Making Medicines Affordable

Patent linkage, Bolar, Paediatric Extension and Data Exclusivity

Beata Stepniewska

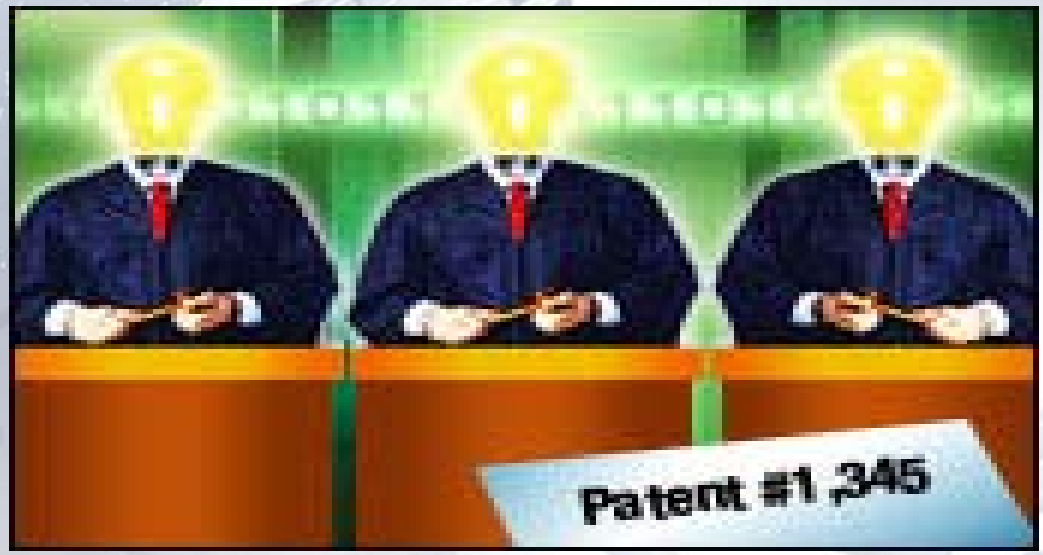
Director of Regulatory Affairs, EGA

Making Medicines Affordable

Latest developments on key provisions since September 2006 (EGA Annual Conference in Budapest)

Making Medicines Affordable

Patent linkage



What do we Understand by Patent Linkage?

- **Patent Linkage is**
  - linking the **marketing approval** or **pricing/reimbursment** status of generic medicines to the patent status of the reference products (RP)

Patent Linkage is Anti - European

- Clear abuse of EU regulatory system - **purposefully confused with US practices** which have no application to the EU system.
- EU Pharmaceutical law clearly allows development, application and registration during patent period.
  - **'Bolar' provision** **(Article 10.6. of Directive 2001/83/EC as amended).**

Different Levels or Types of Patent Linkage Exist

- Notification of generic application to patent holder
- Declaration of non-patent infringement to the Regulatory Authority
- No application allowed or authorisation granted during patent period
- Submission of patent status to Pricing & Reimbursement Authority

Current situation in the EU

- **France**
  - Notification of application to the holder of IP rights
- **Hungary**
  - Declaration that no intention to infringe a patent to be provided at time of application

Current situation in the EU

Italy

- Submission of application possible only 1 year before SPC expiry - for national MA
- For MRP/DCP – the application possible during the patent, but the final MA granted together with price after patent expiry

Italy (cont)

- **Decision issued 23 October 2006 in interlocutory injunction proceeding (Pronova against Chiesi)**
  - The Rome Court held that the filing of the generic application before patent expiry may result in infringement.
    - Filing shall be considered as a preparatory act for marketing
    - MA procedure is not an exception to Bolar
    - Court referred to the IP Code (art 61.5); if no SPC – filing only after expiry of patent
  - Court granted leave for investigative report by a court expert
  - Ruling after completion of technical investigation (date unknown)

Current situation in the EU

- **Slovak Republic**
  - Act 140/ 1998 relating to medicinal products and medical devices came into force 1 June 2006 (new §21a par. 8 g)
    - SUKL shall reject the application if the reference product or active substance used in the reference product is protected by patent or by Supplementary Protection Certificate (SPC).
  - Decree 477/2006 came into force 1 September 2006 with Appendix 23 on patent situation
- **EGA has appealed to the E Commission.**
  - On-going procedure re infringement of EU law by Slovak Rep

