Well-established use applications in EEA

STADA Arzneimittel AG
Regulatory Affairs

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1895
Founded in Dresden as a pharmacists’ association

2005 – 2007
Start and expansion in Eastern Europe: acquisition of Nizpharm and Makiz Pharma, Russia, as well as Hemofarm Group, Serbia

STADA is a global company with more than 50 sales companies in more than 30 countries, divided among four market regions:
• Germany
• Central Europe
• CIS/Eastern Europe
• Asia & Pacific
STADA in Serbia

- STADA represented by Hemofarm
- Founded in June 1960
- Part of STADA since August 2006
- Largest exporter of medicines in Serbia with a market share of 67%
- Approx. 2,500 employees
- Production and office space of over 80,000 m²
- Active in over 30 countries on three continents

Development Centers for the European market:
- Vrsac (Hemofarm, Serbia)
- Bad Vilbel (STADA, Germany)
## Application types in the EEA

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‘Full dossier application’

- **Article 8 (3) - Full Application**
  - Administrative Data (Module 1)
  - Quality documentation
  - Non-clinical data
  - Clinical data

- **Article 10a – Well-established Use Application**
  - Administrative Data (Module 1)
  - Quality documentation
  - Non-clinical and Clinical Data can be replaced by literature
Article 10a – Well-established Use

The Applicant has to show and prove

• the extensive medicinal use (‘Well established Use‘)
• and an acceptable level of safety
• by means of bibliographic data (only) to support the safety and efficacy aspects
• own studies can be submitted as supportive but not as pivotal data
  = Borderline to other types of application e.g. generic application
Article 10a – Well-established Use

- a full and independent application
- at least 10 years of well established medicinal use from the first systematic and documented use of that substance as a medicinal product in the EU
- quantitative aspects of the use
- degree of scientific interest (reflected in the published scientific literature)
- coherence of scientific assessments regarding safety and efficacy
- all documentation = favourable and unfavourable published scientific literature
- search strategy and justification for inclusion of references to be described in detail
WEU Applications: General rules

- no circumvention of data exclusivity
- not for failed Generics
- not for new indications or populations
- not for new pharmaceutical forms
- the concept of
  - comparable pharmaceutical forms
  - bioequivalence/ biowaiver

belongs to Generic Applications
WEU vs. Generic

Well-established use
• as it is a full application, each indication has to be applied for and supported separately
• is an exceptional case

Generic
• all indications of the reference medicinal product are possible (if applied for)
• the choice !
MRP/DCP New applications
January to June 2014

FINALISED Procedures – MRP/DCP per legal basis
Total: 109 MRP and 389 DCP (regarding 201 and 802 products respectively)

Procedures referred to CMDh in 2014 - Per Legal Basis
(excluding referrals for type II variations and Work-Sharing procedures)
WEU Applications: Challenges

Biobliographical Data
• Leave room for interpretation

Bioequivalence study in WEU applications
• Supportive or pivotal?
• Differences between national authorities
  ➢ e.g. possible in UK, not possible in Germany!

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Data exclusivity for WEU marketing authorizations?

Recent decision of the European Court (Case C-104/13):
• MAs granted on basis of Article 10a are also reference medicinal products
• Data exclusivity period is also applicable for WEU-MAs
➢ Obstruction of generic applications
EEA vs. South East Europe (Serbia)

- Well-established use application type came into force with the current Rulebook 2012
- The previous ‘bibliographical application’ is comparable with the new WEU application
- Hemofarm has gained first experience
- Instead of company’s own data in Module 4 and 5 any known data concerning the API, including relevant information from the published literature should be listed

Example:
- Xylometazoline is a well-known API and has been used over 30 years in the treatment of the relevant indications
- Marketing Authorization in Serbia was issued in 10/2014
Conclusions

- Well-established use is a full application
- Authorities have a wider scope for interpretations and objections against WEU applications
- Scientific advice recommended
- Higher risk
- Exceptional case
Questions?

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