16 September 2016
EMA/CHMP/623490/2016
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 18-21 July 2016

Chair: Tomas Salmonson – Vice-Chair: Pierre Demolis

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 this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available.

Of note, this agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the agenda 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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Table of contents

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 as included in the pre-meeting list of participants and restrictions. See (current) July 2016 CHMP minutes for the pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 18-21 July 2016.

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). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Committee welcomed new Danish alternate member Hanne Lomholt Larsen.

1.2. Adoption of agenda

CHMP agenda for 18-21 July 2016

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 20-23 June 2016.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

No items

2.2. Re-examination procedure oral explanations

2.2.1. Sialanar - glycopyrronium bromide - PUMA - EMEA/H/C/003883

Proveca Limited; Symptomatic treatment of sialorrhoea (chronic pathological drooling) in children and adolescents aged 3 to <18 years with neurological disorders.

Scope: Oral explanation and Opinion, report from ad-hoc expert group held on 11 July 2016.

Action: Oral explanation to be held on Tuesday 19 July 2016 at 9.00.

Opinion adopted on 28.04.2016.

An oral explanation was held on Tuesday 19 July 2016 at 9.00.

See also 3.5.1

2.3. Post-authorisation procedure oral explanations

2.3.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0020 & EMEA/H/C/002720/R/0022

MAH: PTC Therapeutics International Limited,

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus,

Scope: Oral explanation, Type II variation

“Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information.”
Request for Supplementary Information adopted on 01.04.2016.

Scope: Oral explanation, Renewal of Marketing Authorisation

Action: Oral explanation to be held on Tuesday 19 July 2016 at 14.00.

Oral explanation held in June 2016. Request for Supplementary Information adopted on 28.04.2016.

Action: For adoption

The CHMP agreed that no Oral Explanation was required at this time.

See also 9.1.1

2.4. Referral procedure oral explanations

2.4.1. Diclofenac 50 mg Tablets - Diclofenac epolamine - EMEA/H/A-29/1434

Altergon Italia srl

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Joseph Emmerich,

RMS: UK, CMS: CZ, FR, SK

Decentralised Procedure number: UK/H/5906/001/DC

Disagreements regarding the demonstration of bioequivalence in the fed state

Scope: Oral explanation

Action: Possible oral explanation to be held on Wednesday 20 July 2016 at 9.00.

An oral explanation was held on Wednesday 20 July 2016 at 9.00

See also 10.4.1

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Cabometyx - cabozantinib - EMEA/H/C/004163

Accelerated assessment

Ipsen Pharma; treatment of advanced renal cell carcinoma (RCC)

Scope: Opinion

Action: For adoption

Known active substance (Article 8(3) of Directive No 2001/83/EC)

List of Questions adopted on 26.05.2016.

The CHMP discussed the wording of the indication.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP agreed by consensus on the one additional year of market protection for a new indication.

The CHMP adopted the similarity assessment report for Cabometyx

The summary of opinion was circulated for information.

3.1.2. Inhixa - enoxaparin sodium - EMEA/H/C/004264

Techdow Europe AB; prophylaxis of thromboembolic disorders of venous origin

Scope: Opinion

Action: For adoption

Similar biological application (Article 10(4) of Directive No 2001/83/EC), Duplicate of Thorinane

List of Outstanding Issues adopted on 28.04.2016. List of Questions adopted on 23.07.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The CHMP noted the letter of recommendation dated 15.07.2016.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.3. Thorinane - enoxaparin sodium - EMEA/H/C/003795

Pharmathen S.A.; prophylaxis of thromboembolic disorders of venous origin

Scope: Opinion

Action: For adoption

Similar biological application (Article 10(4) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 28.04.2016. List of Questions adopted on 23.07.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The CHMP noted the letter of recommendation dated 14.07.2016.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.4. Kisplyx - lenvatinib - EMEA/H/C/004224

Accelerated assessment

Eisai Europe Ltd.; in combination with everolimus for the treatment of unresectable

advanced or metastatic renal cell carcinoma (RCC)

Scope: Opinion

Action: For adoption

Known active substance (Article 8(3) of Directive No 2001/83/EC)

List of Questions adopted on 26.05.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for Kisplyx

3.1.5. Onivyde - irinotecan - Orphan - EMEA/H/C/004125

Baxalta Innovations GmbH; treatment of pancreatic cancer

Scope: Opinion

Action: For adoption

Known active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.02.2016. List of Questions adopted on 24.09.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.6. Tenofovir disoproxil Zentiva - tenofovir disoproxil - EMEA/H/C/004120

Zentiva k.s.; treatment of HIV-1 infection and hepatitis B infection

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Viread

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 28.01.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.7. Truberzi - eluxadoline - EMEA/H/C/004098

Aptalis Pharma SAS; for the treatment of irritable bowel syndrome with diarrhoea

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 24.09.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that eluxadoline is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.8. MysildeCard - sildenafil - EMEA/H/C/004186

MYLAN S.A.S.; treatment of pulmonary arterial hypertension

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Revatio

List of Questions adopted on 01.04.2016.

The Committee confirmed that all issues previously identified in this application had been addressed. It was agreed to finalise the document package by written procedure.

The Committee adopted a positive opinion by written procedure on 28 July 2016 recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for MysildeCard

3.2. Initial applications; Day 180 list of outstanding issues

3.2.1. - bezlotoxumab - EMEA/H/C/004136

indicated for the prevention of Clostridium difficile infection (CDI) recurrence

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to consult a SAG.

The CHMP adopted the BWP report.

3.2.2. - pegfilgrastim - EMEA/H/C/004342

treatment of neutropenia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.3. - chenodeoxycholic acid - Orphan - EMEA/H/C/004061

Sigma-tau Arzneimittel GmbH; treatment of inborn errors of primary bile acid synthesis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.04.2016. List of Questions adopted on 25.02.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.4. - dasabuvir / ombitasvir / paritaprevir / ritonavir - EMEA/H/C/004235

treatment of hepatitis C

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.5. - pegfilgrastim - EMEA/H/C/004023

treatment of neutropenia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.6. - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050

treatment of HIV

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 19.11.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.7. - ivabradine - EMEA/H/C/004117

treatment of angina pectoris

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.8. - parathyroid hormone - Orphan - EMEA/H/C/003861

NPS Pharma Holdings Limited; treatment of hypoparathyroidism

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 28.04.2016, 24.09.2015. List of Questions adopted on 26.03.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.9. - obeticholic acid - Orphan - EMEA/H/C/004093

Intercept Italia s.r.l; treatment of primary biliary cirrhosis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 22.10.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable. The consultation of an ad hoc expert group was not considered at this stage.

3.2.10. - follitropin delta - EMEA/H/C/003994

indicated for controlled ovarian stimulation

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.02.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues.

The CHMP adopted the BWP report.

3.2.11. - edotreotide - Orphan - EMEA/H/C/004140

Advanced Accelerator Applications; Diagnosis of gastro-entero-pancreatic neuroendocrine tumours

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.02.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.12. - tenofovir disoproxil - EMEA/H/C/004049

treatment of HIV-1 infection and hepatitis B infection

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 17.12.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.13. - venetoclax - Orphan - EMEA/H/C/004106

AbbVie Ltd.; treatment of adult patients with chronic lymphocytic leukaemia (CLL)

Scope: Day 180 list of outstanding issues

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.3. Initial applications; Day 120 list of questions

3.3.1. - rurioctocog alfa pegol - EMEA/H/C/004195

treatment of haemophilia A

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application. .