Slovak Republic (cont)

- **Latest changes in the legislation May 2007:**
  - §21a par.8 letter g) deleted from the Act 140/1998.
  - New §22 par.8 was added
    - *"(8) When a decision on registration does not involve original product, decision on registration of medicinal product enters into force the day after a day of expiry of the patent protection of the product or active substance in the product".*
  - Amendment to the Act 140/1998 will come into force on **1 July 2007**
  - Negative impact on pricing/reimbursement procedure
  - EGA will continue to oppose

Current situation in the EU

- **Portugal**
  - Infarmed sued by MSD for granting generics' MA of Alendronic Acid during patent protection period
  - Still on-going case

Sweden

- **T 22250-05 Pfizer v. Stada – Judgement of 1 June 2006 –**
  - **Decision by the Court: Stada infringed patent by seeking reimbursement/asking for a price to the authorities.**
  - **Request of price was considered as as a 'product offer infringing the SPC' even if Stada did not offer the product for sale.**
- **Stada has appealed**
  - Still on-going procedure

Sweden

- Risperidon case- Jansen against MPA and Sandoz
  - Janssen has stated that the Medical Products Agency must consider whether patent protection exists when assessing substitutability
  - Administrative Court of Uppsala on 14 February 2007 rejected Janssen's appeal

Positive Decisions of the Courts (1)

- **Spain**
  - Madrid High Court 2006: application for reimbursement status does not constitute offering as the product is not purchased by the social security system
- **Belgium**
  - Brussels First Instance Court 2006 (MSD against ratiopharm)
    - Application for MA and price and reimbursement as not regarded as patent infringement

Positive Decisions of the Courts (2)

- **Netherlands**
  - Two judgments: Glaxo against Merck and Elly Lilly against Pharmachemie
    - Publication of price on pricing list not considered as patent infringement
- **France**
  - Tribunal de Grande Instance of Paris (30.01.1998) Allen&Hanburys against Scat/ Pharmafarm
    - Putting a medicine on the reimbursement list is not considered as patent infringement

Preliminary Conclusion

- Level of severity of patent linkage is increasing.
- Patent linkage tends to move also into post-authorisation area like pricing and reimbursement.
  - Market entry of generics at patent expiry is threatened
- Pending court decisions will be critical to future developments; originators likely to continue their pressure

WHO Briefing Note
Access to Medicines

March 2006.

- *'Linkage' is also problematic in view of the fact that patents are private rights; as such, they should be enforced by the right holders, not by the government.'*

WHO Contd.

- *'From the perspective of access to medicines, this is a worrying trend; countries should be vigilant and should not 'trade away' their people's right to have access to medicines.'*

Implementation of Bolar provision

Implementation of Bolar at national level

- **Different implementation at national level:**
  - Only in patent law: AT, HU, DE, IT, IRL, MT, RO, SLO, TR, UK, S, ES, FI, FR, CZ
  - Only in pharmaceutical law: PT, LT, SK
  - In patent law and pharma law: BE (different scope), DK, NL,

Scope of Bolar at national level after implementation (1)

- **Different scope at national level:**
  - Limited to generic and biosimilars (Art 10.1-4 Dir) BE (ph law), IRL, UK, LT, PT, NL, ES*
    - * only „clasical" generics in the legal text
  - Broader scope: BE (pt law) HU, DE, IT, MT, RO, SLO, SK*, TR, S, FI, DK, FR, CZ
    - for any medicinal product
      for comparable studies, fixed combination products..
    - for experimental purpose
    - * if full pharmaceutical, preclin/clin studies are performed

Scope of Bolar at national level after implementation (2)

