22 May 2014
EMA/CHMP/263230/2014
Procedure Management and Business Support Division

Committee for Medicinal Products for Human Use (CHMP)

Final Minutes of meeting held on 22-25 April 2014

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

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).

Disclaimers

Some of the information contained in these minutes is considered commercially confidential or sensitive 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 certain aspects of them are considered confidential. Additional details on some of these procedures is published in the CHMP meeting highlights once the procedures are finalised and start of referrals are also available. For orphan medicinal products and products that received an opinion at this meeting, the applicant details are published as this information is already publicly available. The same applies for the product name for products that received an opinion at this meeting. Documents mentioned in these minutes cannot be released at present as they are currently in draft format or are classified as confidential. They will become public when adopted in their final form or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006). Of note, this set of minutes 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.

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AGENDA (EMA/CHMP/169875/2014) and Annex to CHMP agenda of the CHMP plenary session to be held 22-25 April 2014	The agenda and annex were adopted with amendments.
TIMESCHEDULE of the CHMP plenary session to be held 22-25 April 2014	The timeschedule was adopted.
MINUTES (EMA/CHMP/189248/2014) of the CHMP plenary session held 17-20 March 2014	The Minutes of the CHMP plenary session held 17-20 March 2014 were adopted.
MEMBERSHIP ANNOUNCEMENT	The Committee welcomed Filip Josephson as new alternate member from Sweden and George Aislaitner as new alternate member from Greece.
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 22-25 April 2014	The pre-meeting list was noted. See also 21 List of participants
CONFLICT OF INTERESTS	In accordance with the Agency's revised policy and procedure on the handling of conflicts of interests, participants in this meeting were asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests). Discussions, deliberations and voting took place in full respect of the restricted involvement of Scientific Committee members and, where relevant, experts attending the plenary meeting, as announced by the Scientific Committee Secretariat at the start of meeting (see end of document). All decisions taken at this meeting were made in presence of a quorum of members – i.e. 22 or more members were present in the room.
Draft Agenda of CHMP meeting to be held on 19-22 May 2014 CHMP meeting: **for information**	The draft agenda was noted.

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1 ORAL EXPLANATIONS

1.1 Pre-authorisation Procedure Oral Explanations

(EMEA/H/C/002633), Orphan, (tobramycin), Applicant: PARI Pharma GmbH, (treatment of chronic pulmonary infection)
List of Outstanding Issues adopted in October 2013 and March 2014.
List of Questions adopted in February 2013.
The CHMP agreed that no Oral Explanation was needed at this time.
See also 2.2 List of Outstanding Issues - New full applications

1.2 Re-examination Procedure Oral Explanation

No items

1.3 Post-authorisation Procedure Oral explanation

Pradaxa (EMEA/H/C/000829/II/0048/G) (dabigatran etexilate mesilate), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis,
"Extension of indications to two new related indications:
• Treatment of acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and prevention of related death (a VTEt)
• Prevention of recurrent deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and related

death (s VTEp)"
Request for Supplementary Information adopted in September 2013.
An Oral explanation was held on Tuesday 22 April 2014 at 16.00.
See also 4.1 Type II variations – extension of indications; Opinions

1.4 Referral Procedures Oral Explanations

Caustinerf arsenical® and Yranicid arsenical® and associated names, paste for dental use (oral formulations) (EMEA/H/A-31/1382) (lidocaine, ephedrine, arsenic trioxide), SEPTODONT and A.T.O. ZIZINE, Rapporteur: Alar Irs, Co-Rapporteur: Joseph Emmerich,
Article 31 triggered by the ANSM for ephedrine hydrochloride, lidocaine and arsenous anhydride containing medicinal products for topical use, based on genotoxicity data.
List of Outstanding Issues adopted in February 2014.
An Oral explanation was held on Wednesday 23 April 2014 at 12.00.
See also 12.6 Community Interests- Referral under Article 31

Estradiol (topical use) (EMEA/H/A-31/1336)
Re-examination Rapporteur: Arantxa Sancho, Re-examination Co-Rapporteur: Milena Stain, Review of the benefit-risk balance of medicinal products containing estradiol for intravaginal administration and administration on the skin of the vulva due to observed high systemic absorption which may lead to safety issues.
The CHMP agreed that an oral explanation was not needed at this time.
See also 12.7 Re-examination Procedure under Article 32(4) of Directive 2001/83/EC

2 NEW APPLICATIONS

2.1 Opinions – New full applications

Mekinist (EMEA/H/C/002643), (trametinib), Applicant: Glaxo Group Ltd, (treatment of unresectable or metastatic melanoma with a BRAF V600 mutation)
Oral explanation held in March 2014.
List of Outstanding Issues adopted in November 2013.
List of Questions adopted in June 2013.
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.

2.2 Day 180 List of outstanding issues – New full applications

(EMEA/H/C/002272), (clopidogrel / acetylsalicylic acid), (indicated for the prevention of atherothrombotic events)
List of Questions adopted in December 2013.
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.

(EMEA/H/C/002799), Orphan, (obinutuzumab), Applicant: Roche Registration Ltd (treatment of chronic lymphocytic leukaemia)
List of Questions adopted in September 2013.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a List of Outstanding Issues with a specific timetable.
The Committee adopted the BWP report.

(EMEA/H/C/003698), (brinzolamide / brimonidine tartrate), (treatment of open-angle glaucoma or ocular hypertension)
List of Questions adopted in November 2013.
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.

(EMEA/H/C/002633), Orphan, (tobramycin), Applicant: PARI Pharma GmbH, (treatment of chronic pulmonary infection)
List of Outstanding Issues adopted in October 2013 and March 2014. List of Questions adopted in February 2013.
See also 1.1 Pre-authorisation Procedure Oral Explanations
The members were reminded of previous discussions and the legal framework surrounding this procedure.
The CHMP agreed that no Oral Explanation was needed at this time.
The Committee adopted a List of Outstanding Issues with a specific timetable.

