23 January 2024
EMA/CMDh/49856/2024
Human Medicines Division

Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

Draft minutes for the meeting on 12-14 December 2023

Health and safety information

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

Disclaimers

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. Ongoing procedures discussed by the CMDh are considered confidential.

Of note, this set of minutes is a working document primarily designed for CMDh members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the set of 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/729522/2016).

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1. Introduction

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

The Chair opened the meeting by welcoming all participants. The meeting was held in-person with some members connected remotely.

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 meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants for agenda topics was identified. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests 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. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. CMDh membership

The Chair welcomed Laura Ivett Varga, as the new member for Hungary, and Ágnes Gabriella Szádeczkyné Kelemen as new alternate for Hungary.

The Chair thanked Magdolna Nemeth for her contribution as the member for Hungary.

Mathilde Geynet Kovacs (previous alternate) became the new member for France.

1.3. Adoption of draft agenda

The agenda of the meeting was adopted with the following topics under A.O.B:

- Tiotropium Kappler, 18 Mikrogramm Hartkapsel mit Pulver zur Inhalation (DE/H/7377/001/DC)
- Request for extension of clock-stop
- Electronic submission
- Synapse (Art. 31 referral)
- Recommendation for the transition from quadrivalent (QIV) to trivalent influenza (TIV) vaccines
- Transition to IRIS

1.4. Adoption of the minutes

The minutes of the November 2023 meeting, including the comments received and discussed at the meeting, were adopted and will be published on the CMDh website (**Action: EMA**).

2. Organisational issues/Reports from other meetings

2.1. CMDh Working Groups/Working Parties/Task Force

2.1.1. Safety Outcome Survey (SOS) Working Group / WG chair (CZ)

The WG Chair reported from the December 2023 meetings.

The WG dedicated a meeting mainly to the questions raised to the EMA on the process for MAHs to submit updated SmPCs into XEVMPD. It was clarified that SmPC versions cannot be linked to their corresponding variation. EMA was asked to follow up on the accessibility of SmPCs for NCAs. The WG concluded that, the uploaded SmPCs are not useful for the WG's initiative on the publication of SmPC updates following safety variations.

The WG also discussed the PSUSA Pilot on Section 6 with regard to the communication made to the network including instructions on how to report examples and on the extension of the pilot project. The WG also discussed the example of PSUSA/00001493/202303 for furosemide/spironolactone (see section 6.6.2.).

In a second WG meeting another example was discussed regarding PSUSA/00010649/202302 for ibuprofen, ibuprofen lysine (not indicated in ductus arteriosus), ibuprofen / caffeine. It was agreed that if MAHs of products with active substances or combinations of active substances not in the scope of the PSUSA want to implement the PSUSA recommendation, they have to submit a type II variation with their own data/clinical overview. PRAC advice could be sought during such a variation. The WG will share this example with the EMA and offered to collect other examples from the CMDh and to forward them to the EMA.

The WG continued the discussion on the publication of the outcomes of safety variations and considered the possibility of holding a specific meeting with Interested Parties.

2.1.2. Joint GCP IWG/CMDh Working Party / IE

The WP Chair reported from the November 2023 meeting.

The WP discussed CROs of interest (Synapse (Art. 31 referralthe 2023 CRO planned national inspections, meetings with external regulatory bodies, statistical issues on bioequivalence inspections, the 2023 BE forum, the development of the ICH M10 document and the follow-up actions from the GCP inspectors/assessors' workshop in June.

MSs were reminded of the criticality assessment/variations concerning the BE studies related to the Art. 31 referral for the CRO Synapse (see also topic 8.3.4.).

2.1.3. Multilingual packaging Working Group / WG chair (IE)

The WG Chair reported from the November 2023 meeting.

The WG discussed the progress of the pilot on preparation of EU reduced harmonised text.

The WG agreed on a summary of the survey to the Interested Parties that was presented at the ES Presidency meeting in November. The WG is working on the implementation of the outcome of the survey into the CMDh BPG on Multilingual packaging.

