10 December 2018
EMA/32432/2019 Rev.1
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Final ORGAM[1] minutes of the meeting on 4 December 2018

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

4 December 2018, 14:00-16:40 UK time, room 2E

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be 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, the minutes are a working document primarily designed for CHMP 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] The CHMP ORGAM is a meeting to discuss CHMP organisational matters. It is a virtual meeting, which usually takes place on Monday before the CHMP Plenary meeting. CHMP members, working party chairs and national experts together with EMA staff are participating in this forum. Depending on the nature of the issue and availability of documents and experts some ORGAM topics can be discussed at the CHMP Plenary. Please note that the ORGAM meeting is not taking place every month.

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1. Agenda and Minutes

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

1.2. Adoption of agenda

CHMP ORGAM agenda for 4 December 2018 meeting was adopted.

1.3. Adoption of the minutes

CHMP Orgam Minutes of 4 December 2018 meeting will be adopted at the December 2018 CHMP plenary.

2. Working Parties, Committees, SAGs and Drafting Groups

2.1. General

2.1.1. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

No items

2.1.2. Quality Working Party (QWP)

Chair: Keith Pugh/Blanka Hirschlerova

Letter to EDQM from QWP (EMA/CHMP/QWP/785196/2018)

Action: For adoption

The CHMP adopted the letter.

2.1.3. Scientific Advice Working Party (SAWP)

Chair: Robert Hemmings

No items

2.1.4. European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP)

Co-chair: Kaisa Immonen

Summary of the PCWP Plenary Meeting held on 25 September 2018 (EMA/717595/2018)

Action: For information

The CHMP noted the Summary of the PCWP Plenary Meeting held on 25 September 2018.

Summary of the PCWP/HCPWP Joint Meeting held on 25 September 2018 (EMA/717794/2018)

Action: For information

The CHMP noted the Summary of the PCWP/HCPWP Joint Meeting held on 25 September 2018.

2.1.5. European Medicines Agency Human Scientific Committees' Working Party with Healthcare Professionals' Organisations (HCPWP)

Co-chair: Gonzalo Calvo

See 2.1.4

2.1.6. Geriatric Expert Group (GEG)

Chair: Katarina Vučić

No items

2.1.7. Committees

CHMP 2019 Draft Work Plan

Action: For adoption

The CHMP noted the draft work plan and thanked the contributors for the input provided. In case there are no further comments received, the work plan will be considered adopted during the December Plenary.

2.1.8. International Council on Harmonisation (ICH)

No items

2.1.9. Joint CVMP/CHMP ad-hoc expert group on the application of the 3Rs (replacement, reduction and refinement) in the regulatory testing of medicinal products (J 3RsWG)

Chair: Ellen-Margrethe Vestergaard, Co-Chair: Susanne Brendler-Schwaab

No items

2.1.10. Joint CHMP/CVMP/CMDh/CMDv Working Group on Active Substance Master File Procedures (ASMF WG)

Chair: Nienke Rodenhuis

No items

2.1.11. Joint CVMP-CHMP antimicrobial advice ad hoc expert group (AMEG)

Chair: Gérard Moulin

No items

2.1.12. Modelling and Simulation Working Party (MSWP)

Chair: Kristin Karlsson/Flora Musuamba Tshinanu

Call for nomination for 3 new MSWP members:

The following expertise areas need to be filled with 3 new members as a result of departure of the 3 UK members:

- PBPK modelling
- Exposure-response (PKPD) modelling
- Quantitative systems pharmacology (QSP) modelling
- Non-linear mixed effects modelling

Nominations should be sent by **25 January 2018**.

Action: For information

The CHMP noted the call.

2.2. Biologicals

2.2.1. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Niklas Ekman

No items

2.2.2. Biologicals Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Final minutes from October face-to-face meeting held 8-9 October 2018 (EMA/CHMP/BWP/700986/2018)

Action: For information

The CHMP noted the final minutes.

Draft agenda for BWP face-to-face meeting to be held 3-4 December 2018 (EMA/CHMP/BWP/730346/2018)

Action: For information

The CHMP noted the draft agenda.

2.2.3. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

No items

2.2.4. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

No items

2.2.5. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

No items

2.3. Therapeutics

2.3.1. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder/Alar Irs

No items

2.3.2. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

No items

2.3.3. Infectious Diseases Working Party (IDWP)

Chair: Maria Jesus Fernandez Cortizo

Guideline on the evaluation of medicinal products indicated for treatment of bacterial infections, Rev. 3

Action: For adoption for 6 months public consultation

Presented by Mair Powell

Mair Powell presented the guideline. The guideline merges, revises and adds to the guidance previously included in the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections (CPMP/EWP/558/95 Rev 2) and the Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections (EMA/CHMP/351889/2013).

The revisions reflect scientific advice given on the development of antibacterial agents, decisions taken during regulatory procedures and alignments on clinical trial requirements that have resulted from discussions between regulators in the EU, including revised recommendations for primary endpoints, primary analysis populations and non-inferiority margins in trials to support certain infection site-specific indications for use.

The CHMP adopted the guideline for 6 months public consultation.