2.3 Day 120 List of Questions – New full applications

(EMEA/H/C/003768) (daclatasvir), (treatment of chronic hepatitis C virus (HCV))
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/002772) Orphan (dasiprotimut-t), Applicant: Biovest Europe Ltd, (treatment of non-Hodgkin's lymphoma)
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 Committee adopted the BWP report.

(EMEA/H/C/003773) (cangrelor), (percutaneous coronary intervention (PCI) (reduction of thrombotic cardiovascular events (including stent thrombosis) in adult patients with coronary artery disease undergoing PCI. Also indicated to maintain P2Y12 inhibition in adult patients with acute coronary syndromes or in patients with stents who are at increased risk for thrombotic events (such as stent thrombosis) when oral P2Y12 therapy is interrupted due to surgery)
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/003750), Orphan, ATMP, (substance to be reviewed) allogenic human heterologous liver cells), (treatment of urea cycle disorders)
The CHMP was informed about discussions at the CAT.
The CHMP agreed to the List of Questions adopted by the CAT at their April 2014 meeting.
The Committee adopted the BWP report.

(EMEA/H/C/002739) (human alpha1-proteinase inhibitor), (treatment to slow the underlying destruction of lung tissue)
The Committee discussed the issues identified in this application.
The CHMP agreed to consult an ad hoc expert group and adopted a List of Questions to this group.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP report.

(EMEA/H/C/002066) (ciclosporin), (treatment of dry eye disease in adult patients with severe keratitis that does not improve despite treatment with tear substitutes)
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/002788), Orphan, (tolvaptan), Applicant: Otsuka Pharmaceutical Europe Ltd, (treatment of autosomal dominant polycystic kidney 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/003800), Orphan (ketoconazole), Applicant: Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare, (treatment of Cushing's syndrome)
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/002789), Orphan (levofloxacin), Applicant: Aptalis Pharma SAS, (indicated for chronic pulmonary infections)
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 CHMP similarity assessment report.

(EMEA/H/C/003746) (apremilast), (treatment of psoriatic arthritis, psoriasis)

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/002396) (safinamide), (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/002661), Orphan (recombinant l-asparaginase), Applicant: medac Gesellschaft fuer klinische Spezialpraeparate mbH, (combination therapy for B/T cell lymphoblastic leukaemia or B/T cell lymphoblastic lymphoma)
The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The CHMP agreed to an additional clock stop to respond to the List of Questions with a specific timetable.
The CHMP adopted the CHMP similarity assessment report.
The Committee adopted the BWP report.

(EMEA/H/C/003787) (tadalafil), (treatment of erectile dysfunction in adult males)
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/002800), Orphan, (dinutuximab), Applicant: United Therapeutics Europe Ltd (treatment of high-risk neuroblastoma)
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 Committee adopted the BWP report.

(EMEA/H/C/002840) (dalbavancin), (treatment of complicated skin and soft tissue infections (cSSTI) in adults when known or suspected to be caused by susceptible strains of Gram-positive bacteria, including the treatment of bacteraemia associated with these infections)
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/002814) (vorapaxar), (indicated for the reduction of atherothrombotic events)
The Committee discussed 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 new applications for Centralised Procedures

(EMEA/H/C/003906), Orphan (ketoconazole), Applicant: Laboratoire HRA Pharma, (treatment of Cushing's syndrome)
The CHMP adopted the CHMP similarity Assessment Report .

(EMEA/H/C/002418), Orphan (Dexamethasone Acetate), LABORATOIRES CTRS - BOULOGNE BILLANCOURT, (treatment of symptomatic multiple myeloma)
List of Outstanding Issues adopted in September 2013 and February 2014.
List of Questions adopted in May 2013.
The CHMP did not agree to the request from the applicant dated 16 April 2014 for an additional extension of clock stop for the submission of responses to Day 120 List of Questions adopted in March 2014, but accepted a shorter clock stop with a specific timetable.

(EMEA/H/C/003771) (Nonacog Gamma), (treatment of haemophilia B)
The CHMP noted the change to the timetable to submit the responses to the LoQ adopted in March.

(EMEA/H/C/002647) (insulin degludec / liraglutide), (treatment of type 2 diabetes mellitus)
List of Outstanding Issues adopted in March 2014.
List of Questions adopted in October 2013.
The CHMP adopted the preliminary List of experts to SAG CVS.

(EMEA/H/C/002548), Orphan (afamelanotide), Applicant: Clinuvel (UK) Limited, (treatment of phototoxicity in adult patients with erythropoietic protoporphyria)
List of Outstanding Issues adopted in March 2013.
List of Questions adopted in July 2012.
The CHMP adopted a list of experts for the ad-hoc expert group meeting.

(EMEA/H/C/002085) (tilmanocept), (used in the delineation and localisation of lymph nodes)
Oral explanation held in March 2014. List of Outstanding Issues adopted in December 2013, October 2013 and March 2014. List of Questions adopted in May 2013.
The CHMP adopted the list of questions to the SAG Oncology.

2.5 Products in the Decision Making Phase

Masican (EMEA/H/C/002670), Orphan (MASITINIB), Applicant: AB Science, Rapporteur: Jens Ersbøll, Co-Rapporteur: Greg Markey, (treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST))Negative Opinion adopted in March 2014.
The Committee addressed the request from the European Commission for clarification in relation to the CHMP Opinion adopted for Masican at its March 2014 meeting.
The revised opinion together with the assessment report was adopted after the CHMP meeting via written procedure.