The CMDh discussed the WG proposed options to update the BPG regarding the use of multilingual labelling concept in RUP. MSs were encouraged to send comments in writing for agreement in January (**Action: MSs**).

The CMDh was informed about the ongoing discussions on serialisation, product names and how to improve communication between MSs on the assessment of multilingual packages. NL noted that the IWG could be consulted regarding the topic on serialisation.

In addition, the CMDh was informed about the WG response provided to the PRAC Opioid Drafting Group on the possible challenges for multilingual packages for a possible warning on addiction on the labelling of all opioids.

2.1.4. Working Party on Variation Regulation / WP chair (DE)

The WP Chair reported from the December 2023 WP meeting.

CMDv members of the joint CMDh/CMDv Working Party provided an update on the regulatory handling of variations not requiring assessment (VNRAs) and variations requiring assessment (VRAs).

The WP was updated on the progress of the proposed Delegated Act on the Variation Regulation and future amendment of the Variations Guidelines.

The CMDh was informed about the proposed updates of several guidance documents related to variations. The Best Practice Guide (Chapter 6) on grouped variations was revised to allow quality type IA notifications to be included in supergrouping, among other changes in the document.

The Best Practice Guide (Chapter 7) on variation worksharing was updated to enforce the message that product-specific changes cannot be included in variation worksharing procedures. While the 'present' status can differ in the marketing authorisations included in the worksharing, the proposal and outcome must be the same for all products involved in the procedure.

Following a question from a MAH, the WG also revised Question 4.9 of the Questions & Answers on Variations to clarify that a change in the name/address of the MAH can be submitted as a single variation in MRP/DCP, in case the name/address is the same in the MSs concerned. A grouped variation is only needed if the name/address is different in each MS.

The CMDh adopted the proposed changes of the BPG Chapter 6, BPG Chapter 7 and Variations Q&A. The updated documents will be published on the CMDh website (**Action: EMA**).

The WP discussed the discrepancies identified between footnote 7 of the eAF for variations and explanatory notes on the variation eAF regarding the option to provide the "list of concerned products" in a separate Annex to the application form. The WP proposed to update the footnote in line with the explanatory note, i.e. to delete the "Annex option", and communicate this to the EMA (**Action: FR, HR**). The WP also agreed that it is not necessary to include the supergrouping in the explanatory notes (as it is requested for all MRP/DCP products in the eAF anyway) and to amend Question 55 of the Questions & Answers on eAF to delete the option with Annex. The CMDh agreed with the proposed amendments.

As a follow-up to the November meeting with Interested Parties, the WP discussed the delays in implementation of changes following type IA and IB variations. Industry reported about

differences in approval dates. MSs were asked to send examples by email to the WP Chair (**Action: MSs**).

The WP also discussed cases where large, grouped quality variation applications were received resulting in a "new product" with a new quality dossier. It was noted that the submission of a new marketing authorisation application is preferred if the complete quality dossier is modified (e.g. replaced by a complete new module 3). However, the WP agreed that there are no grounds for refusal of such variation applications (as long as the RefMP for generic applications is not changed).

2.2. Meetings with Interested Parties / Chair

The minutes of the meeting with Interested Parties held on 15 November 2023 were agreed by the CMDh. The minutes will be distributed to the IPs for comments in order to be adopted in the January CMDh meeting (**Action: EMA**).

2.3. Spanish Presidency meeting / ES

The Chair thanked the Spanish presidency for organising the Presidency meeting in Madrid. The meeting documents were tabled for information.

ES informed that they intend to circulate the minutes for comments prior to the CMDh plenary meeting in January (**Action: ES**).

2.4. Belgian Presidency meeting / BE

Belgium will take over the EU Presidency in January 2024. The CMDh was informed that the presidency meeting will take place in person in Ghent from 10-12 June 2024.

2.5. HMA Post-Marketing Risk-Assessment Tool Working Group / Chair

The Chair informed the CMDh that no nominations for a CMDh representative in the WG had been received and reiterated the importance of having a CMDh representative in the group, especially with regard to MRP/DCP products. MSs were asked to further consider volunteering (**Action: MSs**) and were reminded that any questions in this regard could be referred to NL and the Chair.

