29 April 2016
EMA/312797/2016
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 29 March - 01 April 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).

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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the pre-meeting list of participants and restrictions. See (current) March 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 29 March – 1 April 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 Slovakian alternate member Jana Schweigertova, replacing Ivana Pankuchova and new Portuguese alternate member Fátima Ventura, replacing Patrícia Silva.

1.2. Adoption of agenda

CHMP agenda for 29 March - 01 April 2016.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 22-25 February 2016.

The CHMP adopted the minutes.

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2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - ixazomib - Orphan - EMEA/H/C/003844

Takeda Pharma A/S; multiple myeloma

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 30 March 2016 at 14.00.

List of Outstanding Issues adopted on 25.02.2016. List of Questions adopted on 17.12.2015.

An oral explanation was held on Wednesday 30 March 2016 at 14.00.

See also 3.2.10

2.1.2. - glycopyrronium bromide - PUMA - EMEA/H/C/003883

treatment of sialorrhoea

Scope: Oral explanation

Action: Oral explanation to be held on Thursday 31 March 2016 at 9.00.

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 25.06.2015.

An oral explanation was held on Thursday 31 March 2016 at 9.00. The presentation focused on data supporting the claim for well-established medicinal use for at least 10 years in the EU as well as the safety data and the overall benefit/risk of the product.

2.1.3. - daclizumab - EMEA/H/C/003862

treatment of multiple sclerosis (RMS)

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 30 March 2016 at 9.00.

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 23.07.2015.

An oral explanation was held on 30 March 2016 at 9.00. The presentation by the applicant focused on justification, why the product should be considered a new active substance (NAS) The Committee noted the correspondence between the EC and applicant.

The Committee adopted the BWP report.

2.2. Re-examination procedure oral explanations

2.2.1. Dropcys - mercaptamine - Orphan - EMEA/H/C/004038

Lucane Pharma; treatment of corneal cystine deposits

Scope: Oral explanation and re-examination Opinion

Action: Oral explanation to be held on Wednesday 30 March 2016 at 11.00.

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

Opinion adopted on 17 December 2015.

An oral explanation was held on Wednesday 30 March 2016 at 11.00.

See also 3.5.1

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Darzalex - daratumumab - Orphan - EMEA/H/C/004077

Accelerated assessment

Janssen-Cilag International N.V.; treatment of patients with relapsed and refractory multiple myeloma

Scope: Opinion

Action: For adoption

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

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 conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that daratumumab 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 restricted medical prescription.

The CHMP noted the letter of recommendation dated 29.03.2016.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.2. Flixabi - infliximab - EMEA/H/C/004020

Samsung Bioepis UK Limited (SBUK); treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

Scope: Opinion

Action: For adoption

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

Oral explanation held on 24.02.2016. List of Outstanding Issues adopted on 25.02.2016. List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 23.07.2015.

The Committee discussed the anti-drug antibodies (ADA) assays and acceptable immunogenicity level for approving biosimilarity.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (19 votes positive out of 32 votes) together with the CHMP assessment report and translation timetable.

The Icelandic Member was in agreement with the CHMP recommendation and Norwegian Member was not.

The divergent position (Agnes Gyurasics, Daniel Brasseur, Daniela Melchiorri, Fatima Ventura, Greg Markey, Jana Schweigertova, Jens Heisterberg, Koenraad Norga, Kristina Dunder, Nevenka Trsinar, Outi Maki-Ikola, Pieter de Graeff, Robert Hemmings, Karsten Bruins Slot) was appended to the opinion.

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

The CHMP noted the letter of recommendation dated 01.04.2016.

The summary of opinion was circulated for information.

3.1.3. Galafold - migalastat - Orphan - EMEA/H/C/004059

Amicus Therapeutics UK Ltd; treatment of patients with Fabry disease

Scope: Opinion

Action: For adoption

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

Oral explanation held on 23.02.2016. List of Outstanding Issues adopted on 25.02.2016, 17.12.2015. List of Questions adopted on 22.10.2015.

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 migalastat 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 restricted medical prescription.

The summary of opinion was circulated for information.

3.1.4. Neparvis - sacubitril / valsartan - EMEA/H/C/004343

Novartis Europharm Ltd; treatment of heart failure (NYHA class II-IV)

Scope: Opinion

Action: For adoption

Informed consent application (Article 10c of Directive No 2001/83/EC)

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 majority (27 positive out of 28 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 (Daniela Melchiorri) was appended to the opinion.

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

The CHMP noted the letter of recommendation dated 30.03.2016

The summary of opinion was circulated for information.

3.1.5. Pandemic influenza vaccine H5N1 MedImmune - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963

MedImmune LLC; prophylaxis of influenza

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.01.2016. 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.

Furthermore, the CHMP considered that pandemic influenza vaccine (H5N1) (live attenuated, nasal) 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 CHMP noted the letter of recommendation dated 31.03.2016.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.6. Palonosetron Accord - palonosetron - EMEA/H/C/004129

Accord Healthcare Ltd; prevention of nausea and vomiting associated with cancer chemotherapy

Scope: Opinion

Action: For adoption

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

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 medical prescription.

The summary of opinion was circulated for information.

3.1.7. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - ATMP - EMEA/H/C/003854

GlaxoSmithKline Trading Services; severe combined immunodeficiency

Scope: Opinion

Action: For adoption

New 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 was updated on discussions and the draft positive opinion issued by the CAT at

their March meeting. The issues previously identified in this application had been adequately addressed.

The Committee adopted a positive opinion based on the opinion taken by the CAT at their March 2016 meeting recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence is a new active substance, as claimed by the applicant.

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

The CHMP noted the letter of recommendation dated 22.03.2016.

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

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.8. Uptravi - selexipag - EMEA/H/C/003774

Actelion Registration Ltd.; treatment of pulmonary arterial hypertension (PAH; WHO Group I)

Scope: Revised Opinion

Action: For adoption

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

Opinion adopted on 28 January 2016.

Letter from the European Commission received 24 February 2016.

The Committee adopted a revised positive opinion recommending the granting of a marketing authorisation by majority (25 positive out of 31 votes) together with the CHMP assessment report and translation timetable.

The divergent position (Sol Ruiz, Concepcion Prieto Yerro, Daniela Melchiorri, Fatima Ventura, Andrea Laslop, Pieter de Graeff, Karsten Bruins Slot) was appended to the opinion.