3 EXTENSION OF MARKETING AUTHORISATION ACCORDING TO ANNEX I OF REG. 1234/2008

3.1 Extension of marketing authorisation according to Annex I of Reg. 1234/2008; Opinions

No items

3.2 Extension of marketing authorisation according to Annex I of Reg. 1234/2008; Day 180 List of outstanding issues

Isentress (EMEA/H/C/000860/X/0044/G)
(raltegravir), MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams, "Grouping of a line extension application to introduce a new pharmaceutical form (100 mg granules for oral suspension) and a type II variation to extend the indication to toddlers and infants from 4 weeks to less than 2 years of age. Consequently, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and separate SmPC is introduced for the new pharmaceutical form. The Package Leaflet and Labelling are updated in accordance. In addition, minor updates are made to SmPC sections 5.1 and 6.1, Labelling and the PL. Furthermore, the product information is brought in line with the latest QRD version 9.3."
List of Questions adopted in December 2013.
The Committee was reminded of the status of this application and its remaining outstanding issues relating to quality aspects for the drug product and clinical aspects.
The Committee adopted List of Outstanding Issues together with a specific timetable.

3.3 Extension of marketing authorisation according to Annex I of Reg. 1234/2008; Day 120 List of Questions

Humalog (EMEA/H/C/000088/X/0125), (insulin lispro), MAH: Eli Lilly Nederland B.V., Rapporteur: Robert James Hemmings, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, "To add a new strength (200 U/ml KwikPen presentation)."
The Committee discussed the issues identified in this application. The members agreed to seek further clarification on some quality related issues especially on the clear labelling of the 200 U/mL strength, as well as on the conduct of some clinical trials.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

Liprolog (EMEA/H/C/000393/X/0092), (insulin lispro), MAH: Eli Lilly Nederland B.V., Informed Consent of Humalog, Rapporteur: Robert James Hemmings, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, "To add a new strength (200 U/ml KwikPen presentation)."
The Committee discussed the issues identified in this application. The members agreed to seek further clarification on some quality related issues especially on the clear labelling of the 200 U/mL strength, as well as on the conduct of some clinical trials.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

Zoledronic acid Teva (EMEA/H/C/002439/X/0008), (zoledronic acid), MAH: Teva Pharma B.V., Generic of Zometa, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PTL: Irene

Garcia Bravo, "Line extension to include a new pharmaceutical form, solution for infusion which has three new presentations."
The Committee discussed the issues identified in this application, mainly relating to the quality part of the dossier as well as the RMP and routine risk minimisation measures as proposed by the PRAC.
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 Reg. 1234/2008

Orfadin (EMEA/H/C/000555/X/0041), Orphan MAH: Swedish Orphan Biovitrum International AB, (nitisinone), Rapporteur: Luca Pani, PRAC Rapporteur: Carmela Macchiarulo, To add an oral suspension 4 mg/ml as additional pharmaceutical form.
The CHMP agreed to the request from the MAH dated 16 April for an additional extension to the clock stop to respond to the List of Questions adopted in December 2013 with a specific timetable.

4 TYPE II VARIATIONS - Extension of indication procedures

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

Gilenya (EMEA/H/C/002202/II/0021), (fingolimod), MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, "Modification of the indication (section 4.1) of Gilenya to extend the patient population to patients with high disease activity despite treatment with at least one disease modifying therapy (DMT). Consequential changes were made in section 4.4 of the SmPC to include safety information relevant to switching from other immunosuppressive or immunomodulatory therapies to Gilenya. The Package Leaflet has been amended accordingly."
Request for Supplementary Information adopted in October 2013 and April 2014.
The Committee discussed the issues identified in this application which mainly related to the wording of the indication.
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 recommendation.
The summary of opinion was circulated for information.

Invega (EMEA/H/C/000746/II/0037), (paliperidone), MAH: Janssen-Cilag International N.V., Rapporteur: Filip Josephson, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue, PRAC Co-Rapporteur: Martin Huber, "Extension of indication to add the treatment of schizophrenia in adolescents 15 years and older. Consequential changes were made in sections 4.2, 4.4, 4.5, 5.1, 5.2 and 5.3 to include efficacy and safety information resulting from the submitted paediatric studies. The Package Leaflet has been amended accordingly. In addition, the list of local representatives in the Package Leaflet has been revised to amend contact details for the representatives of Luxembourg and Belgium."
Request for Supplementary Information adopted in December 2013, June 2013.
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 recommendation.
The summary of opinion was circulated for information.

Javlor (EMEA/H/C/000983/II/0011), (vinflunine ditartrate), MAH: Pierre Fabre Médicament, Rapporteur: Greg Markey, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Julie Williams, "Extension of Indication: in combination with capecitabine for the treatment of adult patients with locally advanced or metastatic breast cancer previously treated with or resistant to an anthracycline and who are taxane resistant."
Request for Supplementary Information adopted in September 2013.
The Committee discussed the issues identified in this application which related to the fact that the effect on PFS was modest and no effect on overall survival or other relevant endpoint had been shown. This does not outweigh the additional toxicity observed therefore, the benefit risk balance is considered to be negative for the claimed indication for the time being.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Kalydeco (EMEA/H/C/002494/II/0009), Orphan, (ivacaftor), MAH: Vertex Pharmaceuticals (U.K.) Ltd., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia, "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC to extend the indication of Kalydeco in the treatment of cystic fibrosis to patients aged 6 years and older who have other gating (class III) mutation in the CFTR gene than G551D. Consequential changes to sections 1 and 4 of the PL."
Request for Supplementary Information adopted in January 2014.
The Committee discussed the issues identified in this application which mainly related to the wording of the indication.
The Committee adopted a 2nd Request for Supplementary Information with a specific timetable.