2.3.4. Oncology Working Party

Chair: Pierre Demolis/Paolo Foggi

Concept paper on the revision of the guideline on the evaluation of anticancer medicinal products in man (EMA/CHMP/755489/2018)

Action: For adoption for public consultation

This Concept Paper introduces Revision 6 proposing amendments and add-ons to the last version of the guideline on the evaluation of anticancer medicinal products in man. It is also proposed to amend the title to 'the guideline on the clinical evaluation of anticancer medicinal products' (currently EMA/CHMP/205/95 Rev.5). The revision 6 proposes a review of the concepts related to biomarkers, which are increasingly used to define malignant diseases and develop new treatment strategies, improve description of the regulatory standards relevant for rare cancers and additional minor amendments to other sections.

The CHMP adopted the concept paper for public consultation.

Draft agenda for the Adobe meeting on 7 November 2018 (EMA/760743/2018)

Action: For information

The CHMP noted the draft agenda.

Draft minutes for the Adobe meeting on 10 October 2018 (EMA/706854/2018)

Action: For information

The CHMP noted the draft minutes.

Question from PDCO to ONCWP: use of extrapolation for adolescent patients with metastatic, unresectable melanoma

Action: For adoption

The CHMP adopted the question to be sent to ONCWP.

2.3.5. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

Guideline on the reporting of physiologically based pharmacokinetic (PBPK) modelling and simulation (EMA/CHMP/658647/2017)

Rapporteur: Susan Cole

Action: For adoption

Susan Cole presented the guideline. The guideline addresses:

- Purpose of the simulation including regulatory use
- Justification of system parameters, incl. library files, physiological parameters of population
- Justification of drug specific parameters- predictability

- Mechanistic description of the system
- Justification of assumptions made and impact on results
- Qualification of the system i.e. the predictive performance of the system for the particular purpose /intended use

The GCG reviewed the guideline and did not have any further comments.

The CHMP adopted the guideline.

Product-specific bioequivalence guidance, Batch 9 and 10

Batch 9 (Final):

- Aliskiren film-coated tablet 150 mg and 300 mg product-specific bioequivalence guidance (EMA/CHMP/291450/2018)
- Lapatinib film-coated tablet 250 mg product-specific bioequivalence guidance (EMA/CHMP/257298/2018)
- Pegylated liposomal doxorubicin hydrochloride concentrate for solution 2 mg/ml product-specific bioequivalence guidance (EMA/CHMP/800775/2017)

Action: For adoption

The Batch 9 (final guidances) and the associated comments received in the public consultation were presented. However the CHMP wanted to take a closer look to lapatinib guidance, due to changes made in the guideline. It was agreed to leave the lapatinib out and further discussions are expected in ORGAM in January.

The CHMP adopted the guidances for aliskiren and liposomal doxorubicin for publication.

Batch 10 (Draft):

- Alectinib hard capsule 150 mg product-specific bioequivalence guidance (EMA/CHMP/790261/2018)
- Cabozantinib tablet 20 mg, 40 mg and 60 mg, capsule 20 mg and 80 mg product-specific bioequivalence guidance (EMA/CHMP/790333/2018)
- Ezetimibe tablet 10 mg product-specific bioequivalence guidance (EMA/CHMP/802491/2018)
- Palbociclib hard capsule 75 mg, 100 mg and 125 mg product-specific bioequivalence guidance (EMA/CHMP/802679/2018)

Action: For adoption for 6 months public consultation

The Batch 10 was presented. In the discussion, it was agreed that alectinib and palbociclib need further discussion.

The CHMP adopted the guidances for cabozantinib and ezetimibe for 6 months public consultation.

2.3.6. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Jörg Zinserling

Guideline on the investigation of subgroups in confirmatory clinical trials (EMA/539146/2013)

Action: For adoption

Main points presented by Rob Hemmings. The CHMP adopted the guideline.

Question and answer on adjustment for cross-over in estimating effects in oncology trials (EMA/713584/2018)

Action: For adoption

Main points were presented. The CHMP adopted the Question and answer document.

BSWP Draft Minutes of BSWP virtual meeting on 19 June 2018

Action: For information

BSWP Draft Minutes of the BSWP virtual meeting on 11 September 2018

Action: For information

The CHMP noted the draft minutes.

Nomination of additional assessors:

Action: For adoption

The CHMP nominated Wolfgang Jacquet and Finbarr Leacy as additional assessors.

Composition of BSWP

Action: For discussion

Presented by Anja Schiel

As an impact of Brexit, there is a loss of 2 UK members (inc. CHMP co-opted member) and 3 UK additional assessors. In anticipation from UK delegates leaving BSWP, proposal to reconsider the nomination of two additional assessors as described in point 2.3.6.5.

As a follow up on CHMP's decision at plenary March 2018 to limit the number of temporary WP participants to 30 delegates – in BSWP, there are currently over 30 participants – BSWP has reviewed the role, contribution and attendance of all BSWP delegates. Six additional assessors who are not actively involved in BSWP activities were identified. They were contacted and enquired about their interest in BSWP.

The CHMP endorsed BSWP's strategy about its composition.