The Icelandic Member was in agreement with the CHMP recommendation, the Norwegian Member was not.

The revised summary of opinion was circulated for information.

3.2. Initial applications; Day 180 list of outstanding issues

3.2.1. - fluticasone propionate / salmeterol - EMEA/H/C/002752

treatment of asthma and COPD

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.

3.2.2. - fluticasone propionate / salmeterol - EMEA/H/C/004267

treatment of asthma and COPD

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.

3.2.3. - bortezomib - EMEA/H/C/004076

treatment of multiple myeloma

Scope: 2nd Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 28.01.2016. List of Questions adopted on 23.07.2015.

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.

The CHMP adopted the CHMP assessment report on similarity.

3.2.4. - pemetrexed - EMEA/H/C/003895

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

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.

3.2.5. - emtricitabine / rilpivirine / tenofovir alafenamide - EMEA/H/C/004156

treatment of HIV-1

Scope: Day 180 list of outstanding issue

Action: For adoption

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 list of outstanding issues with a specific timetable.

3.2.6. - drisapersen - Orphan - EMEA/H/C/003846

BioMarin International Limited; treatment of Duchenne muscular dystrophy (DMD)

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.

3.2.7. - miglustat - EMEA/H/C/004016

treatment of Gaucher disease

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

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.

Furthermore, the Committee adopted list of questions to PKWP.

3.2.8. - grazoprevir / elbasvir - EMEA/H/C/004126

treatment of chronic hepatitis C (CHC) in adults

Scope: 2nd Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 19.11.2015. Day 180 list of outstanding issue adopted 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.

3.2.9. - allogeneic T cells genetically modified to express suicide gene - Orphan - ATMP - EMEA/H/C/002801

MolMed SpA; treatment in haploidentical haematopoietic stem cell transplantation

Scope: Update on outcome from CAT March meeting

Action: For discussion

List of Outstanding Issues adopted on 28.01.2016, 26.03.2015. List of Questions adopted on 24.07.2014.

The CHMP was updated on discussions from the CAT March 2016 Plenary.

The CHMP agreed to the 3rd list of outstanding issues as adopted by the CAT with a specific timetable.

The CHMP adopted the BWP report.

3.2.10. - ixazomib - Orphan - EMEA/H/C/003844

Takeda Pharma A/S; multiple myeloma

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 30 March 2016 at 14.00.

List of Outstanding Issues adopted on 25.02.2016. List of Questions adopted on 17.12.2015.

An oral explanation was held on Wednesday 30 March 2016 at 14.00. The oral explanation focused on clinical efficacy data.

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

See also 2.1.1

3.3. Initial applications; Day 120 list of questions

3.3.1. - abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

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.

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

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

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.

3.3.3. - brodalumab - EMEA/H/C/003959

moderate to severe plaque psoriasis

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.

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

treatment of hepatitis C

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. - pegfilgrastim - EMEA/H/C/004023

treatment of neutropenia

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. - etanercept - EMEA/H/C/004192

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis

Scope: Day 120 list of questions

Action: For adoption

BWP report

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.

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

treatment of angina pectoris

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. - ivabradine - EMEA/H/C/004217

treatment of angina pectoris

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. - ivabradine - EMEA/H/C/004117

treatment of angina pectoris

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. - pegfilgrastim - EMEA/H/C/004342

treatment of neutropenia

Scope: Day 120 list of questions

Action: For adoption

BWP report

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.

3.3.11. - sildenafil - EMEA/H/C/004289

treatment of patients with pulmonary arterial hypertension

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.

3.3.12. - sildenafil - EMEA/H/C/004186

treatment of pulmonary arterial hypertesion

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. - sofosbuvir / velpatasvir - EMEA/H/C/004210

Accelerated assessment

treatment of chronic hepatitis C virus

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.

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

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

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. - rituximab - EMEA/H/C/004112

treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis

Scope: Letter from the applicant dated 9 March 2016 requesting extension of clock stop to respond to the Day 120 List of Questions,

Action: For adoption

List of Questions adopted on 25.02.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the Day 120 List of Questions.

3.4.2. - alectinib - EMEA/H/C/004164

indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive.

Scope: Letter from the applicant dated 7 March 2016 requesting extension of clock stop to respond to the Day 120 List of Questions.

Action: For adoption

List of Questions adopted on 28.01.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the Day 120 List of Questions.

3.4.3. - cabozantinib - EMEA/H/C/004163

treatment of advanced renal cell carcinoma (RCC)

Scope: Assessment Report on similarity

Action: For adoption

The CHMP adopted the similarity assessment report.

3.4.4. - irinotecan - Orphan - EMEA/H/C/004125

Baxter Innovations GmbH; treatment of pancreatic cancer

Scope: Letter from the applicant dated 18 March 2016 requesting an extension of clock stop to respond to List of Outstanding Issues.

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

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Outstanding Issues via written procedure on 23 March 2016.

3.4.5. lenvatinib - EMEA/H/C/004224

in combination with everolimus for the treatment of unresectable advanced or metastatic renal cell carcinoma (RCC)

Scope: Assessment Report on similarity

Action: For adoption

The adoption of the similarity assessment report was postponed.

3.4.6. - aceneuramic acid - Orphan - EMEA/H/C/004176

Ultragenyx UK Limited; treatment of Hereditary Inclusion Body Myopathy (HIBM)

Scope: Letter from the applicant dated 21 March 2016 requesting an extension of clock stop to respond to Day 120 list of questions

Action: For adoption

List of Questions adopted on 28.01.2016The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Day 120 list of questions.

3.4.7. - eryaspase - Orphan - EMEA/H/C/004055

ERYTECH Pharma S.A.; treatment of leukaemia

Scope: Letter from the applicant dated 30 March 2016 requesting an extension of clock stop to respond to Day 120 list of questions

List of Questions adopted on 28.01.2016

Action: For adoption

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the Day 120 list of questions.

3.4.8. - sirolimus - Orphan - EMEA/H/C/003978

Santen Oy; treatment of chronic non-infectious uveitis

Scope: revised List of experts to Ad-hoc expert group meeting to be held 5 April 2016.

Action: For adoption

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 25.06.2015.

The CHMP adopted a revised list of experts to an ad-hoc expert group.

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

3.5.1. Dropcys - mercaptamine - Orphan - EMEA/H/C/004038

Lucane Pharma; treatment of corneal cystine deposits

Scope: Oral explanation and re-examination Opinion

Action: For adoption

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

Opinion adopted on 17 December 2015.