Nexavar (EMEA/H/C/000690/II/0035), Orphan
MAH: Bayer Pharma AG, (sorafenib), Rapporteur: Filip Josephson, Co-Rapporteur: Dinah Duarte, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of the indication for the treatment of progressive, locally advanced or metastatic, differentiated (papillary/follicular/ Hürthle cell) thyroid carcinoma, refractory to radioactive iodine. The SmPC was revised in order to add warnings on the risk of bleeding, hypocalcaemia and TSH suppression as well as reflect relevant non-clinical and clinical safety and efficacy data in patients with differentiated thyroid carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC have been updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 9.0."Request for Supplementary Information adopted in October 2013
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 recommendation.
The summary of opinion was circulated for information.

Pradaxa (EMEA/H/C/000829/II/0048/G) MAH: Boehringer Ingelheim International GmbH, (Dabigatran Etexilate Mesilate), Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis, "Extension of indications to two new related indications:
• Treatment of acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and prevention of related death (a VTEt)
• Prevention of recurrent deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and related death (s VTEp)"
Request for Supplementary Information adopted in September 2013.
See 1.3. Oral explanation in Post-authorisation Procedure Oral explanation.
An Oral explanation was held on Tuesday 22 April 2014 at 16.00. The MAH presented data mainly concerning the benefit/risk in the prevention indication as well as the posology in patients of high age, patients with moderate renal impairment and patients treated concomitantly with P-gp inhibitors.
After the oral explanation the members discussed the outstanding issues and considered them resolved. Furthermore the CHMP discussed the proposal by the MAH for an observational study and agreed that the possible outcome may not provide sufficiently valuable information. Therefore it was agreed not to request the conduct of the observational study. Some amendments of the SmPC were agreed.
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 recommendation.
The summary of opinion was circulated for information.

Prezista (EMEA/H/C/000707/II/0063), (darunavir), MAH: Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Sabine Straus, "Update of section 4.1 of the SmPC for the 100mg/ml oral suspension and the 400mg, 800mg film-coated tablets with information on the use of darunavir with cobicistat as pharmacokinetic enhancer. Consequential changes have been introduced in the SmPC and the PL of all formulations. Update of the Annex II with a correction to the address of one of the manufacturers responsible for batch release. Update of the PL with the local representatives' contact information for France, Romania, Ireland and Cyprus."
The Committee discussed the issues identified in this application which related to clinical and RMP aspects.
The Committee adopted a Request for Supplementary Information with a specific timetable.
A review of the lack of information for potentially severe interactions with antiplatelets and novel oral anticoagulants with Prezista and all antiretroviral SmPC has been agreed by the Committee. The framework of such initiative will be discussed in the near future.

Prolia (EMEA/H/C/001120/II/0030) (denosumab), Applicant: Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus "The MAH proposes to add the following new therapeutic indication: treatment of osteoporosis in men at increased risk of fracture. As a consequence the MAH proposes to update sections 4.1 and 5.1 of the SmPC. The Package Leaflet has been updated accordingly. In addition, the MAH proposes to make an update to the statement in section 5.1 of the SmPC related to the paediatric plan".
Request for Supplementary Information adopted in November 2013.
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 recommendation.
The summary of opinion was circulated for information.

Rienso (EMEA/H/C/002215/II/0008), (ferumoxytol), MAH: Takeda Pharma A/S, Rapporteur: Harald Enzmann, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Martin Huber, , "Extension of indication: all cause iron deficiency anaemia when oral therapy is ineffective or inappropriate or where there is a need for rapid iron repletion
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were proposed to be updated. The Package Leaflet was proposed to be updated accordingly. The MAH took the opportunity to propose minor editorial changes to the SmPC and to propose the update of the Product Information in line with the latest version of the QRD template (9.0)"
Request for Supplementary Information adopted in October 2013.
The Committee discussed the issues identified in this application. These related to the fact that the long term use of Rienso did not seem to be sufficiently justified. In addition, the fatal cases related to hypersensitivity / non-fatal serious hypersensitivity cases should be related to the last PSUR and reporting rates should be calculated. Finally the MAH is asked to include a warning in order to prevent under dosage in overweight subjects.
The Committee adopted a Request for Supplementary Information with a specific timetable.

RoActemra (EMEA/H/C/000955/II/0032), (tocilizumab), MAH: Roche Registration Ltd, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.1 and 5.1 of the SmPC and consequential changes to section 1 of the Package Leaflet in order to extend the indication to the treatment in combination with methotrexate (MTX) of severe, active and progressive RA in adults not previously treated with MTX. In addition the MAH is taking the opportunity to align the PI with version 9 of the QRD template and to correct some typographical errors throughout the PI."
Request for Supplementary Information adopted in November 2013.
The Committee discussed the issues identified in this application which related to efficacy and risk management plan aspects.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Vfend (EMEA/H/C/000387/II/0097), (voriconazole), MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Sabine Straus, , "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the Vfend SmPC to include information pertaining to the proposed new indication in prophylaxis of invasive fungal infections in high risk hematopoietic stem cell transplant recipients. The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity of this variation to update the SmPC, Annex II and PL in line with the latest QRD template"
Request for Supplementary Information adopted in October 2013.
The CHMP noted the report from the chair of the SAG anti-infective.
The Committee discussed the issues identified in this application which related to benefit/risk of the

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

WS0523
Gardasil-EMEA/H/C/000703/WS0523/0047
Silgard-EMEA/H/C/000732/WS0523/0045
(human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)), MAH: Merck Sharp & Dohme Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Pierre Demolis, "Extension of indication to include prevention of premalignant anal lesions and anal cancer. The Package Leaflet is updated accordingly."
The Committee was reminded that this indication had previously been refused in 2010 mainly due to an expected very limited benefit in the general population with respect to prevention of anal cancer (due to low incidence) that did not outweigh potential safety issues.
The Committee agreed that now efficacy had been demonstrated with regards to prevention of anal cancer as more data concerning duration of protection had been gathered. In addition the safety data was reasurring.
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive Opinion by majority (25 positive out of 28 votes) together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendation.
The divergent position (David Lyons, Pieter de Graeff, Juris Pokrotnieks) was appended to the opinion.
The summary of opinion was circulated for information.

