24 July 2018
EMA/HMPC/510355/2018 Corr.[1]
Inspections, Human Medicines Pharmacovigilance & Committees Division

Committee on Herbal Medicinal Products (HMPC)

Minutes for the meeting on 04-05 June 2018

Chair: Marisa Delbò Vice-Chair: Emiel Van Galen

04 June 2018, 14:00 – 19:00, 2F

05 June 2018, 09:00 – 13:00, 2F

Health and safety information

In accordance with the Agency's health and safety policy, delegates are briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in the minutes is considered commercially confidential or sensitive and therefore not disclosed.

Of note, it is a working document primarily designed for HMPC members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

[1] Correction in participant list

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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room).

1.2. Adoption of agenda

HMPC agenda for 04-05 June 2018

Time schedule for 04-05 June 2018

Outcome:
Agenda adopted with proposed additional topics regarding forward planning and future MLWP operations (included under 5.4.1).

Time schedule endorsed.

1.3. Adoption of the minutes

HMPC minutes for 26-27 March 2018

Outcome:
Minutes adopted with minor correction.

2. European Union herbal monographs and list entries

2.1. Report on MLWP activities

2.1.1. Appointment of Rapporteurs and Peer-reviewers

Changes of Rapporteurs and Peer-reviewers for PS review

Adhatoda vasica folium - Rapporteur
Andrographidis paniculatae folium - Rapporteur
Angelicae sinensis radix - Peer-reviewer
Centellae asiaticae herba - Rapporteur

Withaniae somniferae radix - Rapporteur

Outcome:
Endorsed.

2.1.2. Report from the MLWP March 2018 meeting

Report: MLWP Chair/MLWP Vice-Chair
Action: for information
Document: Draft minutes for the MLWP meeting on 28-29 March 2018

2.2. Revised EU herbal monographs and list entries for final adoption

2.2.1. Monograph on Curcumae longae rhizoma and supporting documents

Action: for adoption
Documents: MO, AR, LoR; References: 00/132

Outcome:

Adoption postponed.
The Rapporteur was asked for some editorial improvements in supporting documents mainly linked to references and headings for possible final adoption at the HMPC July meeting.
For adoption, the set of full text references supporting the revised assessment in line with the LoR should be provided.

Some suggestions for improvement of content (editorial adjustments in tables on traditional use, non-clinical part) and format (numbering of references) of the AR were made.

2.2.2. Monograph on Echinaceae pallidae radix and supporting documents

Action: for adoption
Documents: MO, AR, LoR; References: 59/62

Outcome:

Final revised monograph and supporting documents adopted by consensus. The Norwegian delegate was not present during the meeting.

For publication correct names in all languages should be added to the monograph according to the available information in the regularly distributed overview file.

2.2.3. Monograph on Oenotherae biennis oleum and supporting documents

Action: for adoption
Documents: MO, AR, LoR; References: 61/106

Outcome:

Final revised monograph with changes in section 4.6 and supporting documents adopted by consensus. The Norwegian delegate was not present during the meeting.

Before publication Rapporteur to provide the set of full text references supporting the revised assessment in line with the LoR.

2.2.4. Monograph on Pelargonii radix and supporting documents

Action: for adoption
Documents: MO, AR, LoR, OoC MO, OoC AR; References: 99/96; New references

Outcome:

Final revised monograph and supporting documents adopted by majority vote (23 out of 25). The Norwegian delegate was not present during the meeting.

Divergent opinions: Eeva Sofia Leinonen, Astrid Obmann

It was emphasised that the revision was only focused on the reconsideration of clinical data following the acceptance of the Brochitits Severity Score (BSS). The start of the systematic review is scheduled for end of 2019. The assessment outcome was summarised highlighting the difficulties in the clinical assessment with regard to study design/population and statistical significance versus clinical relevance.

Divergent opinions referred to either safety concerns with regard to hepatic symptom detection by self-medicating patients or with regard to the clinical data that were considered sufficient to recognise efficacy and well established use.

2.3. Revised EU herbal monographs and list entries for public consultation

None

2.4. EU herbal monographs, list entries and public statements for final adoption

2.4.1. Public statement on Glycini semen and supporting documents

Action: for adoption
Documents: PS, AR, LoR; References: 52/49

Outcome:

Final Public statement (PS) and supporting documents adopted by consensus. The Norwegian delegate was not present during the meeting.

It was discussed whether there is potentially sufficient information to document 15/30 years of medicinal use. However, no changes in PS and Assessment report were made.