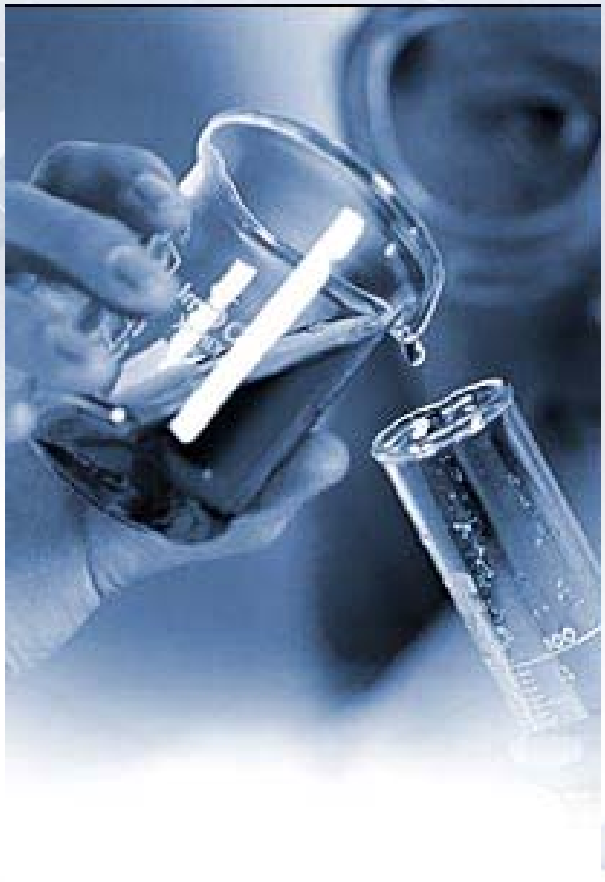
- **Specific scope of Bolar :**
  - All necessary test and trials in the purpose of MA in any country: AT, DE, IT, DK, LT, MT, ES
  - Manufacturing of samples: AT
  - Development of APIs; the preparation and the use of the active pharmaceutical ingredients : IT, ES

What is the meaning of '*Consequential Practical Requirements*'?

- **No clear explanation in the legal text**
  - Only Minutes from the meeting of Council Working Party on Pharmaceuticals (May 2003)
    - *The submission and subsequent evaluation of an application for a marketing authorisation as well as the granting of an authorisation are considered as administrative acts and consequently as falling outside the scope of patent protection.*

Conclusions regarding Bolar

- **Disharmony of exceptions to patent infringement after transposition**
  - Final wording after national implementation is important
- **Still several questions without answers (grey zone)**
  - Where do the commercial activities start?
  - Sufficient incentive for court cases?
- **ECJ might be in favour to Generics as the intention of the new law was to**
  - Increase generics' competition
  - Increase the EU competitiveness



Making Medicines Affordable

Paediatric Medicines Regulation

Status & timetable (1)

- **Publication in EC Official Journal *27* December 06**
  - http://ec.europa.eu/enterprise/pharmaceuticals/paediatrics/
- **Legally <u>into effect since 26 January 2007</u>**
  - direct effect because Regulation does not require transposition into national laws like directives do

    - Some aspects will not take effect until June 2007, or even June 2008

Impact on Generics companies

- **A mix of rewards and insentives**
  - On-patent products:
    - New application
    - Variation/extension for new indication, route of administration, or pharmaceutical form
  - Off- patent products
- **The biggest threat:** 6 month SPC extension
  - 6 months notice
    - ***For 5 years the*** *application for an extension of the SPC* ***shall be lodged not later than*** *6 months before SPC expiry.*

6-month SPC extension

- Reward when PIP fulfilled - whether (new) study reveals should or should not be used in children
- Product must be authorised in all Member States
- Not cumulating with the additional year of market exclusivity which can be gained for a new indication (i.e. 8+2+1)
- Orphan products excluded – market exclusivity extended (from 10) to 12 years

Opportunities for off-patent products

- Paediatric Use Marketing Authorisation “PUMA”
- Funding under EU 7th Framework Programme for Research for off-patent/SPC medicines or active substances

PUMA - incentives

- **Possible to authorise paediatric product separately**
  - with its own 8+2(+1) years data/market exclusivity No need for MA in all MS
  - Brand name may be retained
  - Stand alone or abridged application with cross-reference to adult product
  - Covers exclusivelly paediatric indication(s) and formulation
  - Requirement for separate paediatric product – marked with “a European logo”
  - Reduced fees & free scientific advice
  - Choice of registration procedures