4.2 Update on on-going Type II variation - Extension of indications

Votrient (EMEA/H/C/001141/II/0022) (pazopanib), Applicant: Glaxo Group Ltd, Rapporteur: Jens Ersbøll, Co-Rapporteur: Pieter de Graeff, "Extension of indication for the maintenance treatment of women with stage II-IV ovarian, fallopian tube or primary periotoneal cancer based on the study VEG110655 (AG-OVAR16)."
The CHMP noted the withdrawal of this application.

5 ANCILLARY MEDICINAL SUBSTANCES IN MEDICAL DEVICES

5.1 Opinions/ List of outstanding issues / List of Questions

(EMEA/H/D/002769), (thrombin), (indicated in surgical procedures)
List of Questions adopted in September 2013.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a List of Outstanding Issues with a specific timetable.
The Committee adopted the BWP report.

6 RE-EXAMINATION PROCEDURE (NEW APPLICATIONS) UNDER ARTICLE 9(2) OF REGULATION No 726/2004

Masiviera (EMEA/H/C/002659), Orphan, (masitinib), Applicant: AB Science, (treatment of non resectable locally advanced or metastatic pancreatic cancer)

The CHMP adopted the list of experts to the SAG Oncology meeting to be held on 7th May together with a specific timetable.
Post meeting note: The final list of experts for the SAG Oncology was adopted via written procedure on 2 May 2014.

Nerventra (EMEA/H/C/002546) Applicant: Teva Pharma GmbH, (laquinimod), (treatment of multiple sclerosis)
Negative Opinion adopted in January 2014.
The CHMP adopted a list of questions to the SAG Neurology together with a preliminary list of experts to this SAG meeting to be held on 8th May 2014.
The CHMP adopted a list of questions to the PRAC as well as a list of questions to the SWP.

Translarna (EMEA/H/C/002720), Orphan, Applicant: PTC Therapeutics Limited, (ataluren), Re-examination (treatment of Duchenne muscular dystrophy)

Reasanz (EMEA/H/C/002817) (serelaxin), Applicant: Novartis Europharm Ltd, (treatment of acute heart failure)
Opinion adopted in January 2014.
The CHMP adopted the list of experts for the SAG CVS.
The List of Questions to the SAG will be adopted after the meeting via written procedure.

7 RE-EXAMINATION PROCEDURE (TYPE II VARIATIONS) UNDER ARTICLE 6(9) OF COMMISSION REGULATION EC NO 1085/2003

No items

8 WITHDRAWAL OF APPLICATION

DITELOS (EMEA/H/C/002593) (colecalciferol, strontium ranelate), Les Laboratoires Servier, (treatment of osteoporosis)
The Committee noted the letter from the applicant dated 17 March 2014 informing of the decision to withdraw the MAA.

ISSARLOS (EMEA/H/C/002756) (colecalciferol, strontium ranelate), Les Laboratoires Servier, (treatment of osteoporosis)
See Ditelos (EMEA/H/C/002593)

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.

(H0003839) (veruprevir (ABT-450), ritonavir, ombitasvir (ABT-267)), (treatment of genotype 1 and 4 chronic hepatitis C),
The CHMP agreed to the accelerated assessment request and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

(H0003837), dasabuvir (ABT-333) (treatment of genotype 1 chronic hepatitis C),
The CHMP agreed to the accelerated assessment request and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

(H0003821), Orphan, (nintedanib) (Maintenance treatment of idiopathic pulmonary fibrosis (IPF))
The CHMP agreed to the accelerated assessment request 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.

Herceptin (EMEA/H/C/000278) (trastuzumab), MAH: Roche Registration Ltd, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Greg Markey, (treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)), Falsification of Herceptin 150 mg powder for concentrate for solution for infusion.
The CHMP was informed about cases of falsification of Herceptin and noted the DHPC letter and the EMA press release. The CHMP was also informed about the Minutes of the Incident Network Review teleconference that had taken place the week before CHMP.

Alimta (EMEA/H/C/000564) (pemetrexed), MAH: Eli Lilly Nederland B.V., Rapporteur: Pierre Demolis, Co-Rapporteur: Harald Enzmann, (treatment of malignant pleural mesothelioma and non-small cell lung cancer)
The CHMP was informed about cases of falsification of Alimta.

Remicade (EMEA/H/C/000240) (infliximab), MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, (treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis)
The CHMP was informed about cases of falsification of Remicade.

Pradaxa (EMEA/H/C/000829/ LEG 042)
(Dabigatran Etexilate Mesilate), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jens

Heisterberg, Co-Rapporteur: Pierre Demolis, (prevention of venous thromboembolic events).
The Committee adopted a Request for Supplementary Information with a specific timetable.

SonoVue (EMEA/H/C/000303/II/0025), (sulfur hexafluoride), MAH: Bracco International B.V., Rapporteur: Pierre Demolis, "Update of section 4.3 of the SmPC to delete the contraindications for use in patients with acute coronary syndrome or clinically unstable ischaemic cardiac disease and to insert these patient populations into section 4.4 Special warnings and precautions for use, with editing of the wording as appropriate. The package leaflet was updated accordingly. Furthermore, the MAH took this opportunity to bring the PI in line with the latest QRD template version 9."
Request for Supplementary Information adopted on February 2014, December 2013 and October 2013
The members were informed about recent 5 new cases of severe arrhythmia in stress echocardiography after the last RSI. The Committee discussed whether a contra indication should be included for dobutamine in stress echo and agreed on a simple wording in section 4.4 rather than listing all contraindications as in some national SmPCs.
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 recommendation.
Post meeting note: The final opinion was adopted via written procedure after the Plenary on 2 May 2014.