2.4.2. Monograph on Silybi mariani fructus and supporting documents

Action: for discussion
Documents: MO, AR, LoR, OoC, Presentation

Outcome:

Final monograph (with minor change in section 4.1) and supporting documents adopted by majority vote (21 out of 25). The Norwegian delegate was not present during the meeting.

Divergent opinions: Rachel Cox, Erika Svedlund, Linda Anderson, Astrid Obmann

Rapporteur to adapt AR accordingly and to provide before publication the set of full text references supporting the revised assessment in line with the LoR.

After a summary on previous decisions with regard to the indication, a discussion on options and a *tour de table*, HMPC members agreed on a slightly modified traditional indication

proposed by the Chair according to the answers received by most of the members following the circulation of options in advance of the meeting.

Divergent opinions referred to either safety concerns linked to the wording of the indication or to a possible recognition for well-established use in line with the authorisation status in several Member States.

2.5. EU herbal monographs, list entries and public statements for adoption for release for public consultation

2.5.1. Monograph on Malvae folium and supporting documents

Action: for adoption
Documents: MO, AR, LoR, OoC; References: 149/119

Outcome:

Draft monograph and supporting documents with minor modifications in the MO adopted by consensus for 3 months public consultation.

2.5.2. Monograph on Malvae flos and supporting documents

Action: for adoption
Documents: MO, AR, LoR, OoC; References: 149/119

Outcome:

Draft monograph and supporting documents with minor modifications in the MO adopted by consensus for 3 months public consultation.

2.6. Reviewed EU herbal monographs and list entries for decision on revision

2.6.1. Monograph on Hippocastani semen and supporting documents

Action: for adoption
Document: Review outcome; References: 07/08

Outcome:

The HMPC agreed with the Rapporteur's position and decided by consensus to revise the monograph, assessment report and list of references on Hippocastani semen.

Some relevant new data had been detected including changes in the Ph. Eur. monograph affecting analysis, and potentially specification and marker considerations.

The Rapporteur informed also on a test case to check how PhV data are accessible and useful to incorporate into the review/revision of monographs. A first report is expected in September.

2.6.2. Monograph on Polypodii rhizoma and supporting documents

Action: for adoption
Document: Review outcome; References: 0/0

Outcome:

HMPC agreed with Rapporteurs position that no monograph revision is needed because no new data of relevance were detected that would change the content of the monograph.

The HMPC decided not to revise the monograph, assessment report and list of references on Polypidii rhizoma.

An Addendum to the existing Assessment Report based on the Rapporteurs review report will be published once the final version of procedure EMA/HMPC/124695/2011 Rev. 2 is adopted (see also 4.3.1).

3. Referral procedures

None

4. Guidelines and guidance documents

4.1. Non-clinical/clinical safety and efficacy and multidisciplinary

4.1.1. Guideline on non-clinical documentation in applications for marketing authorisation/registration of well-established and traditional herbal medicinal products (EMEA/HMPC/32116/2005 Rev.1)

Action: for adoption
Documents: Guideline, OoC

Outcome:

Final revised GL and Overview of comments, both with minor changes, adopted by consensus for distribution to Safety WP and CMDh for possible comments before final adoption.

Questions on the legal basis for herbal-specific requirements were discussed as well as the scope of the Guideline.

It was agreed that keeping 'mixed application in scope and title would lead to misinterpretations due to the wide range of possible mixed applications and confusion regarding requirements for products that are not registered or authorised and Art. 16a or Art. 10a, respectively.

4.1.2. Public statement on the use of herbal medicinal products containing estragole

Action: for discussion
Documents: Draft revised PS, OoC; Comments; Combined comments

Outcome:

HMPC noted revised version from MLWP, comments received and update on coordination with Safety WP. Transferred for detailed discussion and agreement to MLWP.

Post-meeting note:

MLWP discussed and agreed by majority to follow the Rapporteur's proposal. Documents and Swedish proposal to be provided to Safety WP for comments and HMPC decision in July 2018.

4.2. Quality

4.2.1. Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products (EMA/HMPC/162241/2005 Rev. 3)

Report: Q DG Chair
Action: for adoption
Documents: Draft revised Guideline; Comments from IE, AT, PT, SE, IT, ES

Outcome:

Draft revised guideline was adopted by consensus.

The committee was informed on the thorough revision process considering other guidelines, Q&As as well as new/ modified Ph. Eur. documents. Many diverse comments were received and considered but not all could be implemented. After public consultation there will be a possibility for final comments. It was noted that after QWP consultation endorsement of the draft is sought for the CHMP and CVMP July meetings before public consultation.