An oral explanation was held on Wednesday 30 March 2016 at 11.00. The presentation and discussion focused on the data provided to support efficacy, the formulation and the stability and microbiological quality after reconstitution.

The CHMP adopted a negative opinion on the re-examination by consensus together with the assessment report.

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

The refusal question and answers document was circulated for information.

See also 2.2.1.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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. Instanyl - fentanyl / fentanyl citrate - EMEA/H/C/000959/X/0030/G

Takeda Pharma A/S; management of breakthrough pain

Rapporteur: Pierre Demolis, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Arnaud Batz

Scope: Opinion

Type II cat. B.II.e.4.b) To add a new improved child resistant multi-dose nasal spray.

3 X Type IB cat. B.II.e.5.d To introduce a new pack size.

Type IA cat. B.II.d.1.a) To tighten the specification limits of the finished product

Additionally, the Applicant took the opportunity to include an editorial change.

Action: For adoption

List of Outstanding Issues adopted on 17.12.2015, 23.07.2015. List of Questions adopted on 26.02.2015.

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.

4.1.2. Trevicta / Paliperidone Janssen - paliperidone - EMEA/H/C/004066/X/0007/G

Janssen-Cilag International NV

Rapporteur: Filip Josephson, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue

Scope: Day 180 list of outstanding issue

“This variation is part of a grouped application consisting of an extension application to introduce four new strengths of a once-every-3-month paliperidone injection formulation (175 mg, 263 mg, 350 mg and 525 mg) together with the variations identified below:

C.I.6.a - extension of indication for to revise the injection frequency to ‘ once-every-3-months’ following prior adequate treatment with XEPLION for at least four months. Consequently, changes to Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are proposed. The PL and RMP are proposed to be revised accordingly.

A.2.a - Change of the Name of the Medicinal Product (Section 1 of the SmPC) from "Paliperidone Janssen" to "TREVICTA”.
6 x C.I.7.b - deletion of all 6 currently authorised Paliperidone Janssen dosage strengths (i.e.

Paliperidone Janssen 25 mg, 50 mg, 75 mg, 100 mg, 150 mg and 150 mg / 100 mg - EU/1/14/971/001-006)."

Action: For adoption

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.

4.1.3. Mabthera - rituximab - EMEA/H/C/000165/X/0101/G

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Doris Stenver

Scope: Day 180 list of outstanding issue

"Grouping of:
Line extension to add a new strength: 1,600 mg solution for subcutaneous injection.

Update of the product information of the 1400 mg solution for subcutaneous injection as a consequence to the line extension application.

Update of the RMP to include new information relevant to chronic lymphocytic leukaemia and update of the educational materials.

Action: For adoption

List of Questions adopted on 26.03.2015.

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

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. Keytruda - pembrolizumab - EMEA/H/C/003820/X/0001/G

Merck Sharp & Dohme Limited

Rapporteur: Daniela Melchiorri

Scope: Opinion

"To introduce concentrate for solution for infusion (25 mg/mL) as additional pharmaceutical form for Keytruda

Action: For adoption

List of Questions adopted on 17.12.2015.

The Committee discussed the issues identified in this application.

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

No items

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. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0025

Takeda Pharma A/S

Rapporteur: Pieter de Graeff, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include new indication for Adcetris (Adcetris is indicated for the treatment of adult patients at increased risk of relapse or progression following ASCT"). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015, 25.06.2015.

The Committee discussed the issues identified in this application. The remaining issues related to the added value of an early maintenance treatment regimen. The Committee considered it relevant to consult SAG Oncology.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

The CHMP adopted a list of questions to the SAG Oncology meeting to be held on 14th April 2016.

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."

Action: For adoption

The Committee discussed the issues identified in this application. The main focus of the discussion was on the observed recurrence and incidence rates of skin cancer in the clinical study.

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

5.1.3. Avastin - bevacizumab - EMEA/H/C/000582/II/0086

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to extend the use of Avastin in combination with erlotinib for the first line treatment of patients with unresectable advanced, metastatic or recurrent non-squamous NSCLC with EGFR activating mutations. As a consequence sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are proposed to be updated. The Package Leaflet and RMP are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015.

The Committee discussed the issues identified in this application, which related to overall survival data.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.4. Caprelsa - vandetanib - EMEA/H/C/002315/II/0016

AstraZeneca AB

Rapporteur: Pierre Demolis

Scope: "Extension of Indication to include paediatric indication population for Caprelsa.
As a consequence, sections 4.1, 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated in update the safety information. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 19.11.2015.

The Committee discussed the issues identified in this application.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.5. Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0067

GlaxoSmithKline Biologicals

Rapporteur: Daniel Brasseur, PRAC Rapporteur: Jean-Michel Dogné

Scope: "Extension of Indication to include prevention against premalignant anal lesions and anal cancer as of 9 years of age for Cervarix.
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 RMP (v.11.0) including the new indication."

Action: For adoption

Request for Supplementary Information adopted on 19.11.2015, 25.06.2015.

The Committee discussed the issues identified in this application.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.6. Halaven - eribulin - EMEA/H/C/002084/II/0028

Eisai Europe Ltd.

Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include the treatment of unresectable liposarcoma in adult patients who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, and 5.1 of the SmPC are updated with the PK, efficacy and safety information. The Package Leaflet and RMP are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in line with the latest QRD template version 9.1."

Action: For adoption

Request for Supplementary Information adopted on 19.11.2015.

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.

5.1.7. Humira - adalimumab - EMEA/H/C/000481/II/0147

AbbVie Ltd.

Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri

Scope: "Extension of Indication to include the treatment of patients with moderately paediatric active Crohn's disease.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated.
In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial corrections to the Labelling."

Action: For adoption

Request for Supplementary Information 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 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.

5.1.8. Ilaris - canakinumab - EMEA/H/C/001109/II/0043

Novartis Europharm Ltd

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to amend the Systemic Juvenile Idiopathic Arthritis (SJIA) indication to include treatment of active Still's disease including Adult-Onset Still's Disease (AOSD) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to bring the annexes in line with the latest QRD template. An updated RMP version 10 was provided as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application, which related to the ongoing clinical trial.

