The Legal Framework for Herbal Medicinal Products in Europe (including reimbursement status)

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Dr. Barbara Steinhoff

European Legislative Network for Medicinal Products

- medicinal products require pre-marketing approval before gaining access to the market
- documentation of quality, safety and efficacy including expert reports
- no difference between herbal and other medicinal products

Medicinal Products in Europe

Marketing authorisation system

- codified Directive 2001/83/EC (includes 65/65/EEC, 75/318/EEC, etc.)
- decentralised system based on mutual recognition (RMS, CMS), applicable for HMP
- efficacy proven by clinical studies and/or "well-established medicinal use"
- future amendment to 2001/83/EC: traditional herbal medicinal products

Bibliographic Application

Art. 10.1 a (ii) of Directive 2001/83/EC

(= Art. 4.8. (a)(ii) of 65/65/EEC):

"The applicant shall not be required to provide the results of pharmacological and toxicological tests or clinical trials if he can demonstrate ... that the constituent or the constituents of the medicinal product have a well established medicinal use, with recognised efficacy and an acceptable level of safety, by means of detailed bibliography."

"Herbal Medicinal Products in the European Union"

- AESGP (1998) on behalf of the European Commission
- regulatory situation in Member States, e.g. implementation of the option of bibliographic applications
- differences in legislation and assessment criteria
- http://pharmacos.eudra.org/F2/pharmacos/comdoc_doc.htm

United Kingdom

- **"full" licences and bibliographic applications**

- **"exempt herbal remedies" = medicines, but not licensed**

United Kingdom

Exempt herbal remedies

- herbalists may prepare/sell tailored herbal products to a particular person after individual consultation *[Section 12 (1)]*
- dried, crushed or comminuted plants without any written recommendation for use *[Section 12 (2)]*

France

- traditionally used herbal medicinal products: simplified registration procedure
- "Cahiers de l'Agence No. 3" (formerly: "Avis aux fabricants")
- positive list of plants and indications (including combinations)
- no studies on efficacy and safety required

  (in some cases reduced toxicity data)
- introduction "traditionally used in ..."

Germany (I)

- **proof of safety and efficacy by pharm/tox and clinical studies or reference to Commission E monographs (bibliographic application acc. to section 5 of the *Arzneimittel-Prüfrichtlinien*)**

- ***Standardzulassung* (herbal teas) without individual application but reference to a standard (quality control, label, leaflet)**

Germany (II)

- **simplified procedure according to section 109a: "traditionally used in ..."**
  - **efficacy proven by long-term use and tradition**
  - **positive list of substances and indications**
  - **safety established**
  - **applicant responsible for quality ("guarantee in lieu of an oath")**

European Regulatory Assessment

Herbal Medicinal Products Working Party (HMPWP) 1997 (EMEA):

- **new guidance on quality, safety, efficacy**
- **e.g. Good Agricultural and Collection Practice (GACP)**
- **e.g. Guidelines on quality and on specifications of HMP**
- **Points to consider on levels of evidence**
- **EMEA website www.emea.eu.int**

Proposed Amendment to Notice to Applicants

- **"scientific monographs on certain substances e.g. those drafted by ESCOP and WHO offer a valuable and updated overview on published scientific literature"**
- **"demonstration of the safety and efficacy of a medicinal product in bibliographical application in accordance with Art. 4.8. (a) ii of Directive 65/65/EEC"**

HMPWP

- preparation of "core data" (formerly "core-SPCs") based on monographs
- levels of evidence I - IV

  according to "Points to consider..." (EMEA/HMPWP/23/99)
- I: meta-analysis, randomised controlled trial
- IV: expert committees, respected authorities

HMPWP

- level I: e.g. for Ispaghula husk
- level IV: e.g. for Calendula flower
- new draft concept paper on levels of evidence (EMEA/HMPWP/1156/03): major, medium, minor claims
- corresponding to levels I / II,III / IV in the area of well-established medicinal use

Traditional Medicinal Products

Proposal for a
Directive of the European Parliament
and of the Council
amending the Directive 2001/83/EC
as regards traditional herbal medicinal products

Amendments of the European Parliament
adopted by the European Commission
on 9 April 2003

AESGP Study 1998

"... several Member States seem to face problems in applying identical rules to all medicinal products in a uniform manner. It is therefore recommended that some clarification of CD 75/318/EEC be incorporated ... for those herbal medicinal products which are safe, of appropriate quality and whose indications are exclusively based on adequate proof of efficacy through documented traditional use. This might include the incorporation of a statement relating to this traditional use …"

Scope and Definitions of the Directive

- traditional herbal medicinal products for human use (also combinations with certain non-herbal substances, "anxillary")
- lower level than "well-established use"
- eligibility criteria
  - indications
    (without intervention of a medical practitioner)
  - specified strength
  - oral, external, inhalation
  - period of traditional use
    (30 years or 15+30 years)

Traditional herbal medicinal products

- eligibility criteria (continued)
  - safety given
  - efficacy plausible on the basis of long-term use and experience
  - quality and GMP requirements are the same as for all medicinal products

List of traditional herbal medicinal products

- Committee sets up a list including e.g.:
  - herbal substances
  - therapeutic indications
  - specified strength
  - route of administration
- reference to list instead of evidence of safety and efficacy (incl. proof of traditional use period)

The Committee

- Committee for Herbal Medicinal Products
- one member nominated by each Member State
- community herbal monographs for herbal medicinal products with well-established medicinal use and traditional herbal medicinal products

Reimbursement Status of non-prescription bound medicines

- Europe: big differences in classification
- in some countries, herbal products are not regarded as medicines (e.g., the Netherlands)
- in some countries, herbal medicinal products are prescription-only, depending on the indication (e.g., Austria)
- ⇒ herbal medicinal products as far as they are classified as non-prescription bound medicines (source: AESGP 2003)

Reimbursement Status of non-prescription bound medicines

Non-prescription bound medicines are re-imbursed when included in a (positive) list or with a special remark for chronic treatment, e.g.

- **France**
- **Austria**
- **Belgium**
- **Denmark**
- **Ireland**
- **Switzerland**
- **United Kingdom**

Reimbursement Status of non-prescription bound medicines

In most of these countries, advertisement to the general public is not permitted for reimbursed medicines, e.g.

- **France**
- **Austria**
- **Belgium**
- **Ireland**
- **Switzerland**

⇒ **otherwise loss of reimbursement status**

Reimbursement Status

The German Situation

- 99 % of hmp are non-prescription bound
- all medicines including non-prescription bound medicines are in principle reimbursable
- exemption: negative lists (specific indications, specific substances/ combinations of substances
- ⇒ herbal medicinal products in principle reimbursable like all other medicines

Reimbursement Status

- but: prescription of medicines for certain indications are not recommended by the doctors' and insurances' organisation ("Bundesausschuss Ärzte und Krankenkassen")
- impact particularly on herbal medicinal products
- traditional medicinal products not reimbursed

Reimbursement Status

Future situation ???

- **all non-prescription bound medicinal products will be excluded from reimbursement**
- **exemption: treatment of certain severe diseases**
- **⇒ herbal medicinal products no longer reimbursed because due to low risks, they are non-prescription bound**