Herbal Medicines
Classification Issues

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Overview of Regulation

• HPRA Regulates medicinal products, medical devices, cosmetics etc.,
• FSAI regulates foods, food supplements
• Herbal ingredients taken by mouth could be present in food supplements or medicinal products
• Classification will depend upon the nature of the herb, the dosage and the purpose for which administered
What is a medicinal product I

• Definition given in Article 1.2 of Directive 2001/83/EC
• Revision in Directive 2004/27/EC
• HPRA guide to definition of a medicinal product for human use based on
  - Composition
  - Claim
  - Presentation
  - Function
What is a medicinal product II

Article I of Directive 2001/83/EC, as amended by Directive 2004/27/EC changed the definition of a medicinal product. The revised definition states that a medicinal product is:

(i) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(ii) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.
HPRA Guideline “Definition of a Human Medicinal Product”

• Developed originally to support enforcement activities

• **Non-legally binding advice – definition is in the Directive**

• Addresses borderline between MP’s and foods, cosmetics, medical devices etc.

• Adjudication by HPRA Classification Committee

• Application form and fee

• Guideline revised 2008 and summer 2014

• Focussed on potential threats to public health
Characteristics of a medicinal product

- Marketing is controlled by valid authorisation or registration
- Protection of consumers is paramount
- Medicines should be of good quality
- Risk of using the product should be reasonable and acceptable in the light of the expected benefit
- Demonstrable therapeutic benefit should be anticipated
Classification process

• Internal or external applications
• Application form on HPRA website www.hpра.ie
• Complete application form in full
• Enclose all labels, leaflets, promotional material
• Pay attention to websites used to promote products
• Submit to Classification Committee Administrator
• Response in writing usually within 28 days
HPRA Classification Committee

- Multidisciplinary scientific in-house committee
- Consists of representatives from Human Medicines, Medical Devices, Compliance Departments
- Expertise in medicine, pharmacy, herbal medicine, toxicology, market surveillance and pharmacovigilance, medical devices, cosmetics.
- Meets once monthly
- Typically >100 applications p.a
- Provides a formal response in writing to the applicant
- Decisions can be appealed to Advisory Committee on Human Medicines
Classification requests on products containing herbal substances

- There has been a growing trend over the last 5 - 10 years of queries on products of plant origin

- IMB Classification requests 2012
  - 164 applications
  - 87 contained herbal substances (53%)

- In addition, collaboration with FSAI reveals many products containing herbal substances notified as foods or food supplements

- HPRA 2014 52% of requests were for herbal products
Traditional herbal medicinal products I

• Based on plants with acceptable safety profile
• Acceptable indications – consistent with safe self-administration
• Concordance with HMPC monographs where available
• Usually oral or topical routes of administration
• Possibility of confusion with food supplements, cosmetics respectively
• Products seen on the market often do not meet these criteria in practice
Traditional herbal medicinal products II

• Products appear on the market containing herbal substances with possible safety concerns

• Some herbal substances restricted as prescription medicines

• Indications are inappropriate and not suitable for self-diagnosis/self-administration

• Products deviate significantly from HMPC monographs

• Many of these products are being marketed inappropriately as food substances or cosmetics

• No THMP applications received in some cases for products containing these herbs
Traditional herbal medicinal products III

- HPRA developed lists of herbal substances acceptable for use in medicinal products for clarity
- “Positive” list includes actual examples from in house applications for THMP’s
- Consistency with indications in HMPC monographs
- Some herbal substances which we would like to see in THMP’s provided the appropriate indication can be found –
  e.g. *Hypericum perforatum*
  *Ginkgo biloba*
  *Senna spp.*
List of medicinal herbs considered to be acceptable as THMPs