PUMA - limitations

- No protection from (off-label) substitution - an already-established practice
- Hence, will probably only work if new formulation
- Reimbursement status not guaranteed (national)
- Considerable investment in trials and development of new formulation without guaranteed market for return

Funding under EU 7th Framework Program

- **Principal conditions:**
  - Up to 6 m Euros per project
    - 3 partners from 3 countries (27 EU plus associated countries: IS, LI, NO, CH, IL, TR, HR)
    - different types of organizations: universities, research centres, SMEs, large companies, etc.
  - Priority list for off-patent products published on EMEA Web (www.emea.europa.eu)
    - Patent status not checked by the EMEA
  - Development can be also covered
  - Deadline for application: **18 September 07**

Useful links

- **Community Research & Development Information Service :**
  - http://cordis.europa.eu/en/home.html
- **Calls for Proposals :**
  - http://cordis.europa.eu/fp7/dc/index.cfm
- **Health :**
  - http://cordis.europa.eu/fp7/dc/index.cfm?fuseaction=UserSite.CooperationCallsPage&id_activity=1
- **Work Programme, incl. Paediatric Medicines**
  - http://cordis.europa.eu/fp7/dc/index.cfm?fuseaction=UserSite.CooperationDetailsCallPage&call_id=10

Making Medicines Affordable

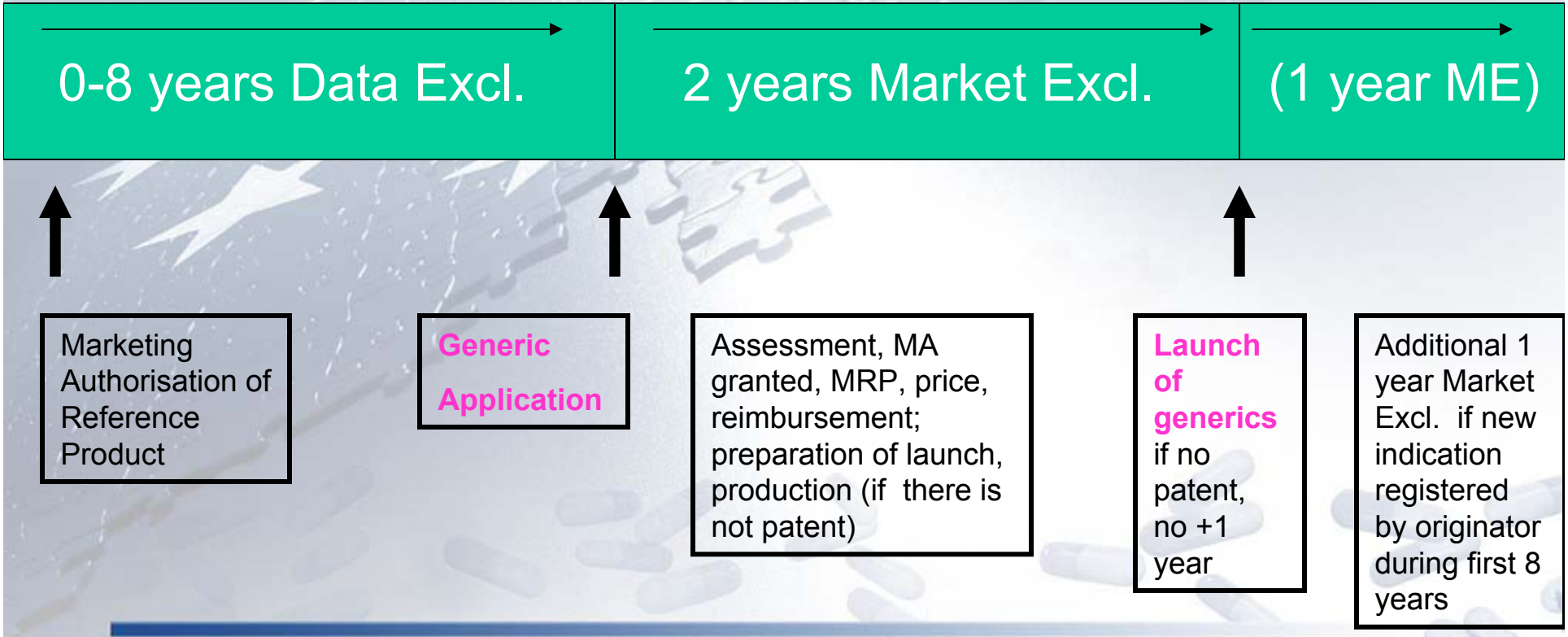
Data Excusivity

New Data exclusivity rules

- **Global Marketing Authorisation:**
  - any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions of Reference Product should be treated as a part of initial MA
- **8+2+(1) formula for all products and all procedures**
- **1 year DE for new indication for well established use substance (WEU)**
