27 April 2015
EMA/223528/2015
Procedure Management and Business Support Division

Committee for medicinal products for human use (CHMP)

Minutes of meeting held on 23-26 March 2015

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

23 March 2015, 13:00 – 19:00, room 2A

24 March 2015, 08:30 – 19:15, room 2A

25 March 2015, 08:30 – 19:45, room 2A

26 March 2015, 08:30 – 14:30, room 2A

Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present following a request for access to documents under 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).

Health & 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 and therefore not disclosed. With regards to therapeutic indications 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. The procedures discussed by the CHMP are on-going and therefore are considered confidential. Additional details on some of these procedures will be published in the CHMP meeting

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highlights once the procedures are finalised and start of referrals will also be available. For orphan medicinal products the applicant details are published as this information is already publicly available. Of note, this agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

Further information with relevant explanatory notes can be found at the end of this document.

For adoption

Agenda (EMA/CHMP/148199/2015 Rev.4) and Annex to CHMP agenda of the CHMP plenary session to be held 23-26 March 2015	The agenda and annex were adopted with amendments.
Timeschedule (EMA/CHMP/169219/2015 Rev.3) of the CHMP plenary session to be held 23-26 March 2015	The timeschedule was adopted.
Minutes (EMA/CHMP/158074/2015) of the CHMP plenary session held 23-26 February 2015	The Minutes of the CHMP plenary session held 23 – 26 February 2015 were adopted.
Minutes of ORGAM meeting held on 16 March 2015 (EMA/CHMP/181631/2015).	The Minutes of the March 2015 CHMP ORGAM meeting held on 16 March 2015, together with all decisions taken at that meeting, were adopted.

For information

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 23-26 March 2015.	The pre-meeting list was noted.
The Committee is asked to note that Tuomo Lapveteläinen was appointed as the new Alternate from Finland replacing Janne Komi in this role.	The CHMP welcomed Tuomo Lapveteläinen as new Finnish alternate.
Draft Agenda of CHMP meeting to be held on 20-23 April 2015.	The draft agenda was noted.

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1. Oral explanations

1.1. Pre-authorisation procedure oral explanations

(EMEA/H/C/002739), (human alpha1-proteinase inhibitor), (treatment of lung disease)
The ad-hoc expert group meeting held on 14 January 2015. List of Outstanding Issues adopted on 20.11.2014.
List of Questions adopted on 25.04.2014. After discussion the CHMP agreed that no Oral explanation was needed at this time.
See also section 2.2. Initial applications; Day 180 List of outstanding issues

(EMEA/H/D/002831), (insulin-like growth factor 1 segment), (hard-to-heal wounds, primarily venous leg ulcers)
List of Outstanding Issues adopted on 25.09.2014. List of Questions adopted on 23.01.2014.
An Oral explanation was held on Wednesday 25 March 2015 at 11.00.
The Committee adopted the BWP Report. The Committee noted that the applicant has withdrawn the request.
See section 8 Withdrawal of initial application

(EMEA/H/C/002772), Orphan, (dasiprotimut-t), Applicant: Biovest Europe Ltd, (treatment of non-Hodgkin's lymphoma (FL))
List of Outstanding Issues adopted on 18.12.2014. List of Questions adopted on 25.04.2014.
An Oral explanation was held on Tuesday 24 March 2015 at 14.00.
The company's presentation focused on the clinical data in support of efficacy and the performed analyses. They also outlined the manufacturing process of the vaccine.
The Committee discussed the available data.
The Committee adopted the BWP Report.

1.2. Re-examination procedure oral explanation

No items

1.3. Post-authorisation procedure oral explanation

Insuman (EMEA/H/C/000201) (Insulin Human), MAH: Sanofi-aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Pieter de Graeff, (treatment of diabetes mellitus), Complete application (stand-alone) - Council Directive 81/851/EEC
After discussion the CHMP agreed that no Oral explanation was needed at this time.
See also section 11. Post-authorisation issues

1.4. Referral procedure oral explanation

No items

2. Initial applications

2.1. Initial applications; Opinions

Akynzeo (EMEA/H/C/003728), (netupitant / palonosetron), Applicant: Helsinn Birex Pharmaceuticals Ltd. (prevention of chemotherapy-induced nausea and vomiting (CINV))
List of Outstanding Issues adopted on 22.01.2015.List of Questions adopted on 22.05.2014.The members discussed the SmPC wording, especially whether contraindications in breast feeding women as well as in pregnancy were required. The members agreed that considering the indication, a strong recommendation against breast feeding was considered sufficient.
The CHMP agreed to include the contraindication in pregnancy.
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 netupitant is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The summary of opinion was circulated for information.

Gardasil 9 (EMEA/H/C/003852), (human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed)), Applicant: Sanofi Pasteur MSD SNC, (treatment of HPV diseases)
List of Outstanding Issues adopted on 18.12.2014.
List of Questions adopted on 24.07.2014.
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 the active substances Human Papillomavirus Type 31 L1 protein, Human Papillomavirus Type 33 L1 protein, Human Papillomavirus Type 45 L1 protein, Human Papillomavirus Type 52 L1 protein and Human Papillomavirus Type 58 L1 protein are new active substances, 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 Committee noted the letter of recommendation dated 26.03.2015.
The summary of opinion was circulated for information.
The Committee adopted the BWP Report.

Lenvima (EMEA/H/C/003727), Orphan, (lenvatinib), Applicant: Eisai Ltd, (treatment of papillary thyroid cancer, treatment of follicular thyroid cancer)
List of Questions adopted on 22.01.2015. Accelerated assessment.The members discussed the starting dose and whether a lower starting dose could be considered . The member noted the proposed post authorisation study to further investigate the starting dose but questioned the proposed timing of finalisation of the study in 2020. The company justified the late finalisation of the study by expected difficult patient recruitment.
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 lenvatinib 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 Committee noted the letter of recommendation dated 23.03.2015.

The summary of opinion was circulated for information.

Synjardy (EMEA/H/C/003770), (empagliflozin / metformin), Applicant: Boehringer Ingelheim GmbH, (treatment of type II diabetes)
List of Questions adopted on 20.11.2014.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.

Voriconazole Hospira (EMEA/H/C/003737), (voriconazole), Applicant: Hospira UK Limited, (treatment of fungal infections)
List of Outstanding Issues adopted on 20.11.2014.
List of Questions adopted on 24.07.2014.
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.