4.2.2. Guideline on quality of herbal medicinal products/traditional herbal medicinal products (EMA/HMPC/201116/2005 Rev. 3)

Report: Q DG Chair
Action: for adoption
Documents: Draft revised Guideline; Comments from IE, AT, PT, SE, IT, ES

Outcome:

Draft revised guideline was adopted by consensus.

See 4.2.1.

4.3. Regulatory / Procedural

4.3.1. Procedure for the review and revision of European Union herbal monographs and European Union list entries (EMA/HMPC/124695/2011 Rev.2)

Action: for adoption
Documents: Draft procedure; Review template; Addendum template

Outcome:

Adoption postponed. Comments and final open questions were noted.
The Procedure was transferred for finalisation to MLWP and ORGAM DG before the final adoption in July 2018.

Final questions/ clarifications by the secretariat were noted. Overall it was confirmed that the principles are already followed for new reviews, while ongoing revisions will be finalised according to previous practice (see also 2.6).

A request for public consultation of the review outcome was not agreed, because the decision to add a monograph revision to the HMPC work programme does not equal an opinion by the HMPC on a monograph. Transparency and possible Interested party

intervention is guaranteed by the Call for data at start of the review, by public consultation when an existing monograph is revised and by possible requests for unscheduled reviews.

4.4. Report on HMPC Drafting Groups activities

4.4.1. Quality DG

Report: Q DG Chair

- Meeting report from Q DG virtual meeting held on 19 Apr 2018
  Action: for adoption
  Document: Meeting report
- Draft agenda for the Q DG virtual meeting to be held 21 Jun 2018
  Action: for information
  Document: Draft agenda

Outcome:

The meeting report was adopted.

Updates were given by the QDG Chair on the forthcoming virtual meeting in June. An additional topic potentially for a quality Q&A was proposed by the HMPC Chair.

4.4.2. ORGAM DG

Report: ORGAM DG Chair

- Meeting report from ORGAM DG virtual meeting held on 23 Apr 2018
  Action: for adoption
  Document: Meeting report
- Agenda ORGAM DG meeting to be held on 19 Jun 2018
  Action: for information
  Document: Draft agenda
- Appointment for new member at ORGAM DG
  Action: for adoption
  Documents: ORGAM mandate

Outcome:

Meeting report was adopted. Updates were given by the ORGAM DG Chair on the forthcoming virtual meeting in June.

HMPC appointed O. Palomino from ES (also MLWP) as new ORGAM DG member.

5. Organisational, regulatory and methodological matters

5.1. Mandate and organisation of the HMPC

5.1.1. Relocation Preparedness to CxMPs - cancelled

5.1.2. Update on the EMA relocation

Action: for information

Document: Presentation

Outcome:

Updates were given with regards to the EMA relocation plan in 2019. Concerns regarding HMPC and subgroup operations in particular MLWP face to face meetings during BCP (business continuity plan) beginning of 2019 were discussed with emphasis on forward planning, organisation, resources and work plan 2019.

5.1.3. Strategic Review and Learning Meetings

Austria Presidency meeting – Vienna, 15-17 Oct 2018
Action: for discussion
Document: Revised Agenda

Outcome:

Updates were given by the Austrian alternate member on the agenda for the SRLM in Vienna.

Members were invited to propose further topics/presentations for the final session.

5.2. Coordination with EMA Scientific Committees or CMDh-v

5.2.1. Scientific Coordination Board Meeting

Report: HMPC Chair
Action: for information
Documents: Minutes 12 April 2018; Agenda 3 May 2018

Outcome:

The Chair highlighted discussions with regard to the business continuity plan (BCP) in 2019 and working party operations and expressed concern with regard to HMPC subgroup meetings and subsequent effects on HMPC output. Clarification was sought to allow preparation and modifications in working methodology as appropriate – partially on the agenda of the Presidency meeting in Vienna (see also 5.1.2 and 5.1.3).

5.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

None

5.4. Cooperation within the EU regulatory network

5.4.1. Coordination with the European Commission

- Clarification of classification on *Saccharomyces cerevisiae* CBS 5926
  Action: for discussion

Outcome:

HMPC noted and discussed the EC response outlining the responsibility of the Member States to classify medicinal products, as well as the HMPC's role to provide scientific advice as regards HMPs and establishment of monographs to facilitate authorisations/registrations.