2.6. International Pharmaceutical Regulators Programme (IPRP) / Chair

The Chair informed the CMDh that no nominations had been received and MSs were asked again to volunteer as CMDh representatives (**Action: MSs**).

2.7. Joint CMDh/CMDv meeting / Chair

The Joint CMDh/CMDv meeting was held on 13 December 2023 in the margins of the CMDh. The groups discussed topics related to reform of the EU pharmaceutical legislation for human medicinal products, MSSG toolkit on regulatory flexibilities, the outcome of the CMDh survey on risk-based approach during DCPs, and CMDv updates on the UPD database, the SmPC template toward QRD v9 and the Guidance to Applicants (GtA).

2.8. PCWP/HCPWP / NO

NO provided a summary of the most relevant topics discussed at the November joint PCWP/HCPWP meeting. The groups discussed, among other topics, the potential impact on the availability of medicines following ECHA's proposal to ban the use of per- and poly-fluoroalkyl substances (PFASs). The CMDh will ask the EMA for an update on ongoing discussions (**Action: EMA**).

The full meeting report, including video recordings, is available on the EMA website.

2.9. Brexit / EMA

EMA provided an update on the implementation of Regulation (EU) 2023/1182 (Windsor Framework) for medicinal products for human use intended to be placed on the market in Northern Ireland and its regulatory impact on CAPs.

The main regulatory impact is foreseen for CAPs which will not be able to be placed on the market in Northern Ireland unless, amongst others, they have an authorisation by the competent authorities of the United Kingdom in accordance with the law of the United Kingdom and under the terms of the authorisation granted by them. Among other consequences, the labelling will need to be updated accordingly, multi-country packs with NI will no longer be valid and parallel distribution with NI will cease to be possible once the Regulation becomes applicable.

To allow preparation of industry, EMA will publish Questions and answers to Stakeholders on the implications of Regulation (EU) 2023/1182 for centrally authorised medicinal products for human use (i.e. excluding NAPs, veterinary medicines and products approved by MHRA under UK law).

[*Post-meeting notes: The Q&A have been published in January 2024: https://www.ema.europa.eu/en/documents/other/questions-and-answers-stakeholders-implications-regulation-eu-2023-1182-centrally-authorised-medicinal-products-human-use_en.pdf*]

It was noted that it is necessary to reflect on potential implications of Regulation (EU) 2023/1182 for NAPs (**Action: SE, IE**) and to continue discussions at a forthcoming meeting.

2.10. HMA meeting / Chair

The Chair reported from the HMA meeting held on 1 December 2023. The highlights from the HMA meeting discussions were presented.

3. General items

3.1. CMDh guidance documents

None

3.2. Variations

3.2.1. Requests for worksharing procedures on Variations

The MSs chosen by the CMDh, based on the recommendations of MAHs, agreed to be reference authorities for the procedures.

3.2.2. Requests for recommendations on unforeseen Variation under Art. 5 of Variation Regulation

None

3.3. GMP

None

3.4. GCP

None

3.5. Presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients

3.5.1. General topics related to nitrosamines

3.5.1.1.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.5.1.2.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.5.1.3.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.5.1.4.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.5.2. Product-specific topics related to nitrosamines

3.5.2.1.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.5.2.2.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.5.2.3.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.6. Paediatric Regulation / Chair

Public PdARs for paed. studies acc. Art. 45
None

Public PdARs for paed. studies acc. Art. 46
None

Art. 46 worksharing
Rapporteurs were appointed for the Art. 46 submissions.

3.7. Request for new active substance status in DCP

3.7.1.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.7.2.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.8. TiO2 (E171) used as excipient / EMA

The interim feedback from EMA to the EU Commission request to evaluate the feasibility of alternatives to replace titanium dioxide (TiO2) in medicinal products and its possible impact on medicines' availability was presented to the CMDh. The input from Interested Parties was sought and taken into consideration while preparing the feedback.