Glybera (EMEA/H/C/002145), Orphan (Adeno-Associated Viral Vector Expressing Lipoprotein Lipase), MAH: uniQure biopharma B.V., Rapporteur: Elaine French, Co-Rapporteur: Egbert Flory, (treatment lipoprotein lipase deficiency), New active substance (Article 8(3) of Directive No 2001/83/EC)
The CHMP noted the additional information.
The CAT timetable was noted.

Rasilez (EMEA/H/C/000780) LEG 37, (aliskiren), MAH: Novartis Europharm Ltd, Rapporteur: Daniela Melchiorri,
The CHMP adopted a List of Questions with a specific timetable.

12 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

Dexamed 5 mg Tablets (EMEA/H/A-29/1375) (dexamfetamine sulphate film coated tablets), Kohne Pharma GmbH, Rapporteur: Greg Markey, Co-Rapporteur: Johann Lodewijk Hillege, Article 29(4) procedure triggered by the Netherlands on the following grounds: enhanced risk for dependence and abuse potential of this product compared to other treatment options in ADHD and lack of convincing evidence for the efficacy in a second line setting – film coated tablets).
The CHMP adopted the final list of experts to the SAG Psychiatry.

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

Amoxil (EMEA/H/A-30/1372) (amoxicillin), MAH: GlaxoSmithKline**,** Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro,
List of Questions adopted in July 2013
The Committee was reminded of previous discussions and remaining outstanding issues. The CHMP adopted a List of Outstanding Issues with a specific timetable.
List of outstanding issues: 25.04.2014; Responses to list of questions: 01.09.2014; Restart of the procedure: 23.09.2014; Assessment report: 08.10.2014; Comments from CHMP: 13.10.2014; List of outstanding issues or CHMP opinion: October 2014 CHMP

Plendil (EMA/H/A-30/1385) (felodipine), Astra Zeneca group of companies and associated companies, Rapporteur: Alar Irs, Co-Rapporteur: Martina Weise,
The Committee started a harmonisation exercise for Plendil and associated names. The review was triggered by the European Commission, due to the need of harmonisation of the Summary of Product Characteristics across Member States.
List of Questions adopted in November 2013.
The Committee was reminded of previous discussions and remaining outstanding issues. The CHMP adopted a List of Outstanding Issues with a specific timetable.
List of outstanding issues: 25.04.2014; Responses to list of outstanding issues: 28.05.2014; Restart of the procedure: 24.06.2014; Assessment report: 09.07.2014; Comments from CHMP: 14.07.2014; 2nd list of outstanding issues or CHMP opinion: July 2014 CHMP

Nasonex (EMEA/H/A-30/1374) (mometasone), nasal spray suspension, MAH: Merck Sharp & Dohme, Rapporteur: Kristina Dunder, Co-Rapporteur: David Lyons,
Nasonex 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.
The CHMP noted the revised timetable adopted via written procedure.
Responses to LoOI: 01.08.2014; Restart of the procedure: 26.08. 2014; Joint or Rapporteurs Assessment report(s): 10.09.2014; Comments from CHMP members: 15.09.2014; List of outstanding issues and/or Oral explanation and/or CHMP opinion: September 2014 CHMP

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

Caustinerf arsenical® and Yranicid arsenical® and associated names, paste for dental use (oral formulations) (EMEA/H/A-31/1382)

(lidocaine, ephedrine, arsenic trioxide), SEPTODONT and A.T.O. ZIZINE, Rapporteur: Alar Irs, Co-Rapporteur: Joseph Emmerich,

Article 31 triggered by the ANSM for ephedrine hydrochloride, lidocaine and arsenous anhydride containing medicinal products for topical use, based on genotoxicity data.

List of Outstanding Issues adopted in February 2014.

See 1.4. Referral Procedures Oral Explanations

An Oral explanation was held on Wednesday 23 April 2014 at 12.00. The MAH presented data on the benefit/risk of the product especially regarding a potential leakage of the product and the usage in the European Union considering other available treatments. After the Oral explanation some members expressed concern on the safety of the product due to possible leakage of the arsenic compound. It was considered that sufficient other therapies exist to achieve anaesthesia even in problematic cases. Other members did see a value of the product in special situations.

The CHMP adopted an opinion by majority (27 votes out of 30 votes), concluding that pursuant to Article 116 of Directive 2001/83/EC the risk-benefit balance is not favourable, and therefore recommending the revocation of the Marketing Authorisations. The assessment report was adopted.

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

The divergent position (John Joseph Borg, Dimitrios Kouvelas, Juris Pokrotnieks) was appended to the opinion.

The EMA communication document was circulated for information.

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097)

Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff,

The CHMP adopted the third monthly update related to the 3rd annual cumulative safety reviews on nephrogenic systemic fibrosis (NSF) Omniscan (GE HealthCare) and interim analysis report submission as requested by CHMP in November 2013 together with assessment report. Furthermore the Inspection report was adopted.

Adrenaline auto injectors (EMEA/H/A-31/1398) Rapporteur: Alar Irs (risk level 2), Co-Rapporteur: Robert Hemmings (risk level 2),

Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients.

The Committee noted the Notification from MHRA dated 2 April 2014.

The CHMP appointed Alars Irs as Rapporteur and Robert Hemmings as Co-Rapporteur .

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

List of Questions: 25 April 2014; Responses to list of questions: 30.06.2014; Restart of the procedure: 26.08.2014; Assessment report: 10.09.2014; Comments from CHMP: 15.09.2014; List of outstanding issues or CHMP opinion: September 2014 CHMP

The CHMP noted the EMA communication document on the start of referral. The CHMP noted that the relevant documentation (i.e Notification from MHRA, Annex I, List of Questions, and Timetable) will be published together with the announcement of the start of the referral.