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

5.1.9. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0016

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indication to broaden the existing indication for chronic lymphocytic leukaemia (CLL) to include all previously untreated patients including those with 17p deletion or TP53 mutation based on the results from the final CSR of study PCYC-1115-CA (MEA 021) for Imbruvica. As a consequence, sections 4.1, 4.6, 4.8, 5.1 and 5.3 of the SmPC are being updated. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and to bring Annex II in line with the latest QRD template version 9.1. Moreover, the updated RMP version 5.0 has been submitted."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2016.

The Committee discussed the issues identified in this application which related to several aspects of the clinical safety and efficacy. The main discussion was on the wording of the indication.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.10. Kyprolis - carfilzomib - Orphan - EMEA/H/C/003790/II/0001/G

Amgen Europe B.V.

Rapporteur: Arantxa Sancho-Lopez

Scope: "Extension of Indication to include new indication for Kyprolis to be used with either lenalidomide and dexamethasone or dexamethasone alone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) updated section 6.6 of the SmPC to include the option to administer Kyprolis in a 100 mL intravenous bag containing 5% glucose solution for injection in line with the extension of indication part of this variation.
Furthermore the MAH took the opportunity to include some editorial changes and harmonisations in the PI."

Action: For adoption

The Committee discussed the issues identified in this application, which related to the survival data.

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

5.1.11. Nevanac - nepafenac - EMEA/H/C/000818/II/0032

Alcon Laboratories (UK) Ltd

Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of indication to include the indication 'reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients' also for the 3 mg/ml strength based on data from the phase III studies C-12-067 and C-12-071. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in SmPC and to update the annexes in line with the latest QRD template. An updated RMP version 7 was provided as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application, which related to endpoints and comparison between two main trials.

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

5.1.12. Opdivo - nivolumab - EMEA/H/C/003985/II/0003

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include treatment in combination with ipilimumab of

advanced (unresectable or metastatic) melanoma in adults based on interim data from study CA209067 and the final CSR of study CA209069. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been revised accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II and Package Leaflet, and to provide a paediatric non-clinical biomarker study as part of the application to fulfil paediatric requirements. Further, an updated RMP version 4.3 was agreed during the procedure and two efficacy measures were added to Annex II upon request by the CHMP."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2016, 22.10.2015.

The CHMP discussed the application, mainly concerning the wording of the indication.

The CHMP agreed to include information on the PFS data in section 5.1 of the SmPC.

The Committee adopted a positive opinion by majority (29 positive out of 31 votes together with the CHMP Assessment Report and translation timetable.

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

The divergent position (Pieter de Graeff, Romaldas Maciulaitis) was appended to the opinion.

The summary of opinion was circulated for information.

5.1.13. Revestive - teduglutide - Orphan - EMEA/H/C/002345/II/0020

NPS Pharma Holdings Limited

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Torbjorn Callreus

Scope: "Extension of Indication to include paediatric population for Revestive.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to update the safety information. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 19.11.2015.

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

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.14. RoActemra - tocilizumab - EMEA/H/C/000955/II/0057

Roche Registration Limited

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with methotrexate (MTX) in the

RoActemra SmPC for the subcutaneous formulation.
As a consequence, section 4.1 of the SmPC is updated. The 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. Moreover, the updated RMP version 18 has been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, which related to efficacy and safety re-analysis.

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

5.1.15. Tysabri - natalizumab - EMEA/H/C/000603/II/0077

Biogen Idec Ltd

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include new indication for Tysabri.
As a consequence, sections 4.1 AND 4.4 of the SmPC are updated in order to provide physicians with more options for treating RRMS patients with high disease activity who fail an initial disease modifying therapy (DMT). Consequential changes to sections 4.2, 4.3, 5.1 and Package Leaflet in Sections 2 and 3 are also proposed."

Action: For adoption

Request for Supplementary Information adopted on 19.11.2015, 25.06.2015.

The Committee discussed the issues identified in this application. The main discussion related to the comparability between the Tysabri-treated patients in the US and the EU and the generation of long-term safety data.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.16. Victoza - liraglutide - EMEA/H/C/001026/II/0038

Novo Nordisk A/S

Rapporteur: Pieter de Graeff, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of Indication to include second-line monotherapy in type II diabetes for Victoza. Additionally, the MAH updated information related to hepatic and renal impairment.
As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated with new efficacy and safety information. The Package Leaflet is updated in accordance.
Furthermore, the Marketing authorisation holder (MAH) took the opportunity to align the PI with the latest QRD template version 9.1."

Action: For adoption

The Committee discussed the issues identified in this application. The main issues concerned the efficacy in hepatic impaired patients as well as updates of the product information.

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

5.1.17. Zontivity - vorapaxar - EMEA/H/C/002814/II/0005

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension of Indication to include treatment of patients with Peripheral Arterial Disease (PAD) and as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of local representative in Luxembourg in the Package Leaflet.
Furthermore, the PI is brought in line with the latest QRD template version 9.1. Moreover, revised RMP version 2.0 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015.

The Committee discussed the issues identified in this application, which related to the clinical efficacy and safety.

The Committee adopted 2nd Request for Supplementary Information with a specific timetable.

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. Humira - adalimumab - EMEA/H/C/000481/II/0146

AbbVie Ltd.

Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

Scope: revised List of experts to Ad- hoc expert group meeting to be held 5 April 2016.

"Extension of Indication to include treatment of non-infectious intermediate, posterior and panuveitis in adult patients for Humira.
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."

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015.

The CHMP adopted a revised list of experts to an ad-hoc expert group meeting to be held 5 April 2016.

5.2.2. Arzerra - ofatumumab - Orphan - EMEA/H/C/001131/II/0041

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Doris Stenver

Scope: List of experts to list of experts to the SAG Oncology meeting to be held 14 April 2016.

"Extension of Indication to include maintenance therapy in Chronic Lymphocytic Leukemia (CLL).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In accordance with the new QRD template version 9.1, the MAH is also taking the opportunity of this procedure to update the Annex II and combine the 2 SmPCs for the 100mg an 1,000mg vials."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015.

The CHMP adopted list of experts to the SAG Oncology meeting to be held 14 April 2016.

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

6.2.1. - human serum albumin - EMEA/H/D/004287

Human serum albumin ancillary action prevents adsorption to the container of various amino acids, vitamins which may be present in trace quantities and acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos. Scavenges embryotoxic components generated prevents adsorption to the container of various amino acids and vitamins, acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos, Scavenges embryotoxic components generated during embryo's metabolism in vitro)

Scope: Letter from the notified body dated 8 March 2016 requesting an extension of timeframe to respond to Day 120 LoQ.

