a prospectively planned, flexible approach to regulation of drugs and biologics. Through **iterative phases of evidence gathering to reduce uncertainties followed by regulatory evaluation and license adaptation**, AL seeks to maximize the positive impact of new drugs on public health by **balancing timely access for patients with the need to assess and to provide adequate evolving information on benefits and harms** so that better-informed patient-care decisions can be made".

Eichler HG et al. Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval. Clin Pharm & Ther 2012, Vol 91 (3), 426-437

EMA-adaptive licensing pilot

- **Other features of adaptive licensing:**
  - 'evidence versus access balance'
  - **earlier regulatory approval** to align with patient needs for **timely access** and for data to inform medical decisions
  - Stepwise learning while **accepting acknowledged uncertainty** about product's efficacy and safety
  - progressive reduction of uncertainty
  - **staged approach to collection of evidence** and **consequent adaptation** of MA
  - More timely and open dialogue between sponsors, **regulators and payers**

EMA-adaptive licensing pilot

- **EMA** is planning to initiate soon a **Pilot Project on Adaptive Licensing** in order to address a range of **technical and scientific questions** and refine the understanding of AL

- The **Commission** services will need to examine the **legal and policy aspects** related to AL in collaboration **with the Member States** and by consultation of relevant stakeholders, as necessary

International developments-among others FDA Breakthrough Therapies

- In July 2012 the FDA Safety and Innovation Act (FDASIA) was signed. FDASIA provides for a new designation - **Breakthrough Therapy Designation**. A breakthrough therapy is a drug:

- intended alone or in combination with one or more other drugs to treat a **serious or life threatening disease or condition** and

- **preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies** on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

- If a drug is designated as breakthrough therapy, FDA will expedite the development and review of such drug.

  - http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/fdasia/ucm329491.htm

Regulatory flexibilities under the current EU legislation for timely access

- Approval with conditions
- Conditional approval*
- Exceptional circumstances*
- Accelerated assessment
- Compassionate use
- Treatment on a 'named-patient basis'

From 2003-2013: 56 conditional/exceptional circumstances MA over a total of 550 MA i.e. 10%

Discussion

The Commission services want to discuss with the Member States the **relation between pharmaceuticals regulatory framework and timely access** of medicines to patients, specifically regarding the following points:

1. Analyse the **perceived problem** and the **reasons** for it and to what extent they are related to marketing authorisation procedures or other policy areas
2. Examine whether **current approaches** to marketing authorisation meet the **objective to ensure timely access** of patients to new medicines
3. Study if there are **ways to improve the situation** within the current legal framework
4. Analyse the perceived **merits and weaknesses** of an **adaptive licensing approach** from the regulatory/policy point of view, including the acceptable levels of uncertainty, possible change of paradigm and the consequences of shifting evidence gathering to the post-authorisation phase
5. Examine how **AL fits within the current legal framework** and principles of legislation
6. Consider whether any **action** would be useful or necessary