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions .

The CHMP agreed to consult the SWP.

The CHMP adopted the BWP report.

3.3.2. - expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue - Orphan - ATMP - EMEA/H/C/004258

S.A.U.; treatment of complex perianal fistula(s)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application. The members were updated on the discussions at the CAT.

The Committee noted the CAT recommendation and scientific discussion together with the list of questions. The CHMP adopted an additional question to the list of questions and an addition to the benefit risk section.

The CHMP adopted the BWP report.

3.3.3. - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

The CHMP agreed to consult a SAG.

3.3.4. - tivozanib hydrochloride monohydrate - Orphan - EMEA/H/C/004131

EUSA PHARMA; treatment of adult patients with advanced renal cell carcinoma (RCC)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.5. - alpha-1-antitrypsin - Orphan - EMEA/H/C/003934

Kamada BioPharma Limited at Fieldfisher LLP; treatment and maintenance therapy of adult patients with congenital deficiency of alpha-1 antitrypsin and lung disease with clinical evidence of emphysema and airway obstruction (FEV1/SVC<70%).

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

3.3.6. - nitisinone - EMEA/H/C/004281

treatment of hepatorenal tyrosinemia type 1

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.7. - pemetrexed - EMEA/H/C/004306

treatment of malignant pleural mesothelioma and non-small cell lung cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with

the list of questions.

3.3.8. - pemetrexed - EMEA/H/C/004488

treatment of malignant pleural mesothelioma and non-small cell lung cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.9. - cariprazine - EMEA/H/C/002770

treatment of schizophrenia

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.10. - pregabalin - EMEA/H/C/004277

treatment of neuropathic pain, epilepsy and Generalised Anxiety Disorder (GAD)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.11. - insulin glargine / lixisenatide - EMEA/H/C/004243

for the treatment of adults with type 2 diabetes mellitus

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

3.3.12. - rolapitant - EMEA/H/C/004196

prevention of nausea and vomiting

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.13. - tofacitinib - EMEA/H/C/004214

treatment of active rheumatoid arthritis

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP agreed to consult a SAG.

3.3.14. - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388

treatment of metastatic colorectal cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.4. Update on on-going initial applications for Centralised procedure

3.4.1. - padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Letter from the applicant dated 8 July 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 26 May 2016.

Action: For information

List of Questions adopted on 26.05.2016

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 26 May 2016.

3.4.2. - pegfilgrastim - EMEA/H/C/004211; treatment of neutropenia

Scope: Letter from the applicant dated 8 July 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 26 May 2016.

Action: For information

List of Questions adopted on 26.05.2016

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 26 May 2016. The CHMP noted that the applicant revised their proposal. The applicant was requested to provide further information .

Post-meeting note: the request for extension of clock stop was agreed and adopted via written procedure after the July Plenary, 25th July 2016.

3.4.3. - iloperidone - EMEA/H/C/004149

treatment of schizophrenia

Scope: Letter from the applicant dated 6 July 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 28.04.2016

Action: For information

List of Questions adopted on 28.04.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 28.04.2016

3.4.4. - ivabradine - EMEA/H/C/004241

treatment of angina pectoris

Scope: Letter from the applicant dated 14 July 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 01.04.2016

Action: For adoption

List of Questions adopted on 01.04.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 01.04.2016

3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004

3.5.1. Sialanar - glycopyrronium bromide - PUMA - EMEA/H/C/003883

Proveca Limited; Symptomatic treatment of sialorrhoea (chronic pathological drooling) in children and adolescents aged 3 to <18 years with neurological disorders.

Scope: Opinion

Action: For adoption

Well-established use application (Article 10a of Directive No 2001/83/EC)

Opinion adopted on 28.04.2016.

The members noted the report from the ad hoc expert group meeting held 11 July 2016. The experts advised on the current treatment options of sialorrhoea and the impact the condition has on the patients and care givers. The ad hoc expert group highlighted that none of the currently used treatments is approved in this indication and outlined the treatment limitations. The group considered the most appropriate patient population as those with severe drooling with less emphasize on the age range. The experts summarised the safety issues expected for this active substance. For children with neurological conditions the experts expected that potential side effects could be well detected by their carers/parents. However a careful dose titration and clear guidance on the identification and management of side effects would be required. The experts acknowledged that robust long term data was lacking and proposed a drug utilisation study to monitor the appropriate usage.

An oral explanation was held on Tuesday 19 July 2016 at 9.00. The presentation focused on the proposed target population and the available clinical data in this population. The safety data was summarised and risk minimisation measures proposed including a drug utilisation study.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (28 positive out of 30 votes) together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The divergent position (Ondrej Slanar, Hanne Lomholt Larsen) was appended to the opinion.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendations dated 19.07.2016.

The summary of opinion was circulated for information.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. - begelomab - Orphan - EMEA/H/C/004144

ADIENNE S.r.l. S.U.; treatment of graft-versus-host disease

Scope: Letter from the applicant dated 4 July 2016 informing of the decision to withdraw the MAA.

Action: For information

List of Questions adopted on 25.02.2016.

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion

4.1.1. Fycompa - perampanel - EMEA/H/C/002434/X/0025

Eisai Europe Ltd.

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams

Scope: "To add a new pharmaceutical form, 0.5 mg/ml oral solution, to the one currently approved (EU/1/12/776/024)."

Action: For adoption

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 17.12.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues

4.2.1. Stelara - ustekinumab - EMEA/H/C/000958/X/0049/G

Janssen-Cilag International N.V.

Rapporteur: Greg Markey, Co-Rapporteur: David Lyons, PRAC Rapporteur: Julie Williams

Scope: "An extension application covering a new pharmaceutical form (concentrate for solution for infusion), a new strength (130mg) and a new route of administration (intravenous use); a type II variation (C.1.6.a) to add a new indication (Crohn`s Disease)."

Action: For adoption

List of Questions adopted on 28.04.2016.

The Committee discussed the issues identified in this application. The main discussion concerned amendments to the RMP, the final wording of the indication, and discussions on a long-term extension study.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

4.2.2. Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/X/0050/G

Bial - Portela & Cª, S.A.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Martin Huber

Scope: "Grouping of a line extension application to add a new pharmaceutical form (50 mg/ml oral suspension) and a type II variation (C.I.6.a New indication (paediatric indication)) to add treatment of children aged 2 years and older. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet.
The application included a revised RMP version 14.0."

Action: For adoption

List of Questions adopted on 19.11.2015.

The Committee discussed the issues identified in this application. A concern was raised on the acceptability of the proposed posology in the extended target population compared to the adult population. The members discussed the data available supporting the new formulation and extension of the indication. They discussed the lack of relative bioavailability data for the tablets and the new oral suspension formulation intended for commercial use which was considered important to fully understand the impact of a possible switch between the different pharmaceutical forms.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question

4.3.1. Xtandi - enzalutamide - EMEA/H/C/002639/X/0029

Astellas Pharma Europe B.V.

Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas

Scope: "To add new pharmaceutical form and strenghts (film-coated tablets 40 mg and 80 mg) to the currently approved presentations for Xtandi."

Action: For adoption

The Committee discussed the issues identified in this application and agreed that further explanations are needed on some issues, which were related to clinical and quality aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No items

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

No items

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

5.1.1. Adempas - riociguat - Orphan - EMEA/H/C/002737/II/0011

Bayer Pharma AG

Rapporteur: Pieter de Graeff, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indication to include pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD).
As a consequence, sections 4.4 and 5.1 of the SmPC are also updated in order to reflect on

the extended indication. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to correct information regarding one of the CYP isoforms involved in the metabolism of riociguat in sections 4.5 and 5.2.
Furthermore, the PI is brought in line with the latest QRD template version 9.1."

Action: For adoption

The CHMP adopted the similarity assessment report.

The Committee discussed the issues identified in this application, which were related to safety issues.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.2. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0020

Biofrontera Bioscience GmbH

Rapporteur: Harald Enzmann,

Scope: "Extension of Indication to include treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerization based on the phase III clinical study ALA-AK-CT007. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet and to bring section 6.6 of the SmPC in line with the latest QRD template."

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016, 23.06.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.3. Humira - adalimumab - EMEA/H/C/000481/II/0154

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension of Indication to include adolescents from 12 years of age for the Humira hidradenitis suppurativa indication. As a consequence, sections 4.1, 4.2, 5.1 and 5.2, of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to age cut-off and need for disease registry.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.4. Orencia - abatacept - EMEA/H/C/000701/II/0097

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of Indication to extend the use of Orencia in combination with methotrexate (MTX) in the treatment of adults with rheumatoid arthritis (RA) who have highly active disease not previously treated with MTX. As a consequence, sections 4.1 and 5.1 of the SmPC (for powder for concentrate for solution for infusion) and sections 4.1, 4.8 and 5.1 of the SmPC (for solution for injection in pre-filled syringe and solution for injection in pre-filled pen) are updated based on results from AVERT study (IM101226). The Package Leaflet is updated accordingly. Moreover, the updated RMP version 20.1 has been agreed."

Action: For adoption

Request for Supplementary Information adopted on 25.02.2016.

The Committee discussed the wording of the indication and confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.5. Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0126

Gilead Sciences International Ltd

Rapporteur: Greg Markey, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams

Scope: "Extension of the indication to add Pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 in adults at high risk. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 28.04.2016.

The Committee discussed the posology and method of administration. The Committee agreed on the final SmPC, PL and agreed that Truvada should be taken with food.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.6. Xalkori - crizotinib - EMEA/H/C/002489/II/0039

Pfizer Limited

Rapporteur: Pierre Demolis, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Claire Ferard

Scope: "Extension of Indication to include treatment of adults with ROS1-positive advanced non-small cell lung cancer (NSCLC) based on the results of Study A8081001 (a multinational, multicenter, open-label, single-arm study of the safety, pharmacokinetics, pharmacodynamics, and antitumor activity of crizotinib in patients with advanced cancer). Consequential changes are proposed to SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 and the Package Leaflet is proposed to be updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Annex II. The application included an updated RMP version 7.0."

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The CHMP adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The updated summary of opinion was circulated for information.

5.1.7. Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0053

Bial - Portela & Cª, S.A.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include the use of Zebinix as monotherapy in adults, in addition to the previously authorised indication as adjunctive therapy. As a consequence, Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. This submission includes an updated RMP (version 15.0). In addition, the MAH is claiming an additional 1-year period of market protection under Article 14(11) of Regulation (EC) No 726/2004.",

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

The Committee discussed the issues identified in this application. The main issues discussed related to assay sensitivity and efficacy results as well as the acceptability of the request for a 1 year of market protection.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.8. Zydelig - idelalisib - EMEA/H/C/003843/II/0011

Gilead Sciences International Ltd

Rapporteur: Kristina Dunder, PRAC Rapporteur: Rafe Suvarna

Scope: Revised Opinion

"Extension of Indication to include new indication for Zydelig to include the combination of idelalisib with ofatumumab. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for United Kingdom and Ireland in the Package Leaflet."

Action: For adoption

Opinion adopted on 25.02.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The CHMP adopted a revised opinion taking into account the outcome of the referral procedure EMEA/H/C/003843/A20/0023 (see 10.1.1.) by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The updated summary of opinion was circulated for information.

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

5.2.1. Lucentis - ranibizumab - EMEA/H/C/000715/II/0061

Novartis Europharm Ltd

Rapporteur: Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Revised assessment timetable

Scope: “Extension of Indication to include treatment of visual impairment due to choroidal neovascularization (CNV) based on 6-month data from the pivotal study CRFB002G2301 (MINERVA). Consequential changes are proposed to SmPC sections 4.1, 4.2, 4.8 and 5.1 and the Package Leaflet is proposed to be updated accordingly.
The application included an updated RMP version 16.0.”, Clockstop extension requested to respond to RSI.

Request for Supplementary Information adopted on 26.05.2016.

Action: For information

The CHMP adopted a revised timetable.

5.2.2. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0012

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus

Scope: “Extension of indication for Translarna to include the treatment of cystic fibrosis resulting from a nonsense mutation in at least one allele of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Consequently, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC were updated. The Package leaflet and RMP are being updated accordingly. The MAH took also the opportunity to implement the QRD template v9.1. and proposed combined SmPC for Translarna 125 mg, 250 mg and 1000 mg granules for oral suspension. Minor editorial changes have been introduced throughout the PI.”

Letter from the applicant requesting an extension of the clock stop to respond to the request for supplementary information adopted in December 2015.

Action: For adoption

The CHMP agreed to the request by the MAH for an extension to the clock stop to respond to the request for supplementary information adopted in December 2015.

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

No items

6. Ancillary medicinal substances in medical devices

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. - PERAMIVIR - H0004299

Treatment of influenza

Scope: Letter from the company dated 25 May 2016 requesting an accelerated assessment

Action: For adoption

Briefing note and Rapporteurs' recommendation on the request for accelerated assessment.

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. - cenegermin - H0004209

Treatment of moderate or severe neurotrophic keratitis

Scope: Briefing note and Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

Letter from the company dated 10.06.2016 requesting an accelerated assessment

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and recommendation on the Request for Accelerated Assessment.

8.2. Priority Medicines (PRIME)

Disclosure of information related to priority medicines cannot be released at present time as these contain commercially confidential information

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 9 recommendations for eligibility to PRIME: 2 were granted and 7 were denied. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0020 & EMEA/H/C/002720/R/0022

MAH: PTC Therapeutics International Limited,

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus,

Scope: Oral explanation, Type II variation

“Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information.”
Request for Supplementary Information adopted on 01.04.2016.

Scope: Oral explanation, Renewal of Marketing Authorisation

Action: Possible Oral explanation to be held on Tuesday 19 July 2016 at 14.00.

Oral explanation held in June 2016. Request for Supplementary Information adopted on 28.04.2016.

Action: For adoption

The CHMP agreed that no Oral Explanation was required at this time.

The CHMP was reminded of the available clinical data including the results of study 020. The members discussed the proposed new study design and its feasibility.

The Committee considered whether more information should be requested from the applicant.