Action: For adoption

List of Questions adopted on 28.01.2016.

The CHMP agreed to the request by the notified body for an extension of timeframe to respond to Day 120 LoQ.

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. Monoclonal Antibody Sgn-30 - EMEA/H/C/004388

treatment of metastatic colorectal cancer

Scope: Letter from the company dated 21 January 2016 requesting an accelerated assessment

Rapporteur's briefing note

Action: For adoption

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

9. Post-authorisation issues

9.1. Post-authorisation issues

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

PTC Therapeutics International Limited,

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus

Scope: Request for Supplementary information

"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."

Action: For discussion

The Committee discussed the final results from the phase III study. The CHMP agreed to the conclusion of the assessment of the data, that the benefit/risk should be re-assessed in the context of the on-going annual review.

The CHMP adopted a list of questions to the MAH with a specific timetable.

The CHMP agreed to consult a SAG with stakeholder/patient involvement and agreed a list of questions to this group.

9.1.2. Onglyza - saxagliptin, saxagliptin / metformin hydrochloride EMEA/H/C/001039/WS0902/0037, Komboglyze- saxagliptin, saxagliptin / metformin hydrochloride - EMEA/H/C/002059/WS0902/0028

AstraZeneca AB,

Lead Rapporteur: Pieter de Graeff

Scope: "Update of section 5.1 of the SmPC, upon request by the CHMP following the assessment of the post-authorisation measures LEG 038.1 (Onglyza) and LEG 015.1 (Komboglyze), with information regarding effect on all-cause mortality. In addition, the MAH took the opportunity to implement minor editorial changes in the Package Leaflet and to update the contact information for the local representative in Poland in the Package Leaflet."

Action: For discussion

The Committee discussed the issues identified in this application, which related to SmPC text.

9.1.3. Voncento - human coagulation factor VIII / human von willebrand factor EMEA/H/C/002493/II/0017/G

CSL Behring GmbH, Rapporteur: Pieter de Graeff, PRAC Rapporteur: Sabine Straus,

Scope: Request for Supplementary information or Opinion, proposal to remove the commitment to conduct a post-marketing study for haemophilia patients

"C.I.4 (type II): Update of section 4.8 of the SmPC in order to update the frequencies of undesirable effects to reflect the final clinical study data from study CSLCT-BIO-08-53 in haemophilia A paediatric patients. The Package Leaflet is updated accordingly. The submission of the final CSR CSLCT-BIO-08-53 also leads to changes to the RMP (ver. 6.1) in order update the Company Core Safety Information (CCSI).
C.I.11.z (type IB): Submission of a revised RMP in order to remove the commitment to conduct a post-marketing study for haemophilia A patients (CSLCT-BIO-12-78) for Voncento as consequence of new data from study CSLCT-BIO-08-53.
In addition, the Marketing authorisation holder (MAH) took the opportunity to combine different strengths in the SmPC and Package Leaflet."
Request for Supplementary Information adopted on 19.11.2015.

Action: For discussion

The Committee discussed the issues identified in this application.

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

9.1.4. Xtandi - enzalutamide - EMEA/H/C/002639/II/0028/G

Astellas Pharma Europe B.V.,

Rapporteur: Arantxa Sancho-Lopez,

Scope: Request for Supplementary information or Opinion
"Update of sections 4.8 and 5.1 of the SmPC based on the results of study 9785-CL-0222 (TERRAIN); an active-controlled study, which evaluated the safety and efficacy of enzalutamide vs bicalutamide in men with metastatic CRPC. The Package Leaflet has been updated accordingly. Further, the MAH provides supportive data from study MDV3100-09 (STRIVE), a second phase 2 study of enzalutamide vs bicalutamide."

Action: For adoption

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.

9.1.5. WS0792 - tenofovir disoproxil, emtricitabine, emtricitabine / tenofovir disoproxil, efavirenz / emtricitabine / tenofovir disoproxil, emtricitabine / rilpivirine / tenofovir disoproxil, elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil Atripla-EMEA/H/C/000797/WS0792/0104 Emtriva-EMEA/H/C/000533/WS0792/0105 Eviplera-EMEA/H/C/002312/WS0792/0061 Stribild-EMEA/H/C/002574/WS0792/0048 Truvada-EMEA/H/C/000594/WS0792/0117 Viread-EMEA/H/C/000419/WS0792/0152

Gilead Sciences International Ltd,

Lead Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna,

Scope: Request for Supplementary information or Opinion, PRAC advice
"Update of section 4.4 of the SmPC in order to delete the HIV class label wording for mitochondrial dysfunction following the review of existing data on mitochondrial toxicity including the Mitochondrial Toxicity in Children (MITOC) Study.The Package Leaflet of Viread, Truvada and Emtriva were updated accordingly."

Request for Supplementary Information adopted on 28.01.2016, 24.09.2015.

Action: For adoption

The CHMP noted the PRAC advice. Patients' representatives were involved in class labelling.

The CHMP adopted positive opinion by consensus. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

9.1.6. WS0769 - lamivudine, lamivudine / zidovudine, abacavir, lamivudine / abacavir / zidovudine, lamivudine / abacavir Combivir-EMEA/H/C/000190/WS0769/0083 Epivir-EMEA/H/C/000107/WS0769/0098 Kivexa-EMEA/H/C/000581/WS0769/0061 Lamivudine ViiV-EMEA/H/W/000673/WS0769/0030 Trizivir-EMEA/H/C/000338/WS0769/0094 Ziagen-EMEA/H/C/000252/WS0769/0087

ViiV Healthcare UK Limited,

Lead Rapporteur: Joseph Emmerich, PRAC Rapporteur: Isabelle Robine,

Scope: Request for Supplementary information or Opinion, PRAC advice "Submission of final CSR for Mitochondrial Toxicity in Children (MITOC) Study (WE027/WWE112888). The MAH took also the opportunity to respond to a LEG on mitochondrial dysfunction to address the request on revision of class labelling of antiretrovirals on mitochondrial toxicity. The present variation does not propose changes in the PI."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2016, 24.09.2015.

The CHMP noted the PRAC advice. Patients' representatives were involved in class labelling.

The CHMP adopted positive opinion by consensus. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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 indolent non-Hodgkin lymphoma (iNHL).

