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

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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
Marketing authorisation system

- 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
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."
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)]
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

Bundesverband der Arzneimittel-Hersteller e.V.
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"
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
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

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

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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
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