The Committee adopted a request for supplementary information on the annual renewal of the conditional marketing authorisation and the Type II variation with a specific timetable.

The Committee considered relevant that the MAH should request for scientific advice. Furthermore the Committee agreed to involve aSAG. The Committee adopted a draft list of questions to the SAG.

9.1.2. Xarelto - Rivaroxaban - EMEA/H/C/000944 – follow up of LEG 37

Bayer Pharma AG, prevention of venous thromboembolism (VTE), prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise,

Scope: Update on ROCKET AF Trial and International Normalized Ratio (INR) device

Action: For adoption

The CHMP reviewed additional analysis and information submitted by the MAH in relation to the ROCKET study, more specific on the INR device used in the study. The additional sensitivity analyses provided by the MAH result in minor or only modest differences in the hazard ratios for the major efficacy and safety outcome as compared to the originally reported results. This is in accordance with the sensitivity analyses performed and assessed in the previous EMA reports related to LEG 37 finalised in January 2016. The additional information submitted in relation to the Covance recheck programme do not alter the January 2016 conclusion of LEG 037.

The CHMP agreed that the conclusion made for LEG 37 and concluded in January 2016 remain valid and that there is sufficient evidence to conclude that the benefit/risk balance remains unchanged and favourable for treatment with rivaroxaban in the prevention of thromboembolism in non-valvular atrial fibrillation. In view of the fact that new data became available and had to be assessed, the CHMP AR contains as well a reminder of the MAH obligation to proactively investigate and report any potentially important concerns that may affect the understanding of the safety profile or the benefit/risk balance of their products.

The CHMP adopted the joint LEG assessment report by consensus.

9.1.3. Ranexa - ranolazine - EMEA/H/C/000805/II/0051

MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Kristina Dunder,

Scope: Request for Supplementary Information / Opinion

"Update of section 5.1 of the SmPC in order to include the data from the final CSR of study RIVER-PCI. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the details of local representative in Bulgaria in the Package Leaflet and to bring the Annex II in line with the latest QRD template version 9.1."

Request for Supplementary Information adopted on 14.04.2016.

Action: For adoption

The Committee discussed the issues identified in this application, which were related to benefit-risk balance in elderly patients.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.4. Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAI GmbH, Rapporteur: Andrea Laslop,

Scope: Request for Supplementary Information / Opinion

"Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI administration. The Package leaflet has been updated accordingly. Additionally, the MAH has taken the opportunity to align the PI with the latest QRD template version 9.1."

Request for Supplementary Information adopted on 23.06.2016, 01.04.2016, 28.01.2016.

Action: For discussion

The Committee discussed the issues identified in this application. The CHMP looked at the available clinical data for the new test in comparison with the available standard test. Some questions were raised on the chosen cut-off point of the new test meal which related to the interpretation of the diagnostic performance of the new test.

The CHMP adopted a 4th request for supplementary information with a specific timetable.

9.1.5. Imbruvica - ibrutinib – Orphan - EMEA/H/C/003791/II/0017/G

MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams,

Scope: Request for Supplementary Information / Opinion

"Update of sections 4.8 and 5.1 of the SmPC in order update the safety and efficacy information following conclusion of studies MCL 3001 and CLL 3001. Annex II has been updated to remove the obligation to submit final CSR of study MCL 3001. The Package Leaflet and RMP are updated accordingly.
In addition, the Marketing authorisation holder (MAH) introduced minor editorial changes

throughout the PI.
Submission of final CSRs for studies MCL 2001 and 1117 in fulfilment of post-authorisation measures.
In addition to the above trials, data from 2 other trials are included in support of the use of ibrutinib in combination with other agents in subjects with relapsed/refractory CLL."
Request for Supplementary Information adopted on 23.06.2016, 25.02.2016.

Action: For discussion

The Committee confirmed that all issues previously identified in this application had been addressed. Furthermore, the submission of the results from the trial CLL3001 leads to an extension of the indication to include combination tyreatment of ibrutinib with bendamustine and rituximab in CLL.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

9.1.6. Praluent - alirocumab - EMEA/H/C/003882/II/0009/G

MAH: sanofi-aventis groupe, Rapporteur: Pieter de Graeff

Scope: Request for Supplementary Information / Opinion

"Update of section 4.2 of the SmPC to include a 300 mg Q4W dosing regimen as a starting dose, based on the results of study CHOICE I (MEA 005).
Section 4.8, 5.1 and 5.2 of the SmPC and the PL have also been updated to reflect the study results.
In addition, the MAH submitted the final study report of study CHOICE II (MEA 009) and additional analysis of the two studies

Action: For discussion

The Committee discussed the issues identified in this application, which were related to dosing regimen.

The CHMP adopted a request for supplementary information with a specific timetable.

9.1.7. ChondroCelect - Characterised Autologous Cartilage Cells Expressing A Specific Marker Profile - EMEA/H/C/000878

MAH: TiGenix NV, Repair of single symptomatic cartilaginous defects

CHMP Coordinators: Jan Mueller-Berghaus, Outi Mäki-Ikola, Rapporteur: Egbert Flory, Co-Rapporteur: Tiina Palomäki,

Scope: Letter from the MAH dated 5 July 2016 informing of decision to withdraw the marketing authorisation as of 30 November 2016.

Action: For information

The CHMP noted the letter from the MAH informing about the withdrawal of the marketing authorisation.

9.1.8. Opgenra - Eptotermin Alfa - EMEA/H/C/000819

MAH: Olympus Biotech International Limited, treatment of spondylolisthesis

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Patrick Salmon,

Scope: Letter from the MAH dated 25 May 2016 informing of decision to withdraw the marketing authorisation.

Action: For information

The CHMP noted the letter from the MAH informing about the withdrawal of the marketing authorisation.

9.1.9. Edistride - dapagliflozin - EMEA/H/C/004161/LEG 001.1
Forxiga - dapagliflozin - EMEA/H/C/002322/LEG 019.1
Ebymect - dapagliflozin, metformin - EMEA/H/C/004162/LEG 001.1
Xigduo - dapagliflozin / metformin EMEA/H/C/002672/LEG 005.1

Applicant: AstraZeneca AB

Scope: Consultation on the assessment of the risk of toe amputation with dapagliflozin-containing medicinal products in the context of the ongoing article 20 of Regulation (EC) No 726/2004 for canagliflozin-containing medicinal products

Action: For information

The CHMP noted the PRAC advice, recommending that the review under Article 20 of Regulation (EC) No 726/2004 of canagliflozin-containing medicines should be broadened to the whole class of SGLT2-inhibitors to allow a review of data on the risk of amputation, including reports from post-marketing and any other sources, and their impact on the benefit-risk balance of authorised SGLT2-inhibitor medicines.

9.1.10. Jardiance - empagliflozin - EMEA/H/C/002677/LEG 006
Synarjy - empagliflozin, metformin – EMEA/H/C/003770/LEG 004

Applicant: Boehringer Ingelheim GmbH

Scope: Consultation on the assessment of the risk of toe amputation with empagliflozin-containing medicinal products in the context of the ongoing article 20 of Regulation (EC) No 726/2004 for canagliflozin-containing medicinal products

Action: For information

The CHMP noted the PRAC advice, recommending that the review under Article 20 of Regulation (EC) No 726/2004 of canagliflozin-containing medicines should be broadened to the whole class of SGLT2-inhibitors to allow a review of data on the risk of amputation, including reports from post-marketing and any other sources, and their impact on the benefit-risk balance of authorised SGLT2-inhibitor medicines.