2.2. Initial applications; Day 180 List of outstanding issues

(EMEA/H/C/004008), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
List of Questions adopted on 20.11.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003904), (atazanavir / cobicistat), (treatment of HIV-1 infected, combination with other antiretroviral medicinal products.)
List of Questions adopted on 20.11.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003984), (bortezomib), (treatment of multiple myeloma)
List of Questions adopted on 23.10.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues .
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003925), (docetaxel), (treatment of breast cancer, non small cell lung cancer, prostate cancer, metastatic gastric adenocarcinoma and head and neck cancer)
List of Questions adopted on 23.10.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003981), (duloxetine), (treatment of major depressive disorder, diabetic peripheral neuropathic pain and generalised anxiety disorder, treatment of major depressive episodes, diabetic peripheral neuropathic pain and generalised anxiety disorder)

List of Questions adopted on 22.01.2015.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003725), Orphan, (panobinostat), Applicant: Novartis Pharmaceuticals UK Limited, (treatment of multiple myeloma)
List of Questions adopted on 25.09.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The Committee discussed the involvement of SAG.
The CHMP adopted a list of Outstanding Issues with a specific timetable.
The CHMP agreed to consult the SAG Oncology and adopted a List of Questions to this group.

(EMEA/H/C/003776), (ferric citrate coordination complex), (treatment of hyperphosphataemia)
List of Questions adopted on 24.07.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003759), (guanfacine), (treatment of ADHD)
List of Questions adopted on 24.07.2014.
Request for an extension of the clock stop received on 27.03.2015
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues.
The CHMP agreed to the request by the applicant for an extension of the clock stop with a specific timetable.
The CHMP agreed to consult the SAG CNS.

(EMEA/H/C/003985), (nivolumab), (treatment of advanced (unresectable or metastatic) melanoma in adults.)
List of Questions adopted on 22.01.2015.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

(EMEA/H/C/004010), (pregabalin), (treatment of neuropathic pain, epilepsy and generalised anxiety disorder)
List of Questions adopted on 18.12.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/004070), (pregabalin), (treatment of epilepsy and generalised anxiety disorder (GAD))
List of Questions adopted on 18.12.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003900), (pregabalin), (treatment of epilepsy and Generalised Anxiety Disorder (GAD))
List of Questions adopted on 18.12.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/002739), (human alpha1-proteinase inhibitor), (treatment of lung disease)
The ad-hoc expert group meeting held on 14 January 2015. List of Outstanding Issues adopted on 20.11.2014. List of Questions adopted on 25.04.2014.
See also section 1.1. Pre-authorisation procedure oral explanations
After discussion the CHMP agreed that no Oral explanation was needed at this time.
The CHMP adopted a 2nd list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

(EMEA/H/C/003794), Orphan, (asfotase alfa), Applicant: Alexion Europe SAS, (treatment of paediatric-onset hypophosphatasia)
List of Questions adopted on 20.11.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

(EMEA/H/C/002801), Orphan, ATMP, (allogeneic t cells genetically modified to express suicide gene), Applicant: MolMed SpA, (treatment in haploidentical haematopoietic stem cell transplantation)
List of Questions adopted on 24.07.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee agreed on the recommendation and scientific discussion as adopted by CAT, together with the updated List of Questions .
The Committee adopted the BWP Report.

2.3. Initial applications; Day 120 List of Questions

(EMEA/H/C/004038), Orphan, (mercaptamine), Applicant: Lucane Pharma, (treatment of corneal cystine deposits)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/002611), (levodopa / carbidopa), (treatment of Parkinson's disease)
The Committee discussed the issues identified in this application
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003861), Orphan, (parathyroid hormone), Applicant: NPS Pharma Holdings Limited, (treatment of hypoparathyroidism)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/004071), Orphan, (dexamethasone acetate), Applicant: LABORATOIRES CTRS, (treatment of symptomatic multiple myeloma in combination with other medicinal products.)
The Committee noted 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 CHMP Similarity Assessment Report .

(EMEA/H/C/003860), (mepolizumab), (treatment of asthma)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/003954), Orphan, (lumacaftor / ivacaftor), Applicant: Vertex Pharmaceuticals (U.K.) Ltd., (treatment of cystic fybrosis)
The Committee noted 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 CHMP Similarity Assessment Report.

(EMEA/H/C/004072), (pemetrexed), (unresectable malignant pleural mesothelioma metastatic non-small cell lung cancer)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

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

(EMEA/H/C/003964), Orphan (Efmoroctocog Alfa), Applicant: Biogen Idec Ltd, (treatment of Haemophilia A)
The CHMP adopted the Rapporteur's request for testing prior to the authorisation.

Heparesc (EMEA/H/C/003750), Orphan, ATMP, (allogenic human heterologous liver cells), Applicant: Cytonet GmbH&Co KG, (treatment of urea cycle disorders (UCD)), List of Outstanding Issues adopted on 18.12.2014. List of Questions adopted on 25.04.2014.
The CHMP noted the timetable. The CHMP noted the overview of updated AR.
The Committee adopted the BWP Report.

(EMEA/H/C/003774), (selexipag), (treatment of pulmonary arterial hypertension (PAH; WHO Group I))
The CHMP adopted the CHMP Similarity Assessment Report .

(EMEA/H/C/003926), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted in November 2014 together with a specific timetable.

(EMEA/H/C/004021), (aripiprazole), Generic, Generic of Abilify, (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
List of Questions adopted on 18.12.2014.
The Committee agreed to the request from the applicant for an extension of clock stop to submit responses to the List of Questions adopted in December 2014 together with a specific timetable.

(EMEA/H/C/002715), (fentanyl), (treatment of acute moderate to severe post-operative pain)

List of Questions adopted on 22.01.2015.
The Committee agreed to the request from the applicant for an extension of clock stop to submit responses to the List of Questions adopted in January 2015 together with a specific timetable.

(EMEA/H/C/003834), Orphan, (idebenone), Applicant: Santhera Pharmaceuticals (Deutschland) GmbH, (treatment of Leber's Hereditary Optic Neuropathy (LHON))
List of Outstanding Issues adopted on 26.02.2015.
List of Questions adopted on 25.09.2014.
The Committee agreed to the request from the applicant for an extension of clock stop to submit responses to the List of Outstanding Issues adopted in February 2015 together with a specific timetable.