- **1 year DE for change of classification**

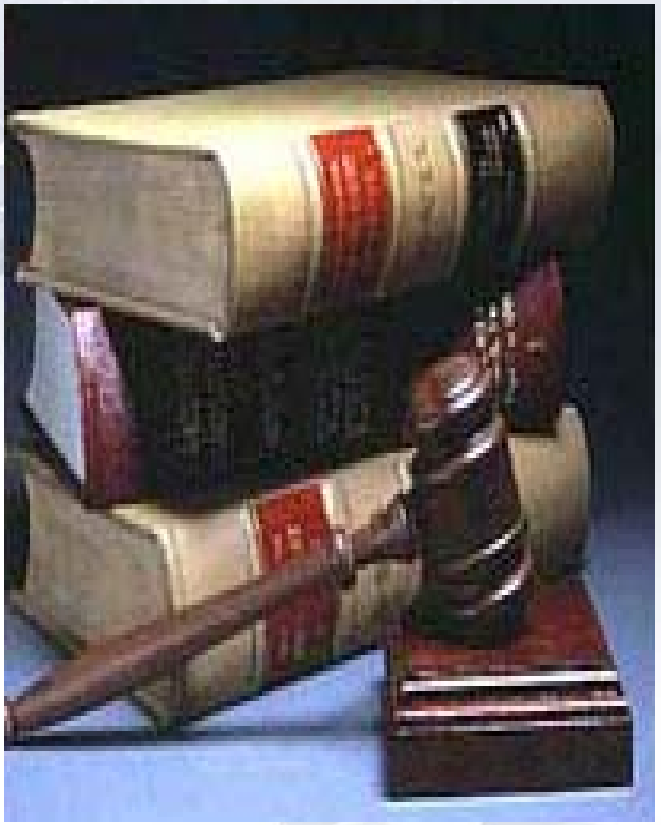
Data exclusivity

- **8 + 2 +(1) formula for all MA procedures**



Request for transitional period from some new MS

- **6 countries have requested the transitional period for 8+2 (+1) DE:**
  - HU, MT, LV, PL, SLO, CY(?)
- **On-going procedure**
  - 6 year DE in new legislation in **HU, PL, LV**
- **Prospective implementation**



Implementation of 8+2+1

- Interpretation of *new indication bringing 'significant clinical benefit'*
  - *Draft guideline on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in order to benefit from an extended (11 years) marketing protection period*
  - Released for consultation (17 February 2006)
  - **Final guideline not yet available**
    - the revised version recently endorsed by the Pharmaceutical Committee with minor changes.

Conclusion on Data Exclusivity

- **To monitor closely:**
  - Transitional period for DE
  - Publication of guidelines
  - Outcome of court cases, particularly on Global Marketing Authorisation

Making Medicines Affordable

Thank you!

Acronyms Used (1)

- EC European Commission
- EMEA European Medicines Agency
- CMD- Coordination Group for Mutual Recognition (MRP) and Decentralised Procedure (DCP)
- MPA- Medicinal Product Agency in Sweden
- SUKL- Medicinal Product Agency in Slovak
- SPC- Supplementary Protection Certificate

Acronyms Used (2)

- SmPC- Summary of Product Characteristics
- SMEs Small and Medium-sized Enterprises
- SPC Supplementary Protection Certificates
- DE - Data Exclusivity
- ME - Market Exclusivity
- BEQ- Bioequivalence
- WHO World Health Organisation