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

Estradiol (topical use) (EMEA/H/A-31/1336) Re-examination Rapporteur: Arantxa Sancho, Re-examination Co-Rapporteur and Milena Stain,
Review of the benefit-risk balance of medicinal products containing estradiol for intravaginal administration and administration on the skin of the vulva due to observed high systemic absorption which may lead to safety issues
See 1.4. Referral Procedures Oral Explanations
The CHMP agreed that an oral explanation was not needed at this time.
The CHMP adopted an opinion by consensus recommending amendments to the SmPC and PL, together with the Assessment Report.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The CHMP noted the EMA public health communication document.

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

Ketoprofen formulation for topical use (EMEA/H/A-107/1259)
(Ketum), Rapporteur: Joseph Emmerich, Co-Rapporteur: Radka Montoniová, The CHMP agreed to the request for a 2-months extension for submission of responses from several MAHs for ketoprofen FUM Art.107 (following outcomes of the March 2014 CHMP meeting) with a specific timetable.
Submissions from MAHs: 02.07.2014; Assessment Report: 10.09.2014; Comments from CHMP: 15.09.2014; CHMP conclusions: September 2014 CHMP

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

Crestor and associated names (EMEA/H/A-29-PAE/1378)
MAH: AstraZeneca, (rosuvastatin), Rapporteur: Pieter de Graeff, Co-Rapporteur: Radka Montoniová, Application to extend the age range of the existing paediatric indication [hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments is inadequate] from patients aged 10 to 17 to patients aged 6 to 17 years.
The CHMP adopted an opinion by consensus recommending the acceptance of the extension of indication. Furthermore amendments to the Product Information were agreed. The Assessment Report was adopted.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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	The Committee noted the report.

PRAC meeting held on 7-10 April 2014: **For information**	The members noted the Summary of recommendations and advices of the PRAC meeting.
List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2014: **For adoption**	The EURD list was adopted.
Early Notification System: April 2014 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

14 INSPECTIONS

14.1 GMP Inspections

Request for GMP Inspections: **For adoption**	*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.
GCP Inspection Programme 2014-2015**: For adoption**	The CHMP adopted the GCP Inspection Programme 2014 - 2015

14.3 Pharmacovigilance Inspections

Request for Pharmacovigilance Inspections: **For adoption**	*Disclosure of information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections.*

14.4 GLP Inspections

Request for GLP Inspections: **For adoption**	*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 ITF: 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.

ITF Briefing Meeting: **For information**	The CHMP noted the ITF Briefing Meeting.

15.3 Eligibility to EMA scientific services

No items

15.4 Requests for CHMP Opinion under Article 57 (1)P of Regulation (EC) NO 726/2004

Update on CHMP opinion under Art. 57 (1)P of Regulation (EC) No 726/2004 Update on EC proposed Medical diagnosis definition	The CHMP agreed with the proposed medical diagnosis definition.

15.5 Nanomedicines activities

No items

16 SCIENTIFIC ADVICE WORKING PARTY (SAWP)

Report from the SAWP meeting held on 31 March-3 April 2014 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 21-23 April 2014: **For information**	The CHMP noted the report.
Letter to CHMP on Classification of levothyroxine and data requirements for levothyroxine	The CHMP noted the letter to CHMP on Classification of levothyroxine and data

applications **Levothyroxine 50 microgram /5ml and 100 microgram/5 ml oral solutions** Data requirements for Art 10a (well-established used) levothyroxine applications and whether levothyroxine should be considered as a narrow therapeutic index drug(NTID) or critical dose drug (CDD) Letter from Chair of CMDh: **for information** List of questions from CMDh to be addressed by CHMP WPs/expert group: **for adoption**	requirements for levothyroxine applications.
Letter dated 12 March 2014 on Qualification of flecainide as NTI drug • List of Questions to CVSWP on flecainide: **For information**	The CHMP noted the letter dated 12 March 2014 on the qualification of flecainide as NTI drug.

18 OTHER COMMITTEES

18.1 Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 8-9 April 2014: **For information**	To be sent in the Post-mail.

18.2 Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 24-25 March 2014: **For information**	To be sent in the Post-mail.

18.3 Paediatric Committee (PDCO)

PIPs reaching D30 at April 2014 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on 23-25 April 2014: **For information**	The CHMP noted the report.

18.4 Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 15-16 April 2014: **For information**	The CHMP noted the Table of Decisions.

19 INVENTED NAME ISSUES

Table of Decisions of the NRG meeting held on 26 March 2014: **For adoption**	The CHMP adopted the Table of Decisions of the NRG meeting held on 26 March 2014.

20 ANY OTHER BUSINESS

Election of BWP Vice Chair	The CHMP agreed to have two BWP Vice Chairs. Ilona Reischl and Nanna Aaby Kruse were both elected as Vice chairs.
Presentation by EC on the Delegated Regulation on Post-Authorisation Efficacy Studies (PAES)	The Committee noted that the Regulation on Delegated Acts was published on 10th April and came into force 10 days after. The Committee noted that the PAES were an exceptional instrument, not to be used as a justification for premature granting of a MA.
EMA presentation on implementation steps on PAES	The Committee noted that a drafting group would be put in place in order to come up with relevant scientific guidance. The participants in this drafting group are Jane Moseley, Kevin Blake, Almath Spooner and Stephen Evans (PRAC). Pierre Demolis and Robert Hemmings were appointed by the CHMP as participants.
Guideline on treatment of Juvenile Idiopathic Arthritis (EMA/CPMP/422/04): **For adoption for 6-months public consultation**	Adopted for 6-months public consultation
Guideline on non-clinical and clinical development of similar biological medicinal products containing recombinant human insulin and insulin analogues (EMEA/CHMP/BMWP/32775/2005_Rev. 1): **For adoption for 3-months public consultation** (2nd consultation).	Adopted for 3-months public consultation
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): **For adoption for 6-month public consultation**	Adopted for 6-months public consultation
Guideline on Influenza Vaccines – Quality Module (EMA/CHMP/BWP/310834/2012): **For adoption** • Overview of comments: **For information**	The CHMP adopted the Guideline on Influenza Vaccines – Quality Module and noted the overview of comments.
Concept paper on Viral safety of blood products with respect to hepatitis E (EMA/CHMP/BWP/78086/2014): **For adoption for 3-month public consultation**	Adopted for 3-months public consultation