The document was agreed by the CMDh and will be sent to the EC after the meeting.

3.8.1. Replacement of TiO2

The CMDh agreed that the change to remove or replace TiO2 cannot be submitted as type IAIN (B.II.a.3.b) since condition 9 is not considered fulfilled as the change is triggered by safety issues. The variation should therefore be submitted as type IB.

3.9. Real World Evidence including DARWIN EU / EMA

The EMA gave an update to the CMDh on Real World Evidence, including DARWIN EU.

MSs were asked to volunteer as new CMDh contact point for the RWE network (**Action: MSs**).

MSs were also encouraged to browse the catalogues of data sources and non-interventional studies which will go live in early 2024 and suggest RWE use cases related to DCP applications (**Action: MSs**).

3.10. Product Management Service (PMS) / DE

The CMDh was informed about the follow-up of the PMS survey. A proposal for final conclusions will be prepared for the January 2024 CMDh meeting (**Action: DE**). MSs that have not yet replied, were asked to do so (**Action: MSs**).

The CMDh was also informed about the PMS undertakings in Q4 2023, the planned undertakings in Q1 2024 and the preparation for the European Shortages Management Platform (ESMP).

3.11. Duration of contraception for morphine-containing medicinal products / DE

Following the finalisation of a variation for a nationally authorised medicinal product containing morphine to update SmPC section 4.6 with the duration of contraception according to the SWP/NcWP recommendation on the duration of contraception following the end of treatment with a genotoxic compound, the CMDh discussed if further discussion at EU level would be needed. While there was support for the outcome of the assessment of the national variation and the same outcome has already been implemented in other variations, it was considered useful to consult NcWP on the mechanism of genotoxicity and the applicability of the NcWP guidance to morphine. A question to NcWP will be prepared for discussion in January (**Action: FR**).

3.12. Harmonisation of marketing authorisations by requesting worksharing procedures / DE

The CMDh discussed a proposal to start a pilot on requesting SmPC harmonisation via variation worksharing procedures for medicinal products that are disharmonised but are not suitable for an Article 30 referral. The proposal is based on actions included in the CMDh MAWP. The harmonisation of product information (PI) is also part of the European's Commission pharmaceutical strategy for Europe.

The pilot should mainly focus on the following disharmonised PI sections: therapeutic indications, posology and method of administration and contraindications. Identified products should be brought to the CMDh for further discussion on whether a variation worksharing procedure to harmonise the SmPC should be requested. Further information on the handling of such a worksharing procedure is given in Q4.21 of the Q&As on variations. A proposal for a standard letter to MAHs was presented.

The CMDh agreed to further explore the possibility of requesting SmPC harmonisation via variation worksharing. Based on the feedback from the MAHs, the pilot can be reviewed in the future. MSs were asked to comment on the proposal and the presented standard letter for further discussion in January (**Action: MSs**). It is also expected to discuss first examples in January. Once the process is more mature, it can also be presented in the next CMDh meeting with Interested Parties.

3.13. Impurity chloromethyl isopropyl carbonate (CMIC) in tenofovir disoproxyl-containing medicinal products / FR

In February 2023, the CMDh published a letter on the CMDh website addressed to MAHs of tenofovir disoproxil-containing medicinal products approved via MRP/DCP, requesting the MAHs to put in place measures (if not already in place) to ensure that levels of CMIC are below the limit of 50 ppm in the active substance.

In the letter, MAHs were requested to inform the national competent authority (in case of a purely national marketing authorisation) or the RMS (in case of an MRP/DCP product) of the strategy to implement this change including the current specification of CMIC impurity in the active substance within 3 months of publication of the letter.

Furthermore, impacted MAHs should submit a variation within 9 months of publication of the letter to ensure compliance with the above-mentioned limit. The submission via a worksharing procedure is strongly recommended, where applicable.

As the deadline has now passed, concerned MAHs are reminded to submit the requested variation as soon as possible, if they have not already done so.