PRAC Rapporteur: Rafe Suvarna, PRAC Co-Rapporteur: Ulla Wändel Liminga

CHMP Rapporteur: Kristina Dunder, CHMP Co-Rapporteur: Pieter de Graeff,

Scope: 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, start of procedure at PRAC

Action: For information

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

Letter from European Commission dated 11 March 2016 informing of an official referral under Article 20 to PRAC and its grounds.

Recommendation to European Commission on interim measure.

The CHMP noted the start of referral at the PRAC.

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

10.2.1. Desloratadine-containing products

Rapporteur: Daniel Brasseur, Co-Rapporteur: Andrea Laslop,

Scope: Letter from Merck Sharp & Dohme (Europe), Inc. dated 16 March requesting two weeks extension of timeframe to submit responses to the List of Questions adopted 17 December 2015.

Prescription status of desloratadine-containing products

Action: For adoption

The CHMP agreed to the request by the applicant for an additional two weeks extension to the timetable to submit responses to the list of questions adopted on 17 December 2015 with a specific timetable:

Submission of responses: 14.04.2016

Re-start of the procedure: 28.04.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 11.05.2016

Comments: 16.05.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 19.05.2016

CHMP list of outstanding issues or CHMP Opinion: May 2016 CHMP

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

No items

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 companiesRapporteur: 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 19.11.2015.

The Committee discussed the therapeutic indication, paediatric age range and posology.

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

Adoption of 2nd LoOI: March 2016 CHMP

Submission of responses: 14.04.2016

Re-start of the procedure: 28.04.2016

Rapporteur and co-rapporteur assessment reports circulated to CHMP: 11.05.2016

CHMP member comments: 16.05.2016

Updated rapporteur and co-rapporteur assessment reports circulated to CHMP: 19.05.2016

Adoption of third list of outstanding issues / CHMP Opinion: May 2016 CHMP

10.5.2. Haldol and associated names (EMEA/H/A-30/1393) (haloperidol), Janssen-Cilag Group of companies and associated companies

Rapporteur: Martina Weise, Co-Rapporteur: Katarina Vučić,

Scope: Opinion or List of Outstanding Issues

Harmonisation due to large differences in sections 4.1 (age; indications) and 4.2 (special population; general dosing) and in other (non)clinical sections of the SmPC (4.3 – 5.3).

Action: For adoption

List of Outstanding Issues adopted 26 March 2015.

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

List of outstanding issues 2: March 2016 CHMP

Submission of responses: 01.07.2016

Re-start of the procedure: 18.08.2016

Joint assessment report circulated to CHMP: 26.08.2016

Comments: 05.09.2016

Updated joint assessment report(s) circulated to CHMP: 08.09.2016

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

Furthermore the CHMP agreed to consult a SAG. The list of questions will be further discussed at the April 2016 CHMP meeting.

In addition they agreed that there is no need to consult the PDCO at this stage.

10.5.3. Haldol decanoate and associated names (EMEA/H/A-30/1405) (haloperidol) Janssen-Cilag Group of companies and associated companies

Rapporteur: Martina Weise, Co-Rapporteur: Katarina Vučić,

Scope: Opinion or List of Outstanding Issues

Harmonisation due to large differences in sections 4.1 (age; indications) and 4.2 (special population; general dosing) and in other (non)clinical sections of the SmPC (4.3 – 5.3).

Action: For adoption

List of Outstanding Issues adopted 26 March 2015.

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

List of outstanding issues 2: March 2016 CHMP

Submission of responses: 01.07.2016

Re-start of the procedure: 18.08.2016

Joint assessment report circulated to CHMP: 26.08.2016

Comments: 05.09.2016

Updated joint assessment report(s) circulated to CHMP: 08.09.2016

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

In addition they agreed that there is no need to consult the PDCO at this stage.

10.5.4. Saroten and associated names - amitriptyline - EMEA/H/A-30/1430

Lundbeck group of companies and associated companies

Rapporteur: George Aislaitner, Co-Rapporteur: Alar Irs,

Scope: List of Outstanding Issues

Harmonisation exercise for Saroten and associated names (amitriptyline). Review triggered by Greece due to the need to harmonise the product information across all Member States, including the therapeutic indication, the posology, the contra-indications, the adverse effects and the recommendations for use.

Action: For adoption

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

Submission of responses: 12.05.2016

Re-start of the procedure: 26.05.2016

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 08.06.2016

Comments: 13.06.2016

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 16.06.2016

CHMP list of outstanding issues/CHMP opinion: June 2016 CHMP

10.5.5. 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: Letter from Bristol-Myers Squibb dated 09 March requesting 2-months extension of timeframe to submit responses to the list of outstanding issues adopted 25.02.2016.

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 agreed to the request by the MAH for an additional 2-months extension to the clock stop to respond to the list of outstanding issues adopted in February 2016 with a specific timetable.

List of outstanding issues: February 2016 CHMP

Responses to LoOI: 15.06.2016

Clock restart: 23.06.2016

Assessment report: 06.07.2016

Comments: 11.07.2016

Updated AR: 14.07.2016

CHMP opinion: July 2016 CHMP

10.5.6. 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: Letter from Bristol-Myers Squibb dated 09 March requesting 2-months extension of timeframe to submit responses to the list of outstanding issues adopted 25.02.2016.

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 agreed to the request by the MAH for an additional 2-months extension to the clock stop to respond to the list of outstanding issues adopted in February 2016 with a specific timetable.

List of outstanding issues: February 2016 CHMP

Responses to LoOI: 15.06.2016

Clock restart: 23.06.2016

Assessment report: 06.07.2016

Comments: 11.07.2016

Updated AR: 14.07.2016

CHMP opinion: July 2016 CHMP

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

10.6.1. Alkem Laboratories Limited, India - EMEA/H/A-31/1436

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey,

Scope: reliability of the data of bioequivalence studies, Appointment of (Co)Rapporteur

Action: For adoption

Amended letter from BfArM in Germany dated 24 March 2016 notifying of an official referral under Article 31 and its grounds.

The CHMP noted the letter from BfArM in Germany dated 24 March 2016 notifying of an official referral under Article 31 and its grounds.

The CHMP appointed Harald Enzmann (interest level 1) as Rapporteur and Greg Markey (interest level 1) as Co-Rapporteur.

The Committee adopted a list of questions to the CRO and a list of questions to the MAHs together with a specific timetable.