10. Referral procedures

10.1. Procedure for Centrally Authorised products under Article 20 Council Regulation (EC) No 726/2004

10.1.1. Zydelig - idelalisib - EMEA/H/C/003843/A20/0023

Gilead Sciences International Ltd; treatment of chronic lymphocytic leukaemia (CLL) and refractory follicular lymphoma (FL)
Rapporteurs for the Article 20 procedure: Rapporteur: Rafe Suvarna, Co-Rapporteur: Ulla Wändel Liminga

CHMP Rapporteurs for Zydelig: Rapporteur: Filip Josephson, Co-Rapporteur: Pieter de Graeff

Scope: Opinion, Report from SAG Oncology held on 12 May 2016

Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on pharmacovigilance data

Action: For adoption

The CHMP noted the report from the SAG Oncology. The CHMP noted the PRAC recommendation.

The CHMP adopted an opinion by consensus based on the PRAC recommendation.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP agreed to the DHPC and communication plan.

The CHMP noted the EMA public health communication.

10.1.2. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free): Daklinza - daclatasvir; Exviera - dasabuvir ; Viekirax - ombitasvir, paritaprevir, ritonavir ; Olysio – simeprevir; Sovaldi - sofosbuvir sofosbuvir, Harvoni - ledipasvir –EMEA/H/A-20/1438

Applicant: Bristol-Myers Squibb Pharma EEIG (Daklinza); AbbVie Ltd (Exviera, Viekirax); Janssen-Cilag International N.V. (Olysio); Gilead Sciences International Ltd (Harvoni, Sovaldi)

CHMP Rapporteurs: Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings (Daklinza), Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege (Exviera, Viekirax), Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Daniela Melchiorri (Olysio); Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs (Sovaldi), Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich (Harvoni)

PRAC Rapporteur: Margarida Guimarães; PRAC Co-rapporteur: Dolores Montero Corominas

Scope: List of Questions to SAG virology as adopted by PRAC

Review of the benefit-risk balance of DAAV following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on

pharmacovigilance data

Action: For adoption

The CHMP agreed to the list of questions to the SAG virology as adopted by PRAC.

10.1.3. Invokana – canagliflozin, Vokanamet - canagliflozin / metformin, Jardiance – empagliflozin, Synjardy - empagliflozin/metformin, Forxiga – dapagliflozin, Edistride – dapagliflozin, Xigduo - dapagliflozin/metformin, Ebymect - dapagliflozin/metformin - EMEA/H/A-20/1442

Marketing authorisation holder: Janssen-Cilag International N.V., AstraZeneca AB, Boehringer Ingelheim international GmbH

SGLT2 Inhibitors in lower amputations treatment of type 2 diabetes mellitus

Rapporteurs: Martina Weise, Kristina Dunder (canagliflozin); Kristina Dunder, Martina Weise (dapagliflozin); Pieter de Graeff, Bart Van der Schueren (empagliflozin)

Scope: Article 20 procedure to PRAC triggered by European Commission on 15 April 2016 for canagliflozin, Signal of potential increased risk of lower limb amputations, was extended to all SGLT2 inhibtors.

Action: For information

The CHMP was updated on the procedure at PRAC.

10.1.4. Gadolinium-containing contrast agents (GdCA): Optimark –gadoversetamide gadobenic acid (CAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1437

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

Rapporteur: Patrick Salmon (Optimark), Co-Rapporteur: Pieter de Graeff (Optimark), PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Doris Stenver

Scope: List of experts for the ad-hoc expert group meeting

Action: For information

The CHMP noted the list of experts as adopted by the PRAC.

10.1.5. Gadolinium-containing contrast agents (GdCA): Optimark –gadoversetamide gadobenic acid (CAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

Lead Rapporteur: Rafe Suvarna,

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

Action: Timetable for adoption

The CHMP adopted the following timetable for assessment of the Annual cumulative reviews.

Start date: 12.09.2016

CHMP Rapporteur AR: 17.10.2016

Comments: 28.10.2016

Updated AR: 03.11.2016

Opinion: November 2016 CHMP

10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004

No items

10.3. Procedure under Articles 5(2) and 10 of the Regulation (EC) No 726/2004

No items

10.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC

10.4.1. Diclofenac 50 mg Tablets - Diclofenac epolamine - EMEA/H/A-29/1434

Altergon Italia srl

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Joseph Emmerich,

RMS: UK, CMS: CZ, FR, SK

Decentralised Procedure number: UK/H/5906/001/DC

Scope: Possible oral explanation / Opinion

Disagreements regarding the demonstration of bioequivalence in the fed state

Action: For adoption

An oral explanation was held on Wednesday 20 July 2016 at 9.00. The presentation by the MAH focused on the bioequivalence data in the fasted condition as well as data on food effects in relation with Diclofenac.

The CHMP adopted an opinion by consensus recommending to refuse the marketing authorisations for the concerned medicinal products.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the EMA question-and-answer document.

See also 2.4.1

10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC

10.5.1. Clenil and associated names - Beclometasone dipropionate - EMEA/H/A-30/1418

Chiesi group of companies and associated companies

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Martina Weise

Scope: List of outstanding issues

Harmonisation exercise for Clenil and associated names (beclometasone dipropionate). The review was triggered by Italy due to the need to harmonise the product information across all Member States, including the therapeutic indication, the target populations and the posology recommendations.

Action: For adoption

List of Questions adopted on 25.06.2015. List of outstanding issues adopted 19 November 2015 and 1 April 2016.

The CHMP discussed the responses to the list of outstanding issues and concluded that further questions related to product information need to be clarified by the marketing authorisation holder.

The CHMP adopted a 3rd list of outstanding issues with a specific timetable.

Submission of responses: 04.08.2016

Re-start of the procedure: 18.08. 2016

Rapporteur and co-rapporteur assessment reports circulated to CHMP: 31.08. 2016

Comments: 05.09.2016

Updated rapporteur and co-rapporteur assessment reports circulated to CHMP: 08.09.2016

Oral explanation/CHMP final opinion: September 2016 CHMP

10.5.2. Durogesic transdermal patches – fentanyl - EMEA/H/A-30/1413

Janssen-Cilag group of companies and associated companies

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise,

Scope: Opinion

Action: For adoption

List of outstanding Issues adopted 28.01.2016, 28.04.2016, 23.06.2016.

The CHMP adopted an opinion by consensus recommending varying the marketing authorisations for the concerned medicinal products.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the EMA question-and-answer document.

10.5.3. Etopophos and associated names– etoposide - EMEA/H/A-30/1417

MAH: Bristol-Myers Squibb group of companies and associated companies

Rapporteur: Greg Markey, Co-Rapporteur: Pieter de Graeff,

Scope: List of Outstanding Issues

Harmonisation exercise for Etopophos and associated names

Action: For adoption

List of outstanding issues adopted 25.02.2016 CHMP, List of Questions adopted on 22.10.2015.

The CHMP discussed the indications, which were considered acceptable, if MAH is making proposed amendments in SmPC.