<table>
<thead>
<tr>
<th>BOTANICAL NAME</th>
<th>COMMON NAME</th>
<th>COMMENT (Plant parts or other comment)</th>
<th>³HMPC MONOGRAPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aesculus hippocastanum L.</td>
<td>Horse Chestnut</td>
<td>Seed</td>
<td>✓ F</td>
</tr>
<tr>
<td>Aloe barbadensis. Miller</td>
<td>Barbados Aloes</td>
<td>Resin contains anthraquinone glycosides (aloin)</td>
<td>✓ F</td>
</tr>
<tr>
<td>(Syn A. vera L.)</td>
<td>Cape Aloes</td>
<td></td>
<td>✓ F</td>
</tr>
<tr>
<td>Aloe ferox Miller</td>
<td></td>
<td></td>
<td>✓ F</td>
</tr>
<tr>
<td>Arctostaphylos uva-ursi L. Spreng</td>
<td>Bearberry</td>
<td>Leaf (Diuretic)</td>
<td>✓ F</td>
</tr>
<tr>
<td>Arnica Montana L</td>
<td>Arnica</td>
<td>Flower</td>
<td>✓ R</td>
</tr>
<tr>
<td>Avena sativa L</td>
<td>Oat</td>
<td>Seeds</td>
<td>✓ F</td>
</tr>
<tr>
<td>Betula pendula ROTH</td>
<td>Birch</td>
<td>Leaf, bark</td>
<td>✓ F</td>
</tr>
<tr>
<td>Borago officinalis L</td>
<td>Borage; Starflower</td>
<td>Oil, leaves if free from pyrrolizidine alkaloids</td>
<td>X</td>
</tr>
<tr>
<td>Capsicum annuum L</td>
<td>Pepper</td>
<td>Fruit</td>
<td>C</td>
</tr>
<tr>
<td>Cassia angustifolia M. Vahl</td>
<td>Senna – Indian (Tinnevelly)</td>
<td>Contains anthraquinone glycosides (laxative)</td>
<td>✓ F</td>
</tr>
<tr>
<td>(Syn Cassia senna L)</td>
<td>Senna – Egyptian (Alexandrian)</td>
<td></td>
<td>✓ F</td>
</tr>
<tr>
<td>Cassia acutifolia Delile</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Traditional herbal medicinal products (IV)

• Development of a second list of herbal substances not considered acceptable in THMP’s

• This (“Negative”) list contains
  - toxic plants
  - plants currently restricted by POM legislation
  - plants for which suitable indications have not been identified

• Clearly such herbal substances on the negative list are not appropriate for inclusion in THMP’s nor in food supplements

• Some plants on the positive list may be considered suitable for inclusion in foods or cosmetics as well as in medicine depending upon usage and dose

• “Negative list” superseded by lists II and III
Herbal medicines registration

• Registration process is feasible and user friendly – for example can use mutual recognition applications

• HPRA is the primary authority for determining method of sale and supply

• No longer bound by the restrictions of existing prescription legislation

• For example Ginkgo biloba *H. perforatum* could be accepted for THM registration provided suitable indication is agreed
Classification of products containing herbal substances - continued

- Many medicinal herbal products are presented as food supplements
- Manufacturers limit claims and assume they escape medicines legislation – not necessarily so
- Active substances containing herbal medicinal substances have been marketed in Ireland without registrations
  - Echinacea
  - Saw Palmetto
  - Black Cohosh
  - Devil’s claw
  - Milk Thistle
Milk Thistle

- *Silybum marianum* (Milk Thistle fruit) normally used for its hepatoprotective effects
- Silymarin and its components esp. silybinin are considered responsible for pharmacological effects
- HMSC has reviewed products containing MT and rejected any serious evidence of food use
- Silymarin present largely in the fruit
- Leaves have also been used for liver and uterine complaints but limited information available
- Leaves do not contain silymarin
Milk Thistle products

- Limited numbers of product applications for THMP status
- Medicinal product – silymarin shows pharmacological activity in range 200 – 500 mg daily dose
- Products containing < 200 mg standardised extract of silymarin probably still likely to possess pharmacological activity
- However HPRA considers products containing less than 200mg silymarin per daily dose acceptable for use in food supplements provided no medicinal claims made since no safety concerns
Herbal Teas – Chamomile and Fennel

- Dried/powdered herbal preparations intended for infusion (decoction or maceration) in hot water
- Usually presented in single dose sachets of 1 -2g
- Such herbal teas not normally considered as medicinal products provided no medicinal claims made
- Problem is promotion and usage in young infants
- IMB received (from a GP) two reports of children given chamomile tea 6 and 9 months – status epilepticus secondary to hyponatraemia diagnosed
- Malnutrition likely where herbal teas being given in place of breast milk/infant formula
Herbal teas continued -

- HMPC monograph for Fennel, not recommended for use in children under 4 – estragole
- Dried herb used in the form of herbal tea
- Fennel tea being used as a carminative
- Traditionally used in infant colic in Eastern Europe
- Matters referred to FSAI, herbal teas should not be used in infants and breast feeding mothers
- Notified Pharmaceutical Society of Ireland who included the recommendation in pharmacist newsletter
Classification of herbal substances vs. foods

• Article 2 (2) of the Directive provides default to medicine in case of doubt
• Conversely Recital 12 (Directive 2004/24) provides for marketing of herbal substances in food supplements
• A balance must be struck to protect the consumer
• Fundamentally physiological functions, claims, mode and presentation of products need to be considered case by case
Conclusion

• Definition of a medicinal product supplemented by the HPRA guideline and CC opinion
• Lists of herbal substances are there to advise on HPRA thinking
• Many herbal substances can continue to be marketed as food supplements with FSAI agreement
• Sometimes modification of literature can bring something out of the medicines arena
• HPRA and FSAI collaborate closely to provide a balanced approach case by case
• If in doubt we are open to advise and negotiation
Questions?

Thank you for your attention
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