2.5. Products in the Decision Making Phase

Mysimba (EMEA/H/C/003687), (naltrexone / bupropion), Applicant: Orexigen Therapeutics Ireland Limited, (indicated for the management of obesity)
Fixed combination application (Article 10b of Directive No 2001/83/EC). Opinion adopted on 18.12.2014. The Committee discussed the release of interim study data in relation to the EPAR.

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

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

No items

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

Norvir (EMEA/H/C/000127/X/0127), (ritonavir), MAH: AbbVie Ltd., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "The MAH applies for a line extension of a new oral powder formulation of Norvir (ritonavir) as a replacement for the currently marketed Norvir oral solution for a more suitable ritonavir formulation for the paediatric population."
List of Questions adopted on 23.10.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues, mainly relating to some quality aspects (graduation of syringe and homogeneity of the suspension). The CHMP adopted a List of Outstanding Issues with a specific timetable.

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

Mabthera (EMEA/H/C/000165/X/0101/G), (rituximab), MAH: Roche Registration Ltd, Rapporteur: Christian Schneider, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Doris Stenver, "Grouping of:
- Line extension to add a new strength 1600 mg solution for subcutaneous injection, a new indication

is proposed for this strength (different from 1400mg strength).
- Type II variation to update the product information of the existing strengths as a consequence to the line extension application
- Type II variation to update the RMP"
The Committee discussed the issues identified in this application, mainly relating to potential off-label use.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions .

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

No items

4. Type II variations - Extension of indication procedures according to Annex I of Commission Regulation (EC) No 1234/2008

4.1. Type II variation; Extension of indication- Opinions or Requests for supplementary information

Fycompa (EMEA/H/C/002434/II/0016), (perampanel), MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams, "Extension of indication as adjunctive treatment of Primary Generalised Tonic-Clonic seizures in patients with epilepsy aged 12 years and older. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to propose minor changes to PL and update the contact details of the Maltese local representative."
Request for Supplementary Information adopted on 18.12.2014.
The Committee discussed the issues identified in this application.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Levemir (EMEA/H/C/000528/II/0070), (insulin detemir), MAH: Novo Nordisk A/S, Rapporteur: Jens Heisterberg, "Update of sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to extend the clinical use of Levemir in children from 2 years to 1 year of age. The Package Leaflet is updated accordingly."
The Committee discussed the issues identified in this application, mainly focusing on the risk minimisation measures.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Qutenza (EMEA/H/C/000909/II/0039), (capsaicin), MAH: Astellas Pharma Europe B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Magda Pedro, "Extension of indication to include treatment of diabetic patients with peripheral neuropathic pain based on the results of studies E05-CL-3004 (STEP) and E05-CL-3002 (PACE). As a consequence sections 4.1, 4.4 and 4.8 of the SmPC have been updated, and Annex II (additional risk minimisation measures) and the Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II, labelling and Package Leaflet. An updated RMP (version 18) was provided as part of the application. The provision of studies STEP and PACE addresses MEA 001.4."

The Committee discussed the issues identified in this application, mainly concerning the difference in effect of Qutenza between patients with and without diabetes as well as the general clinical trial set up.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Rebetol (EMEA/H/C/000246/II/0074), (ribavirin), MAH: Merck Sharp & Dohme Limited, Rapporteur: Joseph Emmerich, "Change of the indication of Rebetol to reflect that ribavirine is indicated in the treatment of hepatitis C in combination with other medicinal products and remove reference to the peginterferon used (2a or 2b) in line with the PRAC recommendation in the PSUR assessment (EMEA/H/C/PSUSA/000100007/201307). As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.7, 4.8, 4.9 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly."
Request for Supplementary Information adopted on 23.10.2014.
The Committee discussed the issues identified in this application, mainly concerning the posology as well as the wording of the indication. In addition the Environmental Risk Assessment was discussed.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Relistor (EMEA/H/C/000870/II/0030), (methylnaltrexone bromide), MAH: TMC Pharma Services Ltd, Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Valerie Strassmann, "The MAH applied for an extension of the indication for the treatment of opioid induced constipation in adult non cancer pain patients. Consequently, the MAH proposed the update of sections 4.1, 4.2, 4.4 and 5.1 of the SmPC. The Package Leaflet was proposed to be updated in accordance."
Request for Supplementary Information adopted on 20.11.2014, 26.06.2014.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)
The Committee discussed the issues identified in this application, which were related to the extension of data protection and the posology.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Revlimid (EMEA/H/C/000717/II/0079), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Arnaud Batz, "Extension of Indication to add treatment of adult patients with relapsed and/ or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. A revised version of the RMP (version 25.0) was provided as part of this application."
The Committee discussed the issues identified in this application. The discussion was mainly on the wording of the indication with specific focus on the appropriate target population as well as the clinical study design. Furthermore the CHMP was updated on discussions at the PRAC concerning the RMP.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Tamiflu (EMEA/H/C/000402/II/0110/G), (oseltamivir), MAH: Roche Registration Ltd, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Bruno Sepodes, "A group of a type II extension of indication to include the treatment of influenza in infants below one year of age and a type IAIN to add a 3 ml plastic oral dispenser (for the Tamiflu 6mg/ml strength)"
Request for Supplementary Information adopted on 23.10.2014.

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.

Tygacil (EMEA/H/C/000644/II/0092), (tigecycline), MAH: Pfizer Limited, Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Miguel-Angel Macia, "Addition of a new restricted indication in children eight year-old and older. The sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated accordingly. The Package Leaflet is also updated. In addition, an updated RMP is proposed." The Committee discussed the issues identified in this application. The discussion focused on the possibility to extrapolate the indication from adults to the paediatric population and on the need for an Environmental Risk Assessment.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Volibris (EMEA/H/C/000839/II/0041), Orphan, (ambrisentan), MAH: Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Radka Montoniová, PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to include an expanded therapeutic indication for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) In addition, the MAH took the opportunity to update Annex II to reflect a change in the PSUR cycle. The Package leaflet is proposed to be updated accordingly."
The Committee discussed the issues identified in this application, mainly relating to the wording of the indication.
The Committee adopted a Request for Supplementary Information with a specific timetable.
The CHMP adopted the CHMP Similarity Assessment Report