The CHMP adopted a 2nd list of outstanding issues with a specific timetable.

Submission of responses: 03.11.2016

Re-start of the procedure: 17.11.2016

Joint Rapporteurs assessment report circulated to CHMP: 30.11.2016

Comments: 05.12.2016

Updated Joint Rapporteurs assessment report circulated to CHMP: 08.12.2016

List of outstanding issues/CHMP opinion: December 2016 CHMP

10.5.4. Vepesid and associated names - etoposide - EMEA/H/A-30/1425

MAH: Bristol-Myers Squibb group of companies and associated companies

Rapporteur: Greg Markey, Co-Rapporteur: Pieter de Graeff

Scope: List of Outstanding Issues

Harmonisation exercise for Vepesid and associated names

Action: For adoption

List of outstanding issues adopted 25.02.2016 CHMP. List of Questions adopted on 22.10.2015.

The CHMP discussed the indications, which were considered acceptable, if MAH is making proposed amendments in SmPC.

The CHMP adopted a 2nd list of outstanding issues with a specific timetable.

Submission of responses: 03.11.2016

Re-start of the procedure: 17.11.2016

Joint Rapporteurs assessment report circulated to CHMP: 30.11.2016

Comments: 05.12.2016

Updated Joint Rapporteurs assessment report circulated to CHMP: 08.12.2016

List of outstanding issues/CHMP opinion: December 2016 CHMP

10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC

10.6.1. Pharmaceutics International – EMEA/H/A-31/1444

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: David Lyons,

Scope: List of Outstanding Issues

Article 31 triggered by the European Commission

List of Questions adopted on 23.06.2016.

The CHMP adopted a list of outstanding issues with a specific timetable.

Submission of responses: 10.08.2016

Re-start of the procedure: 18.08.2016

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 31.08.2016

Comments: 05.09.2016

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 08.09.2016

CHMP list of outstanding issues or CHMP opinion: September 2016 CHMP

10.6.2. Semler Research Centre Private Ltd - EMEA/H/A-31/1443

Rapporteur: Pieter de Graeff, Co-Rapporteur: Concepcion Prieto-Yerro,

Scope: Opinion

Article 31 referral triggered by the UK, Germany, Spain, Denmark and the Netherlands in relation to findings of non-compliance with GCP at the Semler bioanalytical and clinical facilities (JP Nagar Analytical and Sakar Nagar Clinical sites) in Bangalore, India.

Action: For adoption

The CHMP adopted an opinion by consensus concluding that:

- For medicinal products containing abacavir/lamivudine (annex IA of the opinion), bioequivalence to an EU reference medicinal products has been established. Therefore the

marketing authorisations for medicinal products listed in annex IA of the opinion should be maintained, and for the marketing authorisation applications listed in annex IA of the opinion, bioequivalence vis-à-vis the EU reference medicinal product has been established.

- The marketing authorisations listed in annex IB of the opinion should be suspended, and that the marketing authorisation applications listed in annex IB of the opinion do not satisfy the criteria for authorisation as bioequivalence to an EU reference medicinal product has not been established.

  (1) Some of the authorised medicinal products may be considered critical by the individual Member States based on the evaluation of the criticality criteria set out in the opinion. Where on the basis of these criteria the relevant national competent authorities of the Member States consider that a medicinal product is critical, the suspension of the concerned marketing authorisation(s) may be deferred by the period for which the medicinal product is considered critical. This period of deferral shall not exceed twenty-four months from the Commission Decision. Should during this period the Member State(s) consider a medicinal product not critical anymore, the suspension of the concerned marketing authorisation(s) shall apply.

  (2) For these medicinal products considered critical by Member State(s), the marketing authorisations holders shall submit a bioequivalence study conducted vis-à-vis the EU Reference Medicinal Product within 12 months from the Commission Decision.

  (3) Suspension of the MAs should be lifted when bioequivalence to an EU Reference Medicinal Product has been established.

The CHMP assessment report was adopted by CHMP.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the EMA public health communication.

10.6.3. Vancomycin containing products – (vancomycin) - EMEA/H/A-31/1440

Rapporteur: Concepcion Prieto-Yerro, Co-rapporteur: Alar Irs;

Scope: Opinion

Review of the benefit-risk balance following notification by the Spanish Agency of Medicines and Medical Devices of a referral under Article 31 of Directive 2001/83/EC.

List of Questions adopted on 01.04.2016.

The members discussed several sections of the SmPC.

The CHMP adopted a list of outstanding issues with a specific timetable.

Submission of responses: 29.09.2016

Re-start of the procedure: 13.10.2016

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 26.10.2016

Comments: 31.10.2016

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 03.11.2016

CHMP List of outstanding issues/opinion: November 2016 CHMP

In addition the CHMP adopted lists of questions to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and to the Quality Working Party.

10.6.4. Symbioflor 2, Escherichia Coli bacteria (cells and autolysate) - EMEA/H/A-31/1441

Symbiopharm GmbH,

Rapporteur: Harald Enzmann, Co-rapporteur: Milena Stain;

Scope: Letter from the MAH received 23 June 2016 requesting the EMA to suspend the referral.

Reply letter from EMA dated 1 July 2016.

Article 31 triggered by the BfArM in Germany in March 2016 requesting the review of the benefit-risk balance for Symbioflor 2 and associated names following concerns that the effectiveness of the medicine(s) has not been adequately demonstrated.

Action: For information

The Committee did not agree to the request by the MAH for a suspension of the referral procedure.

10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC

No items

10.8. Procedure under Article 107(2) of Directive 2001/83/EC

No items

10.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) (EC) No 1084/2003

No items

10.10. Procedure under Article 29 Regulation (EC) 1901/2006

No items

10.11. Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) No 1234/2008)

No items

11. Pharmacovigilance issue

11.1. Early Notification System

July 2016 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the information.

12. Inspections

12.1. GMP inspections

Disclosure of information related to GMP inspections will not be published as it undermines the purpose of such inspections

12.2. GCP inspections

Disclosure of information related to GCP inspections will not be published as it undermines the purpose of such inspections

12.3. Pharmacovigilance inspections

Disclosure of information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections

12.4. GLP inspections

Disclosure of information related to GLP inspections will not be published as it undermines the purpose of such inspections

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

The CHMP noted the information.

13.2. Innovation Task Force briefing meetings

Disclosure of information related to briefing meetings taking place with applicants cannot be released at present time as deemed to contain commercially confidential information

13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004

Request from EDQM for EMA scientific Opinion under Art. 57 (1)J of Regulation (EC) No 726/2004

Action: For adoption

The CHMP adopted the opinion.

Request from the European Commission for an EMA scientific Opinion under Article 57

Action: For adoption

The CHMP adopted the opinion.

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Outcome of the Expert meeting on ATMPs held on 27th May 2016

Scope: Report presentation to CHMP

Action: For information

Postponed.

14.1.2. New timetable proposal for type II variations involving the PRAC

Action: For discussion

Background document

The CHMP noted the proposal. The proposal is to use the specific 'weekly' timetable finishing on the Thursday of the PRAC for the majority of type II variations involving the PRAC. This excludes variations to be discussed at the CHMP (i.e. extensions of indication) as well as variations leading to an immediate EC Decision (as per current practice). The proposal only applies to non-controversial variations rarely discussed in practice in either committee. There will be 2nd monthly linguistic review after PRAC.