Start of the procedure (CHMP): March, 2016 CHMP

List of questions: March 2016 CHMP

Submission of responses: 12.05.2016

Re-start of the procedure: 26.05.2016

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 08.06.2016

Comments: 13.06.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 16.06.2016

CHMP LoOI/opinion: June 2016 CHMP

10.6.2. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP); gadoversetamide – OPTIMARK (CAP)

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Doris Stenver

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data, Appointment of (Co)Rapporteur

Action: For information

The CHMP noted the start of referral at the PRAC.

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

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

Scope: 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, to ensure the availability of efficacious and safe antibiotics for EU patients.

Scope: Appointment of (Co)Rapporteur, List of Questions and timetable

Action: For adoption

The CHMP noted the notification by the Spanish Agency of Medicines and Medical Devices of a referral under Article 31 of Directive 2001/83/EC.

The CHMP appointed Concepcion Prieto-Yerro (interest level 1) as Rapporteur and Alar Irs (interest level 2) as Co-Rapporteur.

The Committee adopted a list of questions together with a specific timetable.

Notification: 21.03. 2016

Start of the procedure (CHMP): March 2016 CHMP

List of questions: 01.04.2016

Submission of responses: 09.06.2016

Re-start of the procedure: 23.06.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 06.07.2016

Comments: 11.07.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 14.07.2016

CHMP list of outstanding issues / CHMP opinion: July 2016 CHMP

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: Article 31 triggered by the BfArM 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. Appointment of (Co)Rapporteur, adoption of List of Questions, timetable.

Action: For adoption

The CHMP noted the letter from the BfArM in Germany dated 30 March 2016 notifying of official referral under Article 31 and its grounds.

The CHMP appointed Harald Enzmann (interest level 1) as Rapporteur and Milena Stain (interest level 1) as Co-Rapporteur.

The Committee adopted a list of questions together with a specific timetable.

Start of the procedure (CHMP): March 2016 CHMP

List of questions: 01.04.2016

Submission of responses: 12.05.2016

Re-start of the procedure: 26.05.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 08.06.2016

Comments: 13.06.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 16.06.2016

CHMP LoOI/CHMP opinion: June 2016 CHMP

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

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

Action: For information

The CHMP noted the March 2016 ENS.

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 Minutes were noted.

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

Scope: ITF Briefing Meeting

Meeting date: 12 April 2016

Action: For adoption

The CHMP agreed to the ITF meeting.

Scope: ITF Briefing Meeting

Meeting date: 15 April 2016

Action: For adoption

The CHMP agreed to the ITF meeting.

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Joint CHMP-COMP Strategic Review & Learning Meeting to be held in Utrecht, 30 May-1 June 2016 under the Netherland's Presidency of the Council of the European Union

Scope: Agenda topics of the upcoming Strategic Review and Learning meeting

Action: For discussion

Strategic Review and Learning meeting will be held, in part, jointly with the COMP.

The CHMP noted the draft agenda. Comments on the draft agenda topics are awaited from members until 8th April.

14.1.2. Joint CHMP/PDCO membership

Action: For information

The CHMP noted the information that 4 mandates of joint CHMP/PDCO membership are expiring in May 2016 and joint CHMP/PDCO memberships for another three-year mandate are needed.

Post-meeting note: letter was sent out to CHMP members on 11 April 2016: CHMP members are requested to consider putting him/herself (together with his/her alternate) to take on the

joint CHMP/PDCO membership role. Such expressions of interest should be sent by Friday 29 April 2016.

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 **14-17 March 2016**

Action: For information

The CHMP noted the Summary of recommendations and advice.

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

Action: For adoption

The CHMP adopted the list of Union Reference Dates and frequency of submission of Periodic Safety Update Reports.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 22-23 March 2016
Action: For information

The CHMP noted the minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Not applicable this month

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at March 2016 PDCO

Action: For information

The CHMP noted the report.

Report from the PDCO meeting held on 30 March – 1 April 2016

Action: For information

The CHMP noted the report.

Scope: Reflection paper on extrapolation of efficacy and safety in paediatric medicine development

Action: For adoption

The CHMP discussed the draft reflection paper and the framework of public consultation. The CHMP agreed in light with the upcoming workshop (17-18 May 2016) to wait with the public consultation of the paper until the workshop has taken place and any outcome has been implemented in the reflection paper. However, a preliminary version of its draft reflection

paper has been published on EMA website. Discussions at the workshop will contribute to the further development of the draft refection paper which is expected to be released for public consultation by the end of July 2016.

The draft reflection paper outlines a framework for the extrapolation of clinical trial data from adults to children to support the authorisation of new medicines for children.

Extrapolation of data aims to optimise the involvement of children in clinical studies, one of the objectives of the European Union Paediatric Regulation, by predicting how a medicine may work in children and adolescents on the basis of studies conducted in adults or other paediatric populations.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 21-23 March 2016
Action: For information

The CHMP noted the report.

14.2.6. CMDh

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 29-31 March 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 14-17 March 2016. Table of conclusions

Action: For information

The CHMP noted the report.

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

14.3.2. Ad-hoc Influenza Working Group

Scope: EU Strain selection for the Influenza Vaccines for the Season 2016/2017

Action: For adoption

The CHMP adopted the EU Strain selection for the Influenza Vaccines for the Season 2016/2017.

Scope: EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2016/2017

Action: For adoption

Report from the Ad Hoc Influenza working group to the BWP

The CHMP adopted the EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2016/2017. The CHMP noted the report from Ad Hoc Influenza working group to the BWP.

14.3.3. Quality Working Party (QWP)

CHMP: Jean-Louis Robert,

Scope: Questions and answers on API mixtures

Action: For adoption

The CHMP adopted the Q&A. This Questions-and-answers document has been developed to provide information on how to deal with mixtures of API and excipients (called API mix), and to identify situations where it will be acceptable to use the ASMF/CEP procedure and perform manufacture under EU GMP Part II for the API mix.

Scope: Reflection paper on the Dissolution specification for generic oral immediate release products

Action: For adoption for 3-month public consultation

The CHMP adopted the reflection paper for 3-month public consultation. The reflection paper discusses the suitability of the dissolution method and the specifications for in vitro dissolution of orally administered generic drug products with immediate release characteristics. Where applicable, this reflection paper should be read in connection with the principles of relevant guidelines listed as references.

14.3.4. Biologics Working Party (BWP)

CHMP: Sol Ruiz,

Scope: Guideline on process validation for the manufacture of biotechnology-derived active substances and data to be provided in the regulatory submission (EMA/CHMP/BWP/187338/2014)

Action: For adoption

Postponed to April ORGAM.