3.14. Options for harmonisation of posology / IE

The CMDh discussed the response of the MAH following the request sent after the November CMDh meeting to ask the MAH to harmonise SmPC Section 4.2 of their product. In their response the MAH mentioned several ongoing harmonisation exercises, but none of the ongoing procedures addresses the posology. Therefore, the CMDh agreed to insist on the initial request and will provide further details on the identified disharmonised PI (**Action: EMA**).

4. Generic/hybrid marketing authorisations

4.1. Marketing Authorisation Applications for generics of Tecfidera (dimethyl fumarate) / Chair

The EC informed the CMDh about the recent developments regarding the generic marketing authorisations for products containing dimethyl fumarate authorised via the centralised procedure.

4.2. Generics of lenalidomide / EMA

The CMDh noted the feedback from the MWP on the CMDh questions on bioequivalence requirements for generics of lenalidomide. MWP concluded that, based on the applications that triggered the questions, an additional BE study in fed state is not required because of different in vitro dissolution profiles between test and reference product. A change of the existing PSBGL for lenalidomide was not considered necessary.

4.3. Data exclusivity of Art. 10a dossier when generic product is already authorised under the same GMA / SE

The CMDh discussed if a medicinal product authorised under Article 10a of Directive 2001/83/EC (well-established use (WEU)) can potentially benefit from data exclusivity and

market protection when an Article 10(1) generic product is already authorised in the same global marketing authorisation (same company, same active substance.

The CMDh agreed to send the questions to the EC (**Action: EMA**).

5. Referrals

5.1. Referrals to CMDh (pursuant to Art. 29(1) of Directive 2001/83/EC or Art. 13 of Regulation (EC) No 1234/2008)

5.1.1. Art. 29/13 referrals for discussion at CMDh

5.1.1.1.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.1.2. List of questions

5.1.2.1.

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.2. Referrals to PRAC (pursuant to Art. 31 or 107i of Directive 2001/83/EC)

5.2.1. Referral timetables

Tabled for information.

5.2.2. Started referral procedures at PRAC

None

5.2.3. Information on ongoing referral procedures

5.2.3.1. Hydroxyprogesterone (Art. 31)

Tabled for information.

5.2.4. PRAC recommendations for CMDh position

None

5.3. Outcome of referrals to CHMP

None

5.4. Other topics related to referrals

5.4.1. Symbioflor (Art. 31) / DE

DE presented the MAH request for a further postponement of the submission deadline of the efficacy study (imposed condition after Art. 31 referral on Symbioflor). Considering the arguments provided and the exceptional circumstances of the Covid-19 pandemic, the CMDh agreed to extraordinarily accept the proposed submission deadline of December 2027. It was noted that the MAH should endeavour to accelerate recruitment in order to submit the final study report in the shortest possible time. In addition, the CMDh agreed to request the MAH to submit informal annual updates on the status of the recruitment process and the overall progress of the clinical trial (**Action: EMA**).

6. Pharmacovigilance

6.1. Report from the December 2023 PRAC meeting

The EMA reported from the PRAC meeting held from 27-30 November 2023.

It was noted that disharmonisation of the SmPC (among others in section 4.8) of pseudoephedrine-containing medicinal products was noticed during the Art. 31 referral on pseudoephedrine. The CMDh will publish a recommendation for MAHs to keep their PI up to date once an EC decision is issued and the AR is published.

6.2. Periodic Safety Update Reports (PSUR)

6.2.1. PRAC recommendations on PSUSAs for CMDh position[1]

6.2.1.1. Aceclofenac - PSUSA/00000022/202303

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing aceclofenac.

6.2.1.2. Clarithromycin - PSUSA/00000788/202304

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing clarithromycin.

6.2.1.3. Fentanyl (transdermal patches, solution for injection - nationally authorised product only) - PSUSA/00001370/202304

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing fentanyl (transdermal patches, solution for injection - nationally authorised product only).

[1] Subject to adoption via written procedure in advance of the meeting. For discussion/adoption at the plenary if comments are received during written procedure.

6.2.1.4. Gentamicin (systemic use) - PSUSA/00009159/202303

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing gentamicin (systemic use).