A further discussion on *Saccharomyces cerevisiae* CBS 5926 was scheduled for the HMPC July meeting.

- AESGP proposal on the simplification of variations specific to herbal medicinal product
  Action: for discussion
  Document: QDG proposal

  Outcome:

  The Commission welcomed HMPC/QDG position as regards the HMP-specific proposal. Some detailed questions were raised and will be clarified by HMPC/QDG.

  The Commission explained that the herbal proposal is one among several currently brought forward to the Commission. The HMPC position could be helpful as part of a future evaluation of the Variation Regulation and Variation Guidelines. However, a change of the Variation Regulation in the near future is unlikely.

5.4.2. Coordination with European Pharmacopoeia

- EDQM 13A expert group meetings
  Action: for information
- EDQM 13B expert group meetings
  Action: for information
- EDQM TCM expert group meetings
  Action: for information
- EDQM PA working party
  Outcome:

  HMPC noted SoDs and updates on 13A, 13B, TCM and PA expert groups given by the EDQM representative.

  No major progress regarding the ongoing project on 'assay alternatives' at TCM was reported, which first has to be discussed at expert groups 13A and 13B before a draft proposal can be shared with HMPC.

5.5. Cooperation with International Regulators

None

5.6. Contacts of the HMPC with external parties and interaction with the Interested Parties to the Committee

5.6.1. Question on HMPC assessment and national monograph use

Report: HMPC Chair
Action: for adoption
Document: Draft response letter; Hederae helicis folium MO, AR, LoR; Supportive references

Outcome:

HMPC noted modified draft letter and references/information newly provided.

The detailed discussion was postponed to July 2018.

Available information at FR and IT agencies and EMA regarding general safety concerns on use of mucolytics in children below 2 years have been collected and presented and could be added to the AR and LoR. Some inconsistencies in the existing AR, transferability of data, diverse practice in the member states regarding synthetic mucolytics were mentioned. A majority preferred to postpone to the July meeting the discussion whether to follow a precautionary principle or focus on specific available data for contraindications in children and whether it is useful to step into coordination with PRAC and PDCO in this regard. The Chair emphasised that independent from the discussion the letter to the Interested party should be finalised to explain the HMPC assessment outcome.

5.7. Work plan

5.7.1. HMPC work plan 2018

Report: HMPC Chair
Action: for information
Document: Work plan 2018 – current status June 2018

Outcome:

The status of projects on the work plan 2018 was discussed one by one. Project leaders were invited to give an update on their topics in July 2018.

For projects within area 1.3.3. 'Coordination on safety assessments of herbal constituents it was agreed to organise TCs before the HMPC July meeting in order to prepare/outline the next steps such as data collection to follow up on the PS on contamination of HMPs with pyrrolizidine alkaloids (PAs). Based on a concept proposal on what guidance documents should be newly drafted or updated, calls for data should be prepared, both for PAs and polycyclic aromatic hydrocarbons (PAHs), to be presented during the July meeting.

It was reminded that due to less face to face meetings in 2018 and the specific BCP situation (disclaimer in work plans) different working methodologies should be explored such as written communication, TCs or meetings at the margin of HMPC for small groups with focus on the most relevant topics.

5.8. Planning and reporting

None

5.9. Legislation and regulatory affairs

5.9.1. WEU/Bibliographic application regarding Art. 10a Dir. 2001/83/EC for HMPs – Reference to other products

Report: HMPC Chair
Action: for discussion
Document: Comments by EUCOPE received 14 May 2008

Outcome:

HMPC noted comment received after revision and publication of the clinical GL revision regarding HMPC guidance documents and the similarity/comparability issue for herbal products.

Rapporteurs for the clinical GL will draft a response for discussion/adoption at the HMPC July meeting and, if appropriate, a proposal whether alignment of Q&A to the GL is necessary.

The Committee discussed the similarity/comparability issue for herbal products, the history and the different regulatory and scientific dimensions to it. As some different level of detail is given in guidance documents, better explanations may be considered for the Q&A, although an obvious contradiction was not found.

6. Any other business

6.1. Topics for discussion

6.1.1. Questions from NCAs on Public statement on pyrrolizidine alkaloid contaminations

Action: for adoption
Documents: Summarised responses to questions received in May 2017; Literature

Outcome:

The summarised responses with minor changes were adopted by consensus.

HMPC secretariat to provide to the NCAs.