Xalkori (EMEA/H/C/002489/II/0024), (crizotinib), MAH: Pfizer Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Arnaud Batz, "Type II variation to apply for extension of XALKORI indication to the first-line treatment ALK-positive advanced NSCLC (section 4.1 of the SmPC) and to update sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the XALKORI SmPC to include results of the pivotal Study A8081014, a multinational, multicenter, randomized, open-label, Phase 3 study comparing the efficacy and safety of crizotinib to first-line chemotherapy (pemetrexed/cisplatin or pemetrexed/carboplatin) in patients with previously untreated ALK-positive advanced non-squamous NSCLC and updated safety results from Studies A8081001, A8081005 and A8081007. In addition, section 5.1 of the SmPC was revised to include updated overall survival data from Studies A8081001 and A8081005."
The Committee discussed the issues identified in this application, which were related to the study results. The members noted that the choice to administer crizotinib as first line therapy is complex, because the detrimental effect on next line therapies cannot be excluded.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Xultophy (EMEA/H/C/002647/II/0002), (insulin degludec / liraglutide), MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Menno van der Elst, "Extension of indication for Xultophy to include transfer of patients from Glucagon-Like peptide-1 (GLP1) receptor agonist (RA) treatment to Xultophy. Consequently, the MAH proposed the update of sections 4.1, 4.2, 4.4, and 5.1 of the SmPC. The Package Leaflet is updated accordingly."
The Committee discussed the issues identified in this application, mainly relating to some clinical aspects, which required clarification.

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

4.2. Update on on-going type II variation; extension of indications

Vidaza (EMEA/H/C/000978/II/0030), Orphan, (azacitidine), MAH: Celgene Europe Limited, Rapporteur: Pieter de Graeff, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Sabine Straus, "Extension of Indication to add treatment of adult patients aged 65 years or older who are not eligible for HSCT with AML with >30% marrow blasts according to the WHO classification, based on the pivotal phase III study AZA- AML-001. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. A revised RMP version 10.0 was provided as part of the application. The application includes a request for an additional year of market protection for a new indication in accordance with Article 10(1) of Directive 2001/83/EC."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004).
The CHMP adopted the CHMP Similarity Assessment Report.

Kalydeco (EMEA/H/C/002494/II/0027), Orphan, (ivacaftor), MAH: Vertex Pharmaceuticals (U.K.) Ltd., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia, "Extension of indication for Kalydeco to include the treatment of cystic fibrosis in patients aged 18 years and older who have a R117H mutation in the CFTR gene. Consequently, changes are proposed to sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and to the Package Leaflet."
Request for Supplementary Information adopted on 23.10.2014.
The CHMP adopted an updated timetable.

5. Ancillary medicinal substances in medical devices

5.1. Ancillary medicinal substances in medical devices - Opinions / List of outstanding issues / List of Questions

No items

6. Re-examination procedure (new applications) under Article 9(2) of Regulation no 726/2004

No items

7. Re-examination procedure (Type II variations) under Article 16 of Commission Regulation (EC) No 1234/2008 and 9(2) of Regulation (EC) No 726/2004

No items

8. Withdrawal of initial application

Ketoconazole AID-SCFM (EMEA/H/C/003800), Orphan
(Ketoconazole), Applicant: Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare, , Well-established use application (Article 10a of Directive No 2001/83/EC)
The Committee noted the question-and-answer document.

Corluxin (EMEA/H/C/002830), Orphan, (mifepristone), Applicant: FGK Representative Service GmbH, Rapporteur: Patrick Salmon, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Miguel-Angel Macia, (treatment of Cushing's syndrome)
Known active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 20.11.2014.
List of Questions adopted on 20.03.2014.
The Committee noted the letter from the applicant informing of the decision to withdraw the Marketing Authorisation application.

(EMEA/H/D/002831), (insulin-like growth factor 1 segment), , (hard-to-heal wounds, primarily venous leg ulcers)
List of Outstanding Issues adopted on 25.09.2014. List of Questions adopted on 23.01.2014.
See also section 1.1. Pre-authorisation procedure oral explanations
An Oral explanation was held on Wednesday 25 March 2015 at 11.00.
It was agreed that the company will be provided scientific advice.
The Committee adopted the BWP Report.
The Committee noted that the applicant has withdrawn the application.

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

No items

10. Pre-submission issues

Some items in this section are considered commercially confidential or sensitive and therefore not disclosed.
(H0003855), Orphan,(human coagulation factor x), Applicant: Bio Products Laboratory, (Control and Prevention of Bleeding Episodes:
FACTOR X is a blood coagulation factor indicated for control and prevention of bleeding episodes in adults and children (aged 12 years and above) with hereditary factor X deficiency.
Perioperative Management:
FACTOR X is indicated in the perioperative management in adults and children (aged 12 years and above) with hereditary factor X deficiency.),
The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

11. Post-authorisation issues

Some items in this section are considered commercially confidential or sensitive and therefore not disclosed.

BSWP response to letter received from Dr Fuglsang regarding Kinetica software used in BE studies (EMA/108507/2015) The CHMP discussed the BSWP response and concluded that no medically relevant impact could be observed following the assessed studies. The Committee agreed that a response to CMDh should be drafted by BSWP as well as a response letter to Dr Fuglsang.

Rienso (EMEA/H/C/002215) (Ferumoxytol), MAH: Takeda Pharma A/S, Rapporteur: Harald Enzmann, Co-Rapporteur: Romaldas Mačiulaitis, (treatment of iron deficiency with chronic kidney disease (CKD)), New active substance (Article 8(3) of Directive No 2001/83/EC).
The CHMP noted the letter from the MAH dated 24 February 2015 notifying of the decision to withdraw the Marketing Authorisation.
The CHMP agreed that there was no need for specific communication.

Ad-hoc Influenza Working Group: EU Strain selection for the Influenza Vaccines for the Season 2015/2016,
The CHMP adopted the EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2015/2016.
The report from the Ad Hoc Influenza working group to the BWP was adopted.

Xarelto (EMEA/H/C/000944/II/0038), (rivaroxaban), MAH: Bayer Pharma AG, Rapporteur: Kristina Dunder, , "Submission of study results (EINSTEIN cancer analysis) and literature data on the efficacy and safety of rivaroxaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEp) in patients with active cancer as requested by CHMP in December 2014 during variation II-33."
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 members were in agreement with the CHMP recommendation.