6.2.1.5. Nortriptyline - PSUSA/00002192/202303

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing nortriptyline.

6.2.1.6. Piroxicam - PSUSA/00002438/202304

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing piroxicam.

6.2.1.7. Pravastatin - PSUSA/00002500/202303

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing pravastatin.

6.2.1.8. Racecadotril - PSUSA/00002602/202303

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing racecadotril.

6.2.1.9. Venlafaxine - PSUSA/00003104/202305

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing venlafaxine.

6.2.2. Information on PRAC recommendations for PSUSAs for maintenance

None

6.2.3. Information on PRAC recommendations for PSUSAs for CAPs/NAPs or CAPs

None

6.2.4. Outcomes of informal PSUR work sharing procedures / Chair

The CMDh adopted the SmARs of PSUR worksharing procedures for ramipril/bisoprolol and human normal immunoglobulin (IV) (Yimmugo). The SmARs will be published on the CMDh website (**Action: EMA**).

6.2.5. PSUSA Lead Member State appointment

The CMDh appointed the lead Member States for single assessment of PSURs for NAPs to be started until December 2024. The appointed lead member states will be published in the EURD list.

6.2.6. PSUSA Follow-up procedures

None

6.3. Results of post-authorisation safety studies (PASS) imposed in the MA (in accordance with Art. 107q)[2]

6.3.1. PRAC recommendations on PASS results for CMDh position

None

6.4. Lists

6.4.1. Union Reference Date list

The CMDh noted the update of the Union Reference Date list.

6.4.2. List of medicinal products under additional monitoring

The CMDh noted the update of the list of medicinal products under additional monitoring.

6.5. Information from Member States on actions for nationally authorised products related to safety

None

6.6. Other topics related to pharmacovigilance

6.6.1. National variation to update SmPC sections 4.7 and 4.8 of traditional herbal medicinal product containing valerian root / IE

IE informed the CMDh about the receipt of a variation for nationally authorised traditional herbal medicinal product (THMP) containing valerian root to update the PI (SmPC 4.7 & 4.8, PL and the labelling) based on a safety review by the MHRA. The MAH has been asked to provide further supportive data related to the change.

The CMDh discussed if the approach agreed for variations to implement MHRA safety reviews also applies to nationally authorised THMPs and if in this case PRAC advice should be requested or if HMPC should be consulted.

[2] Subject to adoption via written procedure in advance of the meeting. For discussion/adoption at the plenary if comments are received during written procedure.

It was noted that products containing valerian root are authorised in the EU as THMP (Art. 16a) and under other legal bases. At the time of the meeting, it was not yet known if similar variations have also been submitted for other products in other MSs.

It was further noted that ideally PRAC should be involved via a Member States' request for PRAC advice, if appropriate. However, further data would be needed to support such a request to PRAC. MHRA could also be asked to provide their assessment. HMPC would also need to be involved for a potential need to update the existing monograph.

6.6.2. Follow-up of PSUSA on furosemide/spironolactone - PSUSA/00001493/202303 / DK

Following the finalisation of the PSUSA on furosemide/spironolactone in November 2023, questions have been received from MAHs if the warnings included in section 4.5 of the SmPC and section 2 of the PL related to drug-drug interaction between aliskiren and furosemide should also be implemented in medicinal products containing furosemide as mono-component. A PSUSA on furosemide (mono-component) was finalised in September 2023, where the interaction was noted, but not included in the recommendation of the PSUSA as the interaction was already included in the PI of some (but not all) of the products.

MAHs are reminded of their obligation to keep the product information up to date with the current scientific knowledge. MAHs of oral furosemide-containing medicinal products that do not yet have a similar wording in their PI should include the below wording via a type IB variation:

SmPC, section 4.5:

Aliskiren reduces the plasma concentration of orally administered furosemide. It is recommended to monitor the diuretic effect of furosemide when starting and adjusting the dose of concomitant treatment with aliskiren.