6.2. Documents for information

6.2.1. HMPC

Table of Decisions from HMPC meeting held on 26-27 March 2018

Overview of expertise of members HMPC and subgroups

Meeting report from HMPC meeting held on 27-28 March 2018

Overview of status of HMPC assessment work – priority list

Inventory of herbal substances for assessment work

Abbreviations in HMPC agendas/minutes

Common names of herbal substances in all languages

6.2.2. MLWP

- Overview of status of HMPC/MLWP assessment work
- Draft agenda of MLWP meeting to be held on 05-07 June 2018

6.2.3. ARSP

- English template
- English summaries for publication:
  - Black cohosh
  - Agnus castus
  - Calendula
  - Elder flower
  - Mullein flower

No objections were raised with regard to publication of the 5 finalised summaries.

6.2.4. Other

- EU herbal monographs, list entries and public statements post adoption
  - Remaining publication delays:
    - Allii sativi bulbus
    - Pistacia lentiscus (mastix)
    - Cynarae folium
- Conference on 6 June: Reducing the need for antibiotics – The contribution of Complementary and Alternative Medicine

6.2.5. Guideline on quality of water for pharmaceutical use (EMA/150605/2018)

Documents: Guideline; Concept paper, HMPC comments provided 26 April 2018

6.2.6. Feedback on national experiences with HMPC monographs and guidelines

- draft template
- summary feedback, examples feedback received: Cytisine (PL), Harpagophytum (SE)

An updated table with added information was presented. Some open regulatory/procedural questions regarding the use /usability of the collected information for HMPC tasks will be discussed at the ORGAM DG.

6.2.7. EU – India/AYUSH communication

Document: AYUSH reply to EMA

HMPC agreed to prefer the September combined HMPC/MLWP meeting for the possibility that AYUSH experts attend to discuss HMPC data requirements in particular with respect to specific public statements currently under review.

6.2.8. Request from NL regarding products on the EU market containing *Erythrina mulungu* Mart. Ex Benth (*Erythrina verna* Vell)

Document: Questions to all HMPC members

Feedback to be given to the NL delegate directly.

List of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 04-05 June 2018 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Marisa Delbò	Chair	Italy	No interests declared	
Astrid Obmann	Alternate	Austria	No interests declared	
Iliana Ionkova	Alternate	Bulgaria	No interests declared	
Ivan Kosalec	Member	Croatia	No restrictions applicable to this meeting	
Darko Trumbetic	Alternate	Croatia	No interests declared	
Marie Heroutova	Member	Czech Republic	No interests declared	
Martina Holenková	Expert	Czech Republic	No interests declared	
Eeva Sofia Leinonen	Member	Finland	No interests declared	
An Le	Member	France	No interests declared	
Jacqueline Wiesner	Member	Germany	No interests declared	
Ioanna Chinou	Member	Greece	No interests declared	
Zoi(Zoe) Karampourmpouni	Alternate	Greece	No interests declared	
Zsuzsanna Biróné Dr Sándor	Member	Hungary	No interests declared	
Rachel Cox	Alternate	Ireland	No interests declared	
Alessandro Assisi	Member	Italy	No interests declared	
Evita Skukauska	Member	Latvia	No interests declared	
Baiba Jansone	Alternate	Latvia	No interests declared	
Rugille Pilviniene	Member	Lithuania	No interests declared	
Marcel Bruch	Member	Luxembourg	No interests declared	
Emiel Van Galen	Member	Netherlands	No interests declared	
Wojciech Dymowski	Member	Poland	No interests declared	
Ana Paula Martins	Member	Portugal	No interests declared	
Raluca Iavorszky	Member	Romania	No interests declared	
Miroslava Petrikova	Member	Slovakia	No interests declared	
Barbara Razinger	Alternate	Slovenia	No interests declared	
Adela Núñez Velázquez	Member	Spain	No interests declared	
Cristina Martinez Garcia	Expert	Spain	No interests declared	
Karin Erika Svedlund	Member	Sweden	No interests declared	
Malin Kyllikki Hobro Soderberg	Alternate	Sweden	No interests declared	
Linda Anderson	Member	United Kingdom	No interests declared	
Sue Harris	Alternate	United Kingdom	No interests declared	
Ewa Balkowiec Iskra	Co-opted member	Poland	No interests declared	
Silvia Girotto	Co-opted member	Italy	No interests declared	

Gert Laekeman	Co-opted member	Belgium	No interests declared	
Heidi Foth	Co-opted member	Germany	No interests declared	
Melanie Bald	Observer – via TC	EDQM	No interests declared	
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the agenda topics or activities they participated in.