14.1.3. EMA survey on Initial Marketing Authorisation Application (MAA) 2016

Scope: Web-based survey has been announced at the May CHMP and will be performed between September 2016 - February 2017

Action: For discussion

The CHMP noted the information about the survey. A web-based survey will be performed between September 2016 - February 2017. The scope of the survey is Centralised (human), Initial Marketing Authorisation procedures (MAA) targeting: Content & Procedural Questions. The survey will be completed by EMA, Applicants and Rapporteurs. 40-50 IMAA applications are expected to be surveyed at 3 key steps of the centralised evaluation: 1) after validation (EMA/Applicants); 2) late in clock-stop (Rapporteurs) or after LoQ response (Applicants/EMA); 3) after opinion (EMA/Applicants/Rapporteurs). Further discussions are expected.

14.1.4. Review of experience with the Early Background Summary

Scope: An Outcome of a review of experience with the Early Background Summaries. A survey amongst CAT/CHMP/PRAC assessors was conducted following the pilot starting at the end of 2014. The data collection and analysis are completed based on a total 121 responses for the 21 products in scope of the exercise.

Action: For discussion

Postponed.

14.1.5. Time schedule of CHMP August written procedure

Action: For information

The CHMP noted the timetable for the August 2016 written procedure.

14.1.6. Election of CHMP Co-opted members

CHMP re-elected Jean-Louis Robert and Sol Ruiz as Co-opted members to CHMP in area of expertise in Quality (non-biologicals) and Quality and safety (biological), with expertise in advanced therapies (gene, cell and tissue therapies) respectively.

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 04-07 July 2016

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for July 2016

Action: For adoption

The CHMP adopted the EURD list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 13-15 July 2016
Action: For information

The CHMP noted the minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 11-14 July 2016

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at July 2016 PDCO

Action: For information

Report from the PDCO meeting held on 20-22 July 2016

Action: For information

The CHMP noted the reports.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 11-13 July 2016
Action: For information

The CHMP noted the report.

14.2.6. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 18 -20 July 2016

Action: For information

The CHMP noted the report.

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 4-7 July 2016. Table of conclusions

Action: For information

Scientific advice letters: The CHMP noted the report.

Disclosure of information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

Mandate, objectives and rules of procedure of the Scientific advice working party (SAWP) (Doc ref: EMEA/CHMP/SAWP/69686/04 Rev 10) - revision

Action: For adoption

The CHMP adopted the revised mandate.

14.3.2. Respiratory Drafting Group

Scope: Concept Paper for the revision of the Guideline on the clinical development of medicinal products for the treatment of cystic fibrosis (EMEA/CHMP/EWP/9147/2008)

Action: For adoption for 3 months public consultation

At the time when the current guideline was adopted, medicinal products were developed for either the management of the pulmonary disease or the pancreatic exocrine insufficiency associated with CF and, as a consequence, the guideline is mainly focused on these clinical situations. However, the knowledge of the genetic principles and other recent developments in the field of CF has provided huge insight into the pathophysiology of the disease. There are elements in the current guideline which are outdated based on these recent advances.

The CHMP adopted the concept paper for 3 months public consultation.

14.3.3. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: "Updated advice on the use of colistin products in animals within the European Union: development of resistance and possible impact on human and animal health (EMA/231573/2016)

Action: For adoption

Overview of comments received (EMA/390632/2016)

Action: For adoption

Background note on the Request from the Commission for update of the advice on the impact on public health and animal health of the use of antibiotics in animals (colistin) (EMA/723718/2014)

Action: For information

The CHMP adopted the updated advice and the overview of comments received by written procedure on 22 July 2016. The CHMP noted the background note.

14.3.4. Quality Working Party (QWP)

Chair: Jean-Louis Robert,

Scope: Guideline on the Chemistry of Active Substances (EMA/454576/2016)

Action: For adoption

Overview of comments

Action: For information

The CHMP adopted the guideline and noted the overview of comments. The guideline concerns the application of Directive 2001/83/EC with a view to the granting of a marketing authorisation for a medicinal product. This guideline replaces the 'Note for guidance on chemistry of new active substances' (CPMP/QWP/130/96, Rev 1) and 'Chemistry of active substances' (3AQ5a). It has been revised to cover new and existing active substances in one guideline.

14.3.5. CHMP ad-hoc drafting group

Scope: Update on the revision of fixed dose combination guideline

Action: For discussion

The CHMP noted the update.

14.3.6. Safety Working Party (SWP)

Public statement on the use of herbal medicinal products containing pulegone and menthofuran (EMA/HMPC/138386/2005 Rev. 1)

Overview of comments on draft Public statement on the use of herbal medicinal products containing pulegone and menthofuran (EMA/HMPC/258725/2015)

Action: For information

The CHMP noted the public statement.

14.3.7. Central Nervous System Working Party (CNSWP)

Scope: Election of a new core member

Action: For adoption

The CHMP appointed Mario Miguel Rosa (PT) as new core member to the CNS WP by written procedure on 22 July 2016.

Scope: Call for nomination of Chair to CNSWP

Elections will take place in September. The nominations should be sent by 9th September

Action: For information

The CHMP noted the call.

14.3.8. Cardiovascular Working Party (CVSWP)

Scope: Bart Van Der Schueren (CVSWP observer) to attend FDA workshop on PRO in diabetes, 29 August 2016 in Washington

Action: For adoption

The CHMP agreed for Bart Van Der Schueren to attend the FDA workshop.

14.3.9. Name Review Group (NRG)

Table of Decisions of the NRG plenary meeting held on 6 July 2016

Action: For adoption

The CHMP adopted the NRG table of decision.

14.3.10. Guideline Consistency Group (GCG)

Call for nomination of a new member replacing Pierre Demolis. Expressions of interest should be sent by 31 August 2016.

Action: For information

The CHMP noted the call.

14.3.11. Vaccines Working Party

Guideline on Influenza Vaccines. Non-clinical and Clinical Module (EMA/CHMP/VWP/457259/2014)

Action: For adoption

The CHMP adopted the guideline. The guideline will be published. The guideline on influenza vaccines has been organised with the aim of developing a modular guideline that covers the quality, regulatory, non-clinical and clinical aspects of the development of influenza vaccines. The Non-clinical and Clinical Module is intended to replace five separate guidance documents that were in place previously. Two separate modules cover the quality and regulatory requirements for new influenza vaccines. The content of the new guidance takes into account the lessons learned from the 2009/2010 influenza A(H1N1) pandemic, the experience acquired from requests for CHMP Scientific Advice, as well as prior applications for the approval of pandemic vaccines, vaccines intended for pre-pandemic use and for prevention of seasonal influenza.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

14.5.1. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Update on ICH Lisbon meeting held in 11-16 June 2016

Presentation by Milton Bonelli

Action: For information

The CHMP noted the update from ICH Lisbon meeting held in 11-16 June 2016.

Scope: ICH guideline E17: general principles for planning and design of multi-regional clinical trials - Step 3

Action: For adoption for 6 months public consultation

The CHMP adopted the draft guideline for 6 months public consultation.