PL, section 2:

Tell the doctor if you are being treated with medication for:

- high blood pressure (aliskiren)

7. Break-out sessions and CMDh scientific input to applications

7.1. Ticagrelol Doc (PT/H/2812/001-002/DC) / PT

PT informed the CMDh about the break-out session held for Ticagrelol Doc (PT/H/2812/001-002/DC). The application could be finalised positively based on additional data provided by the applicant.

7.2. Vitamina D Alter (PT/H/2794/001-002/DC) / PT

PT informed the CMDh about the break-out session held for Vitamina D Alter (PT/H/2794/001-002/DC). The application could be finalised positively.

8. Miscellaneous

8.1. Report from the November and December CMDv meetings

Tabled for information.

8.2. December 2023 CMDh Press Release

The CMDh press release will be circulated for written agreement (**Action: EMA**).

8.3. A.O.B.

8.3.1. Tiotropium Kappler, 18 Mikrogramm Hartkapsel mit Pulver zur Inhalation (DE/H/7377/001/DC) / DE

DE informed the CMDh about the break-out session held for Tiotropium Kappler, 18 Mikrogramm Hartkapsel mit Pulver zur Inhalation (DE/H/7377/001/DC). The application could be finalised positively based on additional data provided by the applicant.

8.3.2. Request for extension of clock-stop / IT

IT presented a case where an applicant asked for an extension of the clock-stop for up to one year.

It was noted that requests for extension of the clock-stops beyond 6 months and for up to one year should be exceptional but can be agreed by the RMS, if justified. Requests for extensions of clock-stops with a total duration of more than one year and where the RMS is in agreement with the extension should be brought for discussion at CMDh. However, in the end acceptance of the extension is a decision of the RMS.

8.3.3. Electronic submission / PL

The CMDh discussed if the use of eCTD submission units 'closing' and 'corrigendum', which are currently only used for CAP procedures, can be extended to non-CAP procedures. The discussion originated in the Human Harmonisation Group (HHG) and it was considered necessary to get CMDh input.

The CMDh considered that a corrigendum would be difficult to define and there were concerns that the corrigendum could be misused for changes that would usually require a variation. The CMDh therefore agreed not to allow corrigendum sequences for non-CAP procedures.

For the closing sequence, the CMDh agreed that the submission unit can also be used in MRP, DCP and NP, if needed, e.g. when merging documents from parallel variations without adding new changes.

Feedback will be given to HHG.

8.3.4. Synapse (Art. 31 referral) / DE

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

8.3.5. Recommendation for the transition from quadrivalent (QIV) to trivalent influenza (TIV) vaccines / EMA

Following information provided in October, the CMDh was further informed that the EMA Emergency Task Force (ETF) recommended to exclude B/Yam from the live attenuated vaccine since 2024/2025, and to target 2025-2026 for the remaining inactivated vaccines. Industry and EU public health authorities (NITAGs) prefer to avoid a mix of QIVs-TIVs on the market since tenders for QIV are already in place for 2024-2025.

The EMA asked MSs to share their plans on which season they target for the update.

It was noted that the decision on the national vaccination strategies does not lie with the regulatory authorities but in most MSs with the ministries of health.

RMSs of seasonal influenza vaccines were encouraged to discuss the (manufacturing) intentions with the MAHs, i.e. whether they intend to maintain and produce TIV and QIV in parallel or if they will focus on one or the other. The EMA should be kept informed.

8.3.6. Transition to IRIS / EMA

The EMA updated the CMDh on their approach for transferring procedures to IRIS, including timelines, objectives and key changes.

The CTS WG Chair explained that CTS will be adapted to handle the change in procedure numbers for mixed CAP-NAP WS procedures. However, NCAs that use software to automatically allocate procedures in their system, will need to adjust.

The EMA informed the CMDh that the new numbers will apply to new incoming procedures to be managed in IRIS as of 23 January 2024. This has previously been communicated to IT directors.

Although the changes mainly affect CAPs, MSs were asked to check if any problems are expected nationally, e.g. for CAP-NAP WS procedures, and to report any issues to EMA (**Action: MSs**).

