famhp federal agency for medicines and health products

FAMHP GUIDANCE ON MODULE 3 OF THE HOMEOPATHIC MEDICINAL PRODUCT DOSSIER:

"Homeopathic medicinal product" – P-part

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Disclaimer: this guidance is based on HMPWG guidance on module 3. It is completed with some examples or explanations in order to facilitate the compilation of the P-part of the module 3. All possible cases are not presented.

3.2.P. Drug product

3.2.P.1 Description and composition of the drug product

3.2.P.2 Pharmaceutical development

3.2.P.2.1 Components of the drug product

3.2.P.2.2 Drug product

3.2.P.2.2.1 Formulation development

Where applicable, the differences between clinical formulations and formulation (i.e. composition) described in 3.2.P. should be provided.

3.2.P.2.2.2 Overages

3.2.P.2.2.3 Physicochemical and biological properties

3.2.P.2.3 Manufacturing process development

Where applicable, differences with the manufacturing process(es) used to produce pivotal clinical batches clinical should be provided.

3.2.P.2.4 Container closure systems

3.2.P.2.5 Microbiological attributes

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3.2.P.2.6 Compatibility

3.2.P.3 Manufacture

3.2.P.3.1 Manufacturer

3.2.P.3.2 Batch formula

3.2.P.3.3 Description of manufacturing process and process controls

3.2.P.3.4 Controls of critical steps and intermediates

3.2.P.3.5 Process validation and/or Evaluation

3.2.P.4 Control of excipients

3.2.P.4.1 Specifications

3.2.P.4.2 Analytical procedures

3.2.P.4.3 Validation of analytical procedures

3.2.P.4.4 Justification of specifications

3.2.P.4.5 Excipients of human or animal origin

3.2.P.4.6 Novel excipients

3.2.P.5 Control of the drug product

3.2.P.5.1 Specifications

3.2.P.5.2 Analytical procedures

3.2.P.5.3 Validation of analytical procedures

3.2.P.5.4 Batch analysis

3.2.P.5.5 Characterisation of impurities

3.2.P.5.6 Justification of specifications

Microbiological quality:
Ph. Eur. has fixed specific acceptance criteria for pharmaceutical medicinal products administrated by the oromucosal* route of administration. Considering that a lot of homoeopathic medicinal products (pillules, solutions, …) for human use are administered into the oral cavity or onto a specific part of the oral cavity, these acceptance criteria apply to the majority of homoeopathic medicinal products for human use administrated in the mouth (homoeopathic tradition).

**Definition of oromucosal use (EDQM standard terms):*

Administration of a medicinal product to the oral cavity to obtain either a systemic or a local effect. The term oromucosal is only for use when a more specific term (e.g. buccal, gingival, sublingual...) does not apply. Oral use is excluded.

According to EDQM, buccal, gingival and sublingual preparations are oromucosal preparations.

Disintegration time:
The setting of the maximum time of disintegration should arise from results obtained for different batches of the pharmaceutical form. Therefore a disintegration time of 15 minutes does not seem to be appropriate for a sublingual tablet.

3.2.P.6 Reference standards or materials

3.2.P.7 Container closure system
The combination of the container closure specifications and the drug product stability data may be sufficient to demonstrate suitability of the container closure system for storage and shipping of the drug product.

3.2.P.8 Stability
Homeopathic medicinal products: if no identification or assay of the active substance is possible due to the degree of dilution, stability data of the pharmaceutical form may be considered (see annex 1 of Directive 2001/83: Directive 2003/63/EC).

3.2.P.8.1 Stability summary and conclusion

3.2.P.8.2 Post-approval stability protocol and stability commitment

3.2.P.8.3 Stability data

Product information

Concerning the homeopathic medicinal products containing ethanol and intended to be administered to children, following recommendations should be made:

- Ethanol administration to children should be minimized and the benefit/risk -ratio should be determined keeping in mind the target population. All medicinal products containing ethanol, should not be used in neonates and infants below 2 years unless adequate justification is given.
- The concomitant use of multiple medicinal products that contain ethanol should be avoided.
- The dose interval should be kept as long as possible, however it should be at least 4 hours to avoid accumulation. The whole treatment period should be as short as possible. For children below 6 years of age, adequate justification must be provided if the treatment exceeds one week.
- Appropriateness and safety of alternatives to ethanol should be considered and continued efforts should be made to have ethanol replaced in preparations intended for pediatric use.

Harmful impairment of psychomotor functions can already occur when blood ethanol concentration is above 0.125 g/L. Therefore, the recommendation is that a 0.125 g/L blood ethanol concentration should not be exceeded following a single dose of medicinal product containing ethanol.

- A childproof closure is recommended for medicinal products with an ethanol content greater than 5%. The need for a childproof closure should however not only be related to the concentration but also to the total amount of ethanol present in the medicinal product. A childproof closure is required for containers that contain amounts of ethanol that could produce a blood ethanol concentration greater than 1g/l, when accidentally ingested as a whole.

- Information regarding the ethanol content of the homeopathic medicinal product should be provided in a clear and explicit manner in the package leaflet. For homeopathic medicines the concentration of ethanol can be reduced by mixing the dose in a quantity of water and giving the mixture in a timeframe of several hours. This should be reflected in a recommendation for the correct use in the leaflets.

- Interactions for combinations / concomitant medications likely to be used in pediatric population should be taken into account. Ethanol may enhance the absorption and pharmacological effect of some drugs, such as sedatives, and affect the elimination of others by inducing and/or inhibiting the cytochrome P450-dependent elimination pathways. In addition, ethanol may, in the presence of, e.g., some antibacterials, cause a disulfiram-like reaction. Administration of drugs containing ethanol in children should/must be subject to prior medical evaluation, in particular to check for the lack of contraindications/interactions, unless justified.

References and related documents

HMPWG - GUIDANCE ON MODULE 3 OF THE HOMEOPATHIC MEDICINAL PRODUCT DOSSIER
(HMA-website http://www.hma.eu/uploads/media/HMPWG_dossier_guidance_mod3.pdf)

FAMHP POSITION ON ETHANOL CONTENT IN MEDICINAL PRODUCTS USED IN CHILDREN (including herbal medicinal products and homeopathic medicinal products)
(FAMHP-website http://www.fagg-afmps.be/en/binaries/Ethanol%20in%20Children-position-FAMHP-2010-06-22_tcm292-102688.pdf)

History

Version	Date of application	Reason for change
1	4/12/2012	Initial version
2	19/09/2013	Clarification, disclaimer