Simponi (EMEA/H/C/000992/II/0063), (golimumab), MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the SmPC sections 4.2 and 5.1 in order to reflect the data from a multicentre, placebo-controlled, double-blind, randomised-withdrawal, parallel group study (GO KIDS) in children (2 to 17 years of age) with active polyarticular juvenile idiopathic arthritis (pJIA). The Package leaflet is proposed to be updated accordingly. This procedure includes also an update to the RMP."
The Committee discussed the issues identified in this application
The Committee adopted a Request for Supplementary Information with a specific timetable.

Rotarix (EMEA/H/C/000639/II/0062), (human rotavirus, live attenuated), MAH: GlaxoSmithKline Biologicals S.A., Rapporteur: Daniel Brasseur, PRAC Rapporteur: Jean-Michel Dogné, Procedure Manager: Malgorzata Zienowicz, EPL: Manuela Mura, "To submit the final report of genetic stability study EPI-ROTA-014 VS BE – 112560 that addresses the Post-Approval Measure ME2 005.2 in which the MAH commits to monitor for the potential occurrence of genetic drifts and shifts in the vaccine strain in post-marketing settings."
Request for Supplementary Information adopted on 24.07.2014, 20.03.2014. **PRAC led variation**

The Committee discussed the issues identified in this application, which were related to the genetic drifts (point mutations) in the vaccine strain and the occurrence of genetic shifts (re-assortments) between vaccine and naturally circulating wild-type strains in the population.
The Committee adopted a Request for Supplementary Information with a specific timetable.
The CHMP agreed to the List of Questions adopted at the PRAC to be sent to the VWP.

Yondelis (EMEA/H/C/000773/S/0042), Orphan, (trabectedin), MAH: Pharma Mar, S.A., Rapporteur: Christian Schneider, PRAC Rapporteur: Torbjorn Callreus,
The Committee discussed the issues identified in this application, which were related to converting the exceptional marketing authorisation to a full MAA as the Specific obligation was considered fulfilled.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive opinion to switch to full 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.

Insuman (EMEA/H/C/000201) (Insulin Human), MAH: Sanofi-aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Pieter de Graeff, (treatment of diabetes mellitus), Complete application (stand-alone) - Council Directive 81/851/EEC
See also section 1.3. Post-authorisation procedure oral explanation
After discussion the CHMP agreed that no Oral explanation was needed at this time, but kept open to arrange a TC with the MAH later during the CHMP Plenary.
The Committee agreed the wording of the DHPC.

Buccolam (EMEA/H/C/002267)
(Midazolam Hydrochloride), MAH: ViroPharma SPRL, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey,(treatment of prolonged, acute, convulsive seizures in in children (aged below 18 years)).

12. The CHMP adopted the closing report on the supply shortage. Referral procedures

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

No items

12.2. Requests for CHMP Opinion under Article 5(3) and 57 (1)p of Regulation (EC) No 726/2004

No items

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

No items

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

Merisone 50 mg and 150 mg film coated tablets and MYOSON 50 mg and 150 mg film coated tablet (EMEA/H/A-29/1411)

(tolperisone)

Applicant /MAH: Meditop Pharmaceutical Co.Ltd.

Rapporteur: Agnes Gyurasics , Co-Rapporteur: Johann Lodewijk Hillege, RMS: HU, CMS: DE, NL, BE, LU, Mutual recognition procedures: HU/H/0373/001-002/MR and HU/H/0377/001-002/MR

Scope: Lack of bioequivalence studies to evaluate the food effect.

List of Questions adopted 22.01.2015.

The Committee discussed the available results from fasting state bioequivalence studies and whether the formulation may have an effect on bioequivalence in the fed status.

The CHMP adopted the PKWP response to CHMP question on Article 29(4) referral for Merisone and Myoson.

Iogol and associated names soft capsules, 25 / 50 mg (EMEA/H/A-29/1414)

(diclofenac epolamine); Applicant: Regiomedica GmbH, RMS: DE, CMS: AT, BE, CZ, EL, ES, HU, IT, PL, SK, UK, Decentralised procedure number: DE/H/3633/002-003/DC

Scope: Disagreements regarding the demonstration of bioequivalence with the reference product

The members noted the letter from BfArM in Germany dated 6 March 2015 notifying of an official referral under Article 29 (4) and its grounds.

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

The CHMP adopted a List of Questions with a specific timetable.

Notification: 06.03.2015; Start of procedure (CHMP) and adoption of list of questions: 26.03.2015; Submission of responses: 14.05.2015; Re-start of the procedure: 28.05.2015; Rapporteur and co-rapporteur assessment reports circulated to CHMP: 10.06.2015; Comments: 15.06.2015; List of outstanding issues/ CHMP opinion: June 2015 CHMP

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

Ikorel / Dancor and associated names (EMEA/H/A-30/1380)

(nicorandil), Sanofi-Aventis group of companies and associated companies / Merck group of companies and associated companies, Rapporteur: Joseph Emmerich, Co-Rapporteur: Pieter de Graeff,

Scope: Ikorel / Dancor was included in the list of products for SmPC harmonisation, drawn up by the CMDh, in accordance with Article 30(2) of Directive 2001/83/EC. List of Outstanding Issues adopted on 25.09.2014 and 22.01.2015

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

The CHMP adopted an opinion by consensus recommending changes to the SmPCs, labelling and package leaflets. The assessment report was adopted.

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

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

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

Rapporteur: Martina Weise, Co-Rapporteur: Ivana Mikacic,

Scope: 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).
The CHMP adopted a List of Outstanding Issues with a specific timetable.
List of outstanding issues (LoOI): March 2015 CHMP; Responses to LoOI: 01.06.2015; Restart of the procedure: 23.06.2015; Assessment report: 08.07.2015; Comments from CHMP: 13.07.2015; List of outstanding issues 2 or CHMP opinion: July 2015 CHMP

Haldol decanoate and associated names (EMEA/H/A-30/1405) (haloperidol) Janssen-Cilag Group of companies and associated companies
Rapporteur: Martina Weise, Co-Rapporteur: Ivana Mikacic,
Scope: 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).
The CHMP adopted a List of Outstanding Issues with a specific timetable.
List of outstanding issues (LoOI): March 2015 CHMP; Responses to LoOI: 01.06.2015; Restart of the procedure: 23.06.2015; Assessment report: 08.07.2015; Comments from CHMP: 13.07.2015; List of outstanding issues 2 or CHMP opinion: July 2015 CHMP