9. Other topics and dates for next meeting

9.1. Draft meeting schedule and draft time schedule for referrals

The meeting schedule for January 2024 was tabled for information.

☞More information about acronyms and abbreviations used in this document can be found on the CMDh website: http://www.hma.eu/457.html

List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 12-14 December 2023 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Kora Doorduyn - van der Stoep	Chair	Netherlands	No interests declared	
Jascha Johann Hörnisch	Member	Austria	No interests declared	
Roselien Poppe	Member	Belgium	No interests declared	
Teodor Nikolov	Member	Bulgaria	No interests declared	
Sabina Uzeirbegović	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Member	Cyprus	No interests declared	
Natasa Kiza	Alternate	Cyprus	No interests declared	
Jitka Vokrouhlická	Member	Czechia	No interests declared	
Zuzana Fliegerová	Alternate	Czechia	No interests declared	
Katrine Damkjær Madsen	Member	Denmark	No interests declared	
Anne Kristine Hejlesen	Alternate	Denmark	No restrictions applicable to this meeting	
Heili Tikk	Member	Estonia	No interests declared	
Kairi Laius	Alternate	Estonia	No interests declared	
Tea Linhola	Member	Finland	No interests declared	
Pauliina Ikäheimo	Alternate	Finland	No interests declared	
Mathilde Geynet Kovacs	Member	France	No interests declared	
Susanne Winterscheid	Member	Germany	No interests declared	
Wiebke Hoppensack	Alternate	Germany	No interests declared	
Eleftheria Nikolaidi	Member	Greece	No interests declared	
Stavroula Mamoucha	Alternate	Greece	No interests declared	
Laura Ivett Varga	Member	Hungary	No interests declared	
Agnes Gabriella Szadeczkyne Kelemen	Alternate	Hungary	No interests declared	
Orn Gudmundsson	Member	Iceland	No interests declared	
Ragnhildur Heidarsdottir	Alternate	Iceland	No interests declared	
Nicole Kavanagh	Member	Ireland	No interests declared	
Laura Galatti	Member	Italy	No interests declared	
Marco Franceschin	Alternate	Italy	No interests declared	
Maija Cirkina	Member	Latvia	No interests declared	
Iveta Eglite	Alternate	Latvia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Neringa Kalinauskaitė	Alternate	Lithuania	No interests declared	
Mylene Ferrier	Member	Luxembourg	No interests declared	
Helen Vella	Member	Malta	No interests declared	
Paula Cardona Xuereb	Alternate	Malta	No interests declared	
Priscilla Schoondermark	Member	Netherlands	No interests declared	
Ingrid Bijsmans	Alternate	Netherlands	No interests declared	
Suzanne Gordon	Member	Norway	No restrictions applicable to this meeting	
Nina Malvik	Alternate	Norway	No interests declared	
Andrzej Czeslawski	Member	Poland	No interests declared	
Pawel Pawlowski	Alternate	Poland	No interests declared	
Marta Marcelino	Member	Portugal	No interests declared	
Rui Pedro da Costa Vilar	Alternate	Portugal	No interests declared	
Cristian Dan Georgescu	Member	Romania	No interests declared	
Daniela Elena Popa	Alternate	Romania	No interests declared	
Miroslava Horváth Petriková	Member	Slovakia	No interests declared	
Petra Gubova	Alternate	Slovakia	No interests declared	
Marjeta Jordan	Member	Slovenia	No interests declared	
Nevenka Prpar	Alternate	Slovenia	No interests declared	
Veronica García Morales	Member	Spain	No interests declared	
Elisa Sulleiro	Alternate	Spain	No restrictions applicable to this meeting	
Christin Olofsson	Member	Sweden	No interests declared	
Adam Andersson	Alternate	Sweden	No interests declared	
Dino Soumpasis	Chair of CTS WG	Germany	No interests declared	
Maria Luisa Casini	Chair of the PhV WS WP	Italy	No interests declared	
Jayne Crowe	Chair of GCP Inspectors Working Group/CMDh Working Party	Ireland	No interests declared	
Ad hoc experts* and a representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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