2.3.7. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus/Romaldas Mačiulaitis

Concept paper on a Guideline for allergen products development in moderate to low-sized study populations (EMA/CHMP/251023/2018)

Presented by Andreas Bonertz via Adobe

Action: For adoption for 6 months public consultation

Several guidelines applicable for allergen products are available and provide advice on quality and clinical development according to the current knowledge. However, for the evaluation according to these guidelines, a sufficient number of patients are needed for clinical trials which cannot be achieved in case of allergies of low prevalence or where clinical co-allergies are common. There is an unmet medical need for effective diagnosis and disease modifying treatment by allergen immunotherapy (AIT) for patients suffering from these allergies, in contrast to allergies of high prevalence for which currently defined test and therapy allergens are available.

It has become clear that there is a need to clarify the EU regulatory expectations with regard to the data on quality, safety and efficacy for test and therapy allergens to provide sufficient scientific evidence for the approval of such allergen products.

The GCG had reviewed the concept paper.

The CHMP adopted the concept paper for 6 months public consultation.

2.3.8. Scientific Advisory Groups (SAGs)

No items

2.3.9. Drafting Groups (DGs)

No items

2.3.9.1. Gastroenterology Drafting Group (GDG)

Chair: Mark Ainsworth

No items

2.3.9.2. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

No items

2.3.9.3. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

No items

2.3.9.4. Excipients Drafting Group

Chair: Dominique Masset

No items

2.3.10. Additional agenda points

2.3.10.1. Innovation Task Force

EC request for EMA opinion on the definitions of pharmacological, immunological, metabolic and medical diagnosis.

Action: For discussion

EMA presented on the new EC request received under Article 57 for scientific opinion on the definitions of pharmacological, immunological, metabolic and medical diagnosis. The CHMP was invited to send comments in writing.

2.3.10.2. Guideline Consistency Group (GCG)

Chair: Aranzazu Sancho-Lopez

No items

2.3.10.3. IPRF Nano Working Group

Chair: Harald Enzmann

No items

3. Organisational, regulatory and methodological matters

3.1. Regulatory Issues / new legislation

3.1.1. Proposal to harmonise the rules for chairmanship across WPs (two-term rule)

Presentation

Action: For discussion/adoption

The CHMP adopted the proposal for harmonisation of the rules of procedure across Working Parties. The 2-term rule across all (CHMP) scientific working parties will be harmonised. The phrase will be introduced 'which may be renewed once' in rules of procedure for BWP, QWP, SAWP and SWP.

4. Any Other Business

4.1. EMA emerging health threats plan

EMA emerging health threats plan (EMA/262604/2016)

Presentation

Action: For information

The health threats plan was presented. The objectives of the plan are:

- initiate and coordinate scientific and regulatory activities by involving all interested parties within the EMA and the EU Medicines Regulatory network;

- coordinate discussions on development, authorisation and post-authorisation follow-up of relevant medicinal products;
- effectively communicate relevant information to healthcare professionals, patients and regulatory partners;
- support international partners, stakeholders involved in research/development of medicinal products and public health authorities outside of Europe.

The EMA teams involvement, activities and staff were presented according to the emergency levels. In addition, different EMA expert groups would be used. Rapid "Scientific Advice" procedures can be convened. The document will be published.

The CHMP noted the EMA emerging health threats plan.

4.2. Ebola in Democratic Republic of the Congo (DRC)

Presentation

Action: For information

Ebola outbreak in DRC was presented. This is the 2nd consecutive Ebola outbreak.

The CHMP noted the presentation.

4.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

4.3.1 WS1278: OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042 Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053

Bristol-Myers Squibb Pharma EEIG

Initial Lead Rapporteur: Paula Boudewina van Hennik, Initial Lead Co-Rapporteur: Jorge Camarero Jiménez

Scope: "Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The Package Leaflet and the Risk Management Plan (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Yervoy and Opdivo product information."

Action: For discussion

Report from the SAG-Oncology meeting held 08 November 2018.

Opinion adopted on 15.11.2018. The final opinion documents were sent for adoption via written procedure on 28.11.2018.

The CHMP discussed the assessment report and its updated wording.

5. List of participants

CHMP Chair:

Harald Enzmann

CHMP members:

Bruno Sepodes (Vice-Chair)

Agnes Gyurasics

Concepcion Prieto Yerro

Ewa Balkowiec Iskra

Greg Markey

Kristina Dunder

Outi Mäki-Ikola

Robert James Hemmings

Simona Badoi

Katarina Vučić

Martina Weise

Jayne Crowe

CHMP alternate members:

Christophe Focke

Nithyanandan Nagercoil

Fátima Ventura

Milena Stain

Bjorg Bolstad

Dana Gabriela Marin

Filip Josephson

Jorge Camarero Jiménez

Mark Ainsworth

Natalja Karpova

Paula Boudewina van Hennik

Peter Kiely

Experts:

Andreas Bonertz

Anne Hasle Buur

Henrike Potthast

Olga Kholmanskikh

Pierre Demolis

Sabine Mayrhofer

Susan Cole

A representative from the European Commission attended the meeting

The meeting was run with support from the relevant EMA staff