Scope: ICH guideline M4E(R2): ICH M4E(R2): Revised Guideline on CTD-Efficacy - B/R sections - Step 4

Action: For adoption

The CHMP adopted the guideline for implementation in 6 months.

Scope: ICH guideline S9 Q&A: Nonclinical evaluation for anticancer pharmaceuticals - Step 3

Action: For adoption for 6 months public consultation

The CHMP adopted the draft Q&A document for 6 months public consultation.

14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee

No items

14.7. CHMP work plan mid-year report

Mid-year report

Action: For information

The CHMP noted the mid-year report and updates on the activities. Furthermore it was highlighted that work should be started with 2017 Work Plan.

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Concept paper on the revision of the 'Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products'

Scope: concept paper developed by a multi-disciplinary expert group, agreement on press-release and timeframe for revision (EMA/CHMP/446302/2016)

Action: For adoption

The CHMP adopted the concept paper for 2 months public consultation. The current guideline mainly focuses on non-clinical aspects of drug development and the use of animal data and reflects the practice at the time it was developed which focused on a single ascending dose (SAD) design for first-in-human (FIH) trials. Since then, integration of the non-clinical data available before FIH administrations and the pharmacokinetic (PK), pharmacodynamic (PD) and human safety data emerging during a trial has also evolved. Consequently, the practice has evolved and many FIH trials are now performed with integrated protocols potentially combining a number of different study parts, e.g. single and multiple ascending doses (SAD and MAD), food interaction, different age groups and early proof of concept or early proof of principle parts. FIH and early phase CTs with multiple study parts are, therefore, increasingly being submitted for regulatory review to National Competent Authorities as part of a single CT application.

15.1.2. Workshop on update of TB Guideline to be held on 25 November 2016

Scope: the European Medicines Agency is organising a workshop on Development of antimycobacterial medicinal products which will take place on 25th November 2016.

Action: For information

The CHMP noted the information. The workshop will bring together experts and stakeholders from the academic, regulatory and industrial sectors to discuss key issues and new developments in the field of development of antimycobacterial medicinal products. The presentations and discussions will support the finalisation of the newly drafted Addendum to the note for guidance on evaluation of medicinal products indicated for treatment of bacterial infections to specifically address the clinical development of new agents to treat disease due to Mycobacterium tuberculosis.

16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/ experts following evaluation of declared interests for the 18 – 21 July 2016 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Alternate	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Ines Baotic	Member	Croatia	No restrictions applicable to this meeting	
Katarina Vučić	Alternate	Croatia	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Hanne Lomholt Larsen	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Pierre Demolis	Member (Vice-Chair)	France	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No interests declared	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Karsten Bruins Slot	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Nela Vilceanu	Member	Romania	No interests declared	
Jan Mazag	Member	Slovakia	No interests declared	
Jana Schweigertova	Alternate	Slovakia	No restrictions applicable to this meeting	
Nevenka Tršinar	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Arantxa Sancho-Lopez	Alternate	Spain	No restrictions applicable to this meeting	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
John Johnston	Expert - in person*	United Kingdom	No interests declared	
Kai Dallmeier	Expert - in person*	Belgium	No interests declared	
Maria Concepción Payares	Expert - via telephone*	Spain	No interests declared	
Nele Berthels	Expert - in person*	Belgium	No interests declared	
Valérie Lescrainier	Expert - in person*	Belgium	No interests declared	
Tomas Radimersky	Expert - in person*	Czech republic	No interests declared	
Paula van Hennik	Expert - in person*	Netherlands	No interests declared	
Peter Mol	Expert - via telephone*	Netherlands	No interests declared	
Kristina Bech Jensen	Expert - in person*	Denmark	No interests declared	
Olga Kholmanskikh	Adobe Presenter	Belgium	No interests declared	
Shirley Hopper	Expert - in person*	United Kingdom	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Rafe Suvarna	Expert - in person*	United Kingdom	No interests declared	
Barbara Spruce	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Daniel O'Connor	Expert - in person*	United Kingdom	No interests declared	
Inga Bellahn	Expert - in person*	United Kingdom	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Sylvia Kuhn	Adobe Presenter	Germany	No restrictions applicable to this meeting	
Elmer Schabel	Adobe Presenter	Germany	No interests declared	
Clemens Mittmann	Expert - via telephone*	Germany	No interests declared	
Janet Schriever	Adobe Presenter	Germany	No interests declared	
Violeta Stoyanova-Beninska	Expert - in person*	Netherlands	No interests declared	
Veronika Ganeva	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Benoy Daniel	Expert - via telephone*	United Kingdom	No interests declared	
Anabel Cortés Blanco	Expert - via telephone*	Spain	No interests declared	
Stephan Lehr	Adobe Presenter	Austria	No restrictions applicable to this meeting	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Agustin Portela Moreira	Expert - in person*	Spain	No interests declared	
David Perez Caballero	Expert - via telephone*	Spain	No interests declared	
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Maria Escudero Galindo	Expert - in person*	Spain	No restrictions applicable to this meeting	
Nathalie MORGENSZTEJN	Expert - via telephone*	France	No interests declared	
Antonio López Navas	Expert - via telephone*	Spain	No interests declared	
Carolien Versantvoort	Expert - via telephone*	Netherlands	No interests declared	
Macarena Rodriguez Mendizabal	Expert - via telephone*	Spain	No interests declared	
Maura O'Donovan	Expert - via telephone*	Ireland	No interests declared	
Zane Neikena	Adobe Presenter	Latvia	No interests declared	
Representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the product(s) they have been invited to talk about.

17. Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 2)*

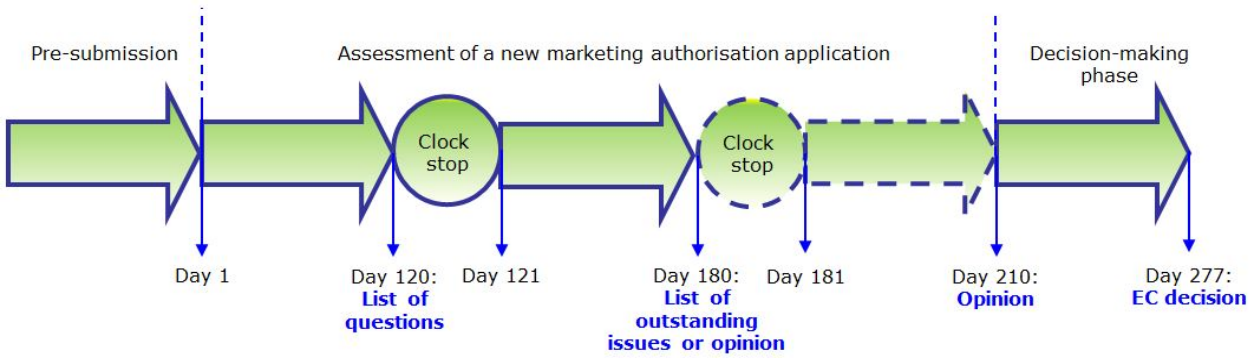
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

Initial applications *(section 3)*

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 4)*

Extensions of marketing authorisations are applications for the change or addition of new strengths,

formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 5)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 6)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 3.5)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section5.3)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 3.7)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 8)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 9)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a

particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 12)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 13)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 14.3.1)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 14.2)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 14.3)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/