14.3.5. Cardiovascular Working Party (CVSWP)

CHMP: Pieter de Graeff

Scope: Draft guideline on clinical investigation of new medicinal products for the treatment of acute coronary syndrome (EMA/CHMP/207892/2015)

Action: For adoption for 6 months public consultation

The CHMP adopted the guideline for 6-months public consultation. The present guideline update includes the following changes: 1) guidance addressing both STEMI and NSTEMI, as well as unstable angina, 2) update in their definitions, 3) risk stratification using different scoring systems, 4) investigated endpoints, and 5) clinical developments of new medicinal products beyond the acute stage, including agents other than antiplatelets and anticoagulants.

14.3.6. Infectious Diseases Working Party (IDWP)

Lead: Maria Fernandez Cortizo

Scope: Concept paper on an addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address paediatric-specific clinical data requirements (CPMP/EWP/558/95 rev 2)

Action: For adoption for public consultation

The CHMP adopted the concept paper for 3-months public consultation. The concept paper proposes the development of an addendum to the Guideline on the Evaluation of New Anti-bacterial Medicinal Products (CPMP/EWP/558/95 Rev 2) to address the clinical development of antibacterial medicinal products for use in the paediatric population.

14.4. Cooperation within the EU regulatory network

14.4.1. Letter from the European Commission on a definition for 'principal molecular structural features'

Scope: Proposal for 'principal molecular structural features' (PMSF) definition

Letter from the European Commission, requesting a definition for 'principal molecular structural features' as referred to in Art 3(3)c of Reg (EC) No 847/2000 on similar active substance

Action: For adoption

The CHMP discussed the proposal and amendments and adopted the CHMP-CAT Joint document. The response contains proposals for chemical and biological medicinal products based on input from QWP and BWP whilst the proposal for the ATMPs was drafted and adopted by CAT at their March meeting.

14.5. Cooperation with International Regulators

No items

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

No items

14.8. Planning and reporting

14.8.1. New marketing authorisation applications for 2016 with appointed rapporteurs

Action: For information

The CHMP noted the report.

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Zika virus: Viral safety of plasma-derived and urine-derived medicinal products with respect to Zika virus

CHMP: Sol Ruiz

Scope: BWP report

Action: For adoption

The CHMP noted the update and adopted the report.

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 29 March – 1 April 2016 meeting 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	
Daniel Brasseur	Member	Belgium	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	
Panayiotis Triantafyllis	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Radka Montoniová	Alternate	Czech Republic	No interests declared	
Jens Heisterberg	Member	Denmark	No restrictions applicable to this meeting	
Sinan B. Sarac	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	France	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	(Vice-Chair)			
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	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
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	
Helen Vella	Alternate	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Nela Vilceanu	Member	Romania	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	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	member			
Patricia Diaz Ramos	Expert - in person*	Spain	No interests declared	
Theis Moeslund Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Alan Fauconnier	Expert - via telephone*	Belgium	No interests declared	
Macarena Rodriguez Mendizabal	Expert - via telephone*	Spain	No interests declared	
Christine Greiner	Expert - via telephone*	Germany	No interests declared	
Marina Fertek	Expert - in person*	Czech Republic	No restrictions applicable to this meeting	
Odoardo Maria Olimpieri	Expert - via telephone*	Italy	No restrictions applicable to this meeting	
Valérie Lescrainier	Expert - in person*	Belgium	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Gabriele Schlosser-Weber	Expert - via telephone*	Germany	No interests declared	
Henning Brohmann	Expert - via telephone*	Germany	No interests declared	
Jörg Zinserling	Expert - via telephone*	Germany	No interests declared	
Leon van Aerts	Expert - in person*	Netherlands	No interests declared	
Margarida Menezes-Ferreira	Expert - via telephone*	Portugal	No interests declared	
Mário Miguel Rosa	Expert - via telephone*	Portugal	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ângelo Ferreira da Silva	Expert - via telephone*	Portugal	No interests declared	
Paulo Paixao	Expert - via telephone*	Portugal	No interests declared	
Katharina Hausteiner-Melichar	Expert - via telephone*	Austria	No interests declared	
Sean Jones	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Mirza Catibusic	Expert - via telephone*	Ireland	No interests declared	
Caroline Laborde	Expert - in person*	France	No interests declared	
Aurelie Beon	Expert - in person*	France	No restrictions applicable to this meeting	
Cecile Ollivier	Expert - via telephone*	EMA	No interests declared	
Andrew Thomson	Expert - via telephone*	EMA	No interests declared	
Annie Eyre-Brook	Expert - via telephone*	United Kingdom	No interests declared	
Joseph Lim	Expert - via telephone*	United Kingdom	No interests declared	
Sean Jones	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Felix Carvalho	Expert - via telephone*	Portugal	No interests declared	
Sabine Lenton	Expert - via telephone*	United Kingdom	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)*

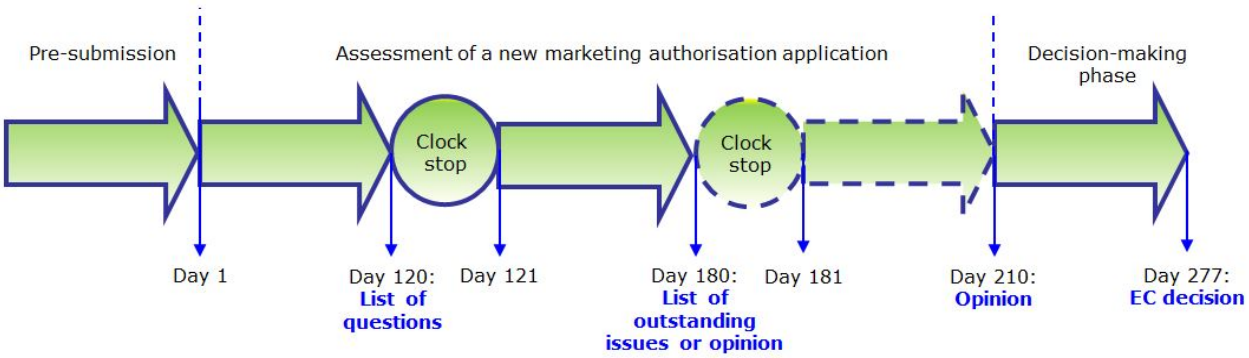
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (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/