Novantrone and associated names (EMEA/H/A-30/1399) (mitoxantrone), MEDA group of companies and associated companies.
Rapporteur: Pieter de Graeff, Co-Rapporteur: Robert Hemmings,
Scope: Harmonisation exercise for Novantrone and associated names.
The CHMP adopted a List of Outstanding Issues with a specific timetable.
List of outstanding issues: March 2015 CHMP; Submission of responses: 27.04.2015; Re-start of the procedure 26.05.2015; Rapporteur/co-rapporteur assessment reports circulated to CHMP: 10.06.2015 Comments: 15.06.2015; List of outstanding issues/CHMP opinion: June 2015 CHMP

Amoxil and associated names (EMEA/H/A-30/1372)
(amoxicillin), MAH: GlaxoSmithKline, Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro,
Scope: Harmonisation of the national summary of product characteristics, labelling and package leaflet.
List of Questions adopted on 25.07.2013. List of Outstanding Issues adopted 23.10.2014, 25.04.2014.
The Committee adopted a revised assessment timetable for the responses to the 3rd List of Outstanding Issues adopted on 26 February 2015:
Responses: 27 April 2015; Restart of the procedure: 26 May 2015; Assessment report: 10 June 2015 Comments from CHMP: 15 June 2015; Forth list of outstanding issues or CHMP opinion: June 2015 CHMP

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

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097)
Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff, ,
The CHMP noted the request for an extension to the deadline to the responses to the CHMP request dated 12 February 2015 and the reasons thereof stated.
The CHMP agreed to grant a four weeks extension of the initial deadline.

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

GVK Biosciences (EMEA/H/A-31/1408) Rapporteur: Harald Enzmann, Co-Rapporteur: Christian Schneider.
Article 31 procedure triggered by the European Commission concerning GVK Biosciences Private Limited (GVK Bio), Swarna Jayanthi commercial complex, Ameerpet, Hyderabad 500 038, India following critical GCP deficiencies reported during an inspection performed by the ANSM (Agency for Medicines and Health Products Safety, France) on 19-23 May 2014. Opinion adopted on 22.01.2015. Hubert Leufkens (interest level 1) was appointed as the Re-examination Rapporteur and Karsten Bruins Slot (interest level 1) as the Re-examination Co-Rapporteur on 12 March 2015.
Post meeting note: The Committee adopted the timetable for the re-examination procedure via written procedure on 31 March 2015 after receipt of the detailed grounds.
Re-examination - Receipt of detailed grounds from MAHs by: 30.03.2015; Re-examination - Start of re-examination procedure: 31.03.2015; Re-examination – Rapporteur assessment report and co-rapporteur assessment report circulated to CHMP: 27.04.2015; Re-examination – comments: 06.05.2015; Re-examination - Joint Assessment Report: 12.05.2015; Re-examination - Oral explanation/CHMP final opinion: May 2015 CHMP

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

No items

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

No items

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

No items

12.11. 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

13. Pharmacovigilance issues

Summary of recommendations and advice of PRAC meeting held on 9-12 March 2015: **For information**	The Committee noted the report. The members noted the Summary of recommendations and advices of the PRAC meeting.
List of Union Reference Dates and frequency of	The EURD list was adopted.

submission of Periodic Safety Update Reports (EURD list) for March 2015: **For adoption**	
Early Notification System: March 2015 Early Notification System on Envisaged CHMP Recommendations for Regulatory Action (based on Identified Safety Concerns) Accompanied by Communication to the General Public: **for information**	See individual items
Gilenya (EMEA/H/C/002202) (Fingolimod Hydrochloride), MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, (treatment of multiple sclerosis), New active substance (Article 8(3) of Directive No 2001/83/EC).Signal of occurrence of one case of progressive multifocal leukoencephalopathy (PML) without prior natalizumab use DHPC: **For discussion**	Note: The PRAC proposed a DHPC and a potential SAG consultation, with LOQs sent to the company to respond in 30 days. The CHMP adopted the DHPC letter and communication plan.

14. Inspections

14.1. GMP inspections

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

14.2. GCP inspections

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

Risk Assessment Template • Background note for March CHMP: **For discussion** • Explanatory Notes for Pilot Procedure: **For adoption**

14.3. Pharmacovigilance inspections

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

14.4. GLP inspections

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

15. Innovation Task Force

15.1. Minutes of Innovation Task Force: For information

15.2. Briefing meetings (Innovation Task Force)

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

15.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004 of the European Parliament and of the Council

Request from EDQM for EMA scientific Opinion under procedure Art. 57 (1)J of Regulation (EC) No 726/2004 • CHMP scientific opinion: **For adoption**	The CHMP adopted the opinion.
Request from DG Internal Market, Industry, Entrepreneurship and SME's, Unit I/4 (ex-SANCO B2) under procedure Art. 57 (1) of Regulation (EC) No 726/2004 for EMA scientific Opinion • Final CHMP scientific opinion: **Adopted by written procedure**	The CHMP noted the opinion adopted via written procedure.

15.4. Nanomedicines activities

12th TC of the international nanomedicines working group: **For information**	The CHMP noted the update from the 12th TC of the international nanomedicines working group. Harald Enzmann was appointed as CHMP sponsor to be involved in this working group.

16. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 9-12 march 2015. Table of conclusions: **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.*

17. Satellite Groups

17.1. Coordination Group for Mutual Recognition and Decentralised Procedures

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 23-25 march 2015: **For information**	The CHMP noted the report.
CMDh question to CHMP (PKWP) regarding potential risk of longer half-life of acitretin, • PKWP response: **For adoption**	Postponed to April CHMP
CMDh question to CHMP (BSWP) dated 10 March 2015 regarding bioequivalence study used in aripiprazole generic application procedures • BSWP response: **For adoption**	The CHMP adopted the BSWP response.

18. Other Committees

18.1. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 17-19 March 2015: **For information**	To be sent in the Post-mail.
COMP input on the Revision of the 2003 Communication on Orphan Medicinal Products: **For information**	The COMP has been asked by the EC to assist the EC with the revision of the 2003 Commission Communication on Regulation (EC) No 141/2000 on orphan medicinal products (2003/C 178/02). The COMP is requested to provide observations on significant benefit, the procedure for designation, re-evaluation and removal of the orphan designation from the Community Register, Orphan MAs, Market exclusivity and similarity. Comments are expected by mid April 2015.

18.2. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 9-12 March 2015: **For information**	To be sent in the Post-mail.

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at March 2015 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on	The CHMP noted the report.