Guideline on non-clinical local tolerance testing of medicinal products (EMA/CHMP/SWP/187944/2014 Rev. 1): **For 3-month public consultation**	Adopted for 3-months public consultation
Questions and answers on the withdrawal of the 'Guideline on pharmacokinetics and metabolic studies in the safety evaluation of new medicinal products in animals (3BS11A)' (EMA/CHMP/SWP/191104/2014): **For adoption**	Adopted
Draft Minutes SWP Meeting on 11-12 February (EMA/CHMP/SWP/131453/2014): **For information**	The CHMP noted the draft Minutes.
Revised SWP Work plan 2014 (EMA/CHMP/SWP/743862/2013): **For adoption**	The CHMP adopted the revised SWP Work Plan 2014.
ToD/Minutes of the BSWP plenary meeting held on 6-7 March 2014 (EMA/141899/2014): **For information**	The CHMP noted the ToD/Minutes.
Survey results from "Alliance for Safe Biologic Medicines" on prescribing habits and knowledge of biosimilar medicines: **For information** • INN / naming topic and WHO activities • ADRs reporting	The members were informed about a survey on identification and traceability of biosimilars. A distinguishable INN was discussed. Furthermore the members were updated on a reflection paper on pharmacovigilance considerations for biological as well as biological qualifier agreed by the INN Committee in April 2014.
2014 initial MAAs submission planning update: **For discussion**	The members were informed that in future quarterly reports of planned MAAs with already appointed Rapporteurs will be circulated to the members in order to keep them informed about expected MAA submissions.
Class labelling for antiretroviral medicinal products regarding mitochondrial dysfunction, lactic acidosis and lipodystrophy. Update on regulatory framework	The Committee noted the update on the regulatory framework for these class labelling actions which will consists of Post Authorisations Measures lead by the PRAC.
Draft guideline on literature monitoring: **For information**	The CHMP noted the draft guideline on literature monitoring.
Respiratory Working Group to finalise Asthma Guideline – List of Members: **For adoption**	The CHMP adopted the list of members. During the discussion further nominations from CHMP members were received. It will be discussed whether more members can be considered although it was highlighted not to extend the group too much.

21 **List of participants:** *including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 22-25 April 2014 meeting.*

CHMP Chair	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
Tomas Salmonson	Sweden	Full involvement	

CHMP Member	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
Andrea Laslop	Austria	Full involvement	
Daniel Brasseur	Belgium	Full involvement	
Mila Vlaskovska	Bulgaria	Full involvement	
Ivana Mikačić	Croatia	Full involvement	
Panayiotis Triantafyllis	Cyprus	Full involvement	
Ondřej Slanař	Czech Republic	No participation in discussions, final deliberations and voting on:	Humalog (EMEA/H/C/000088/X/0125) (insulin lispro)
			Liprolog (EMEA/H/C/000393/X/0092) (insulin lispro)
			Prezista (EMEA/H/C/000707/II/0063) (darunavir)
			Invega (EMEA/H/C/000746/II/0037) (paliperidone)
			(EMEA/H/C/003698) (brinzolamide / brimonidine tartrate)
			(EMEA/H/C/003746) (apremilast)

CHMP Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/ substance
			(EMEA/H/C/002647) (insulin degludec / liraglutide)
			Plendil (EMA/H/A-30/1385) (felodipine)
		No participation in final deliberations and voting on:	Vfend (EMEA/H/C/000387/II/0097) (voriconazole)
			Ketoprofen formulation for topical use (EMEA/H/A-107/1259)
Jens Heisterberg	Denmark	No participation in final deliberations and voting on:	Invega (EMEA/H/C/000746/II/0037) (paliperidone)
Alar Irs	Estonia	Full involvement	
Outi Mäki-Ikola	Finland	No participation in final deliberations and voting on:	(EMEA/H/C/003746) (apremilast)
			Prolia (EMEA/H/C/001120/II/0030) (DENOSUMAB)
			Serelaxin (EMEA/H/C/002817) (Serelaxin)
			Crestor and associated names (EMEA/H/A-29-PAE/1378)
			Rienso (EMEA/H/C/002215/II/0008) (ferumoxytol)
Pierre Demolis	France	Full involvement	
Harald Enzmann	Germany	Full involvement	
Dimitrios Kouvelas	Greece	Full involvement	
Agnes Gyurasics	Hungary	Full involvement	
David Lyons	Ireland	Full involvement	
Juris Pokrotnieks	Latvia	No participation in discussions, final deliberations and voting on:	Rienso (EMEA/H/C/002215/II/0008) (ferumoxytol)

CHMP Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/ substance
Romaldas Mačiulaitis	Lithuania	Full involvement	
Jacqueline Genoux-Hames	Luxembourg	Full involvement	
John Joseph Borg	Malta	Full involvement	
Pieter de Graeff	Netherlands	Full involvement	
Karsten Bruins Slot	Norway	Full involvement	
Piotr Fiedor	Poland	Full involvement	
Bruno Sepodes	Portugal	Full involvement	
Nela Vilceanu	Romania	Full involvement	
Jan Mazag	SLOVAKIA	Full involvement	
Stanislav Primožič	Slovenia	Full involvement	
Concepcion Prieto Yerro	Spain	Full involvement	
Kristina Dunder	Sweden	Full