18-20 March 2015: **For information**	

18.4. Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 19-20 March 2015: **For information**	The CHMP noted the Table of Decision.

19. Invented name issues

NA

20. Any other business

Revision of the Ph. Eur. Monograph on Human Plasma (pooled and treated for virus inactivation) (1646) 'S/D Plasma': **For adoption and transmission to CMDh** • Report from BWP drafting group (EMA/CHMP/BWP/102099/2015)	The CHMP adopted the Report from BWP drafting group.
Update on activities related to revised RMP Assessment process in 2015 • Implementation of the revised RMP assessment process: **For discussion**	The CHMP noted the update on the activities related to revised RMP Assessment process in 2015 Comments on the revised RMP process should be sent by 10 April 2015.
EU Network Training Centre - website containing the first catalogue of trainings accessible to the entire Network (http://euntc.eudra.org/index.html)	The CHMP was informed about the European central platform for exchange of scientific and regulatory training information across the European Medicines Regulatory Network. The aim is to promote harmonisation of standards for assessment and to foster collaboration, sharing of best practices, and lessons learned across the Network. Feedback on the training platform is welcomed in order to further improve the website. Any questions can be sent to networktraining@ema.europa.eu The CHMP members welcomed this new initiative.
Agenda of the Strategic Review & Learning CHMP/CAT meeting under Latvian EU presidency to be held in Ljubljana, Slovenia, from 26 - 28 May, 2015: **For information**	The CHMP agreed to the agenda.
CHMP 2015 work plan (EMA/394100/2014)**: For adoption**	The CHMP adopted the CHMP 2015 work plan.
Peer Review: Best Practice (EMA/742633/2014)**:**	The CHMP adopted the best practice guide on

For adoption	peer review. It was proposed to perform a compliance check after 6 months. The best way to distribute the document will be considered by EMA. The proposal was made to include the guide in the invitations to the peer reviewer TCs.
Guideline on clinical investigation of medicinal products for the treatment of Multiple Sclerosis (EMA/CHMP/771815/2011): **For adoption** • Overview of external comments received (EMA/CHMP/154617/2015): **For information**	The guideline is intended to provide guidance for the evaluation of drugs for the treatment of multiple sclerosis. The guideline primarily focuses on treatments aimed to modify disease progression. In addition some remarks are made concerning the treatment of relapses, repair and restoration of functioning and symptomatic improvement. Products aimed to treat complications of the neurological dysfunction are out of the scope of this guidance. The CHMP adopted the guideline on MS and noted the overview of comments.
Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products (EMA/CAT/80183/2014): **For adoption for external consultation until end of July 2015**	The guideline defines scientific principles and provides guidance for the development and evaluation of gene therapy medicinal products (GTMP) intended for use in humans and presented for marketing authorisation. Its focus is on the quality, safety and efficacy requirements of GTMP. The CHMP adopted the Guideline for public consultation.
Guideline on clinical investigation of medicinal products other than NSAIDs for treatment of rheumatoid arthritis: **For 2nd release for public consultation**	The CHMP adopted the Guideline for public consultation.
European Medicines Agency/European Generic medicines Association joint workshop on the impact of the revised EMA guideline on the pharmacokinetic and clinical evaluation of modified-release dosage forms: **For information**	The Committee noted the joint workshop.
Proposal for a pre-marketing risk-based model for medicinal product testing – Pilot procedure: **For adoption**	The CHMP were informed about the pilot procedure and risk-assessment template tool. The procedure foresees that the assessors complete the risk-assessment template by day 80. New applications between July and December 2015 will be validated. A review of the risk-based model will be performed in 2016 with a report to HMA on the outcome of this plot phase expected in October 2016. Further clarification on the scope as well as on the implications of workload were requested by the members. The members were

	asked further look at the proposal. Sol Ruiz and Jean-Louis Robert were appointed CHMP sponsors. Further discussion expected at the April Plenary.
Update on Review and Reconnect process on Referrals	The updated process would benefit from earlier dialogue between national competent authorities and EMA on defining clear scope and establishing guidance on the best use of regulatory tools for handling an issue/procedure. Best use of network resources and support to (co-)rapporteurs and assessors will be provided together with involvement of a multidisciplinary team at EMA. Implementation is prioritised for pharmacovigilance (PhV) referrals which is now completed. The proposals for implementation include revised templates and process improvements such as strengthening (pre-) draft notification phase with early notification of the MAHs concerned, earlier Rapporteurship appointment for PhV referrals, preparation of the start of procedure, timelines, and a strengthening assessment phase. Training via webinar will be provided in April 2015.

21. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 23-26 March 2015 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	Full involvement	
Andrea Laslop	Member	Austria	Full involvement	
Milena Stain	Alternate	Austria	Full involvement	
Daniel Brasseur	Member	Belgium	Full involvement	
Bart Van der Schueren	Alternate	Belgium	Full involvement	
Mila Vlaskovska	Member	Bulgaria	Full involvement	
Ana Dugonjić	Alternate	Croatia	Full involvement	
Panayiotis Triantafyllis	Member	Cyprus	Full involvement	
Radka Montoniová	Alternate	Czech Republic	Full involvement	
Jens Heisterberg	Member	Denmark	Full involvement	
Christian Schneider	Alternate	Denmark	Full involvement	
Outi Mäki-Ikola	Member	Finland	Full involvement	
Tuomo Lapveteläinen	Alternate	Finland	Full involvement	
Pierre Demolis	Member (Vice-Chair)	France	Full involvement	
Joseph Emmerich	Alternate	France	Full involvement	
Harald Enzmann	Member	Germany	Full involvement	
Martina Weise	Alternate	Germany	Full involvement Connected via TC	
Dimitrios Kouvelas	Member	Greece	Full involvement	
George Aislaitner	Alternate	Greece	Full involvement	
Agnes Gyurasics	Member	Hungary	Full involvement	
Melinda Sobor	Alternate	Hungary	Full involvement	
Kolbeinn Gudmundsson	Member	Iceland	Full involvement	
David Lyons	Member	Ireland	Full involvement	
Patrick Salmon	Alternate	Ireland	Full involvement	
Daniela Melchiorri	Member	Italy	Full involvement	
Natalja Karpova	Alternate	Latvia	Full involvement	
Romaldas Mačiulaitis	Member	Lithuania	Full involvement	
John Joseph Borg	Member	Malta	Full involvement	
Pieter de Graeff	Member	Netherlands	Full involvement	
Johann Lodewijk Hillege	Alternate	Netherlands	Full involvement	
Karsten Bruins Slot	Member	Norway	Full involvement	
Piotr Fiedor	Member	Poland	Full involvement	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bruno Sepodes	Member	Portugal	Full involvement	
Dinah Duarte	Alternate	Portugal	Full involvement	
Nela Vilceanu	Member	Romania	Full involvement	
Jan Mazag	Member	Slovakia	Full involvement	
Stanislav Primožič	Member	Slovenia	Full involvement	
Concepcion Prieto Yerro	Member	Spain	Full involvement	
Arantxa Sancho-Lopez	Alternate	Spain	Full involvement	
Kristina Dunder	Member	Sweden	Full involvement	
Filip Josephson	Alternate	Sweden	Full involvement	
Greg Markey	Member	United Kingdom	Full involvement	
Rafe Suvarna	Alternate	United Kingdom	Full involvement	
Robert James Hemmings	Co-opted member	United Kingdom	Full involvement	
Hubert Leufkens	Co-opted member	Netherlands	Full involvement	
Jan Mueller-Berghaus	Co-opted member	Germany	Full involvement	
Jean-Louis Robert	Co-opted member	Luxembourg	Full involvement	
Sol Ruiz	Co-opted member	Spain	Full involvement	
Theis Moeslund Jensen	Expert - in person*	Denmark	Full involvement	
Kenneth Skov	Expert - in person*	Denmark	Full involvement	
Laszlo Tothfalusi	Expert - in person*	Hungary	Full involvement	
Jana Schweigertova	Expert - in person*	Slovakia	Full involvement	
Luisa Becedas	Expert - in person*	Sweden	Full involvement	
Ingela Hägglund	Expert - in person*	Sweden	Full involvement	
Anders Lindblom	Expert - in person*	Sweden	Full involvement	
Patricia Diaz Ramos	Expert - in person*	Spain	Full involvement	
Jorge Camarero Jimenez	Expert - in person*	Spain	Full involvement	
Valerie Lescrainier	Expert - in person*	Belgium	Full involvement	
Karolina Kwiatek	Expert - in person*	Netherlands	Full involvement	
Sabine Mayrhofer	Expert - in person*	Germany	Full involvement	
Marc Martin	Expert - in person*	France	Full involvement	
Sujata Sengupta	Expert - in	Netherlands	Full involvement	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	person*			
Joost Romme	Expert - in person*	Netherlands	Full involvement	
Tamar Wohlfarth	Expert - in person*	Netherlands	Full involvement	
Elspeth Gray	Expert - in person*	United Kingdom	Full involvement	
James Mcblane	Expert - in person*	United Kingdom	Full involvement	
John Johnston	Expert - in person*	United Kingdom	Full involvement	
Nithyanandan Nagercoil	Expert - in person*	United Kingdom	Full involvement	
Dirk Mentzer	Expert - via telephone*	Germany	Full involvement	
Jan Welink	Expert - via telephone*	Netherlands	Full involvement	
Esther Nijholt-Faber	Expert - via telephone*	Netherlands	Full involvement	
Peter Caspers	Expert - via telephone*	Netherlands	Full involvement	
Andre Elferink	Expert - via telephone*	Netherlands	Full involvement	
Marco van Teijlingen	Expert - via telephone*	Netherlands	Full involvement	
Anita Volkers	Expert - via telephone*	Netherlands	Full involvement	
Leon van Aerts	Expert - via telephone*	Netherlands	Full involvement	
Leon Bongers	Expert - via telephone*	Netherlands	Full involvement	
Valeria Raia	Expert - via telephone*	Italy	Full involvement	
Michael Pfleiderer	Expert - via telephone*	Germany	Full involvement	
Lucas Rems	Expert - via telephone*	Germany	Full involvement	
Christine Greiner	Expert - via telephone*	Germany	Full involvement	
Janet Schriever	Expert - via telephone*	Germany	Full involvement	
Henrike Potthast	Expert - via telephone*	Germany	Full involvement	
Elmer Schabel	Expert - via telephone*	Germany	Full involvement	
Benoy Daniel	Expert - via telephone*	United Kingdom	Full involvement	
David Wright	Expert - via telephone*	United Kingdom	Full involvement	
Marie-Christine Bielsky	Expert - via telephone*	United Kingdom	Full involvement	
Jens Ersbøll	Expert - via telephone*	Denmark	Full involvement	
Una Riekstina	Expert - via	Latvia	Full involvement	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	telephone*			
A 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.

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 1)*

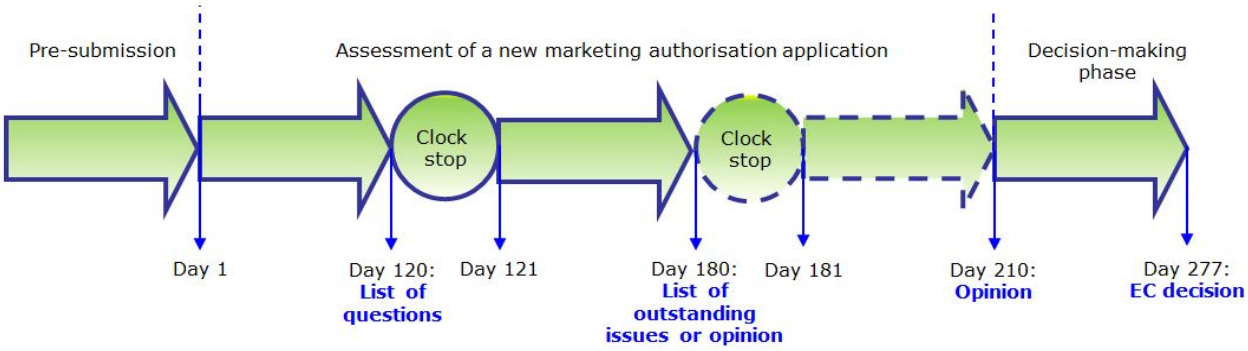
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section 12) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

New applications *(section 2)*

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

Section 2.1 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 2.2 (**Day 180 List of outstanding issues**) and 2.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 2.4, **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 2.5, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 3)*

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 4)*

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 3. 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 5)*

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 6)*

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 *(section 7)*

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 8)*

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 9)*

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 10)*

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 11)*

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 12)*

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 13)*

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 14)*

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 15)*

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 16)*

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 17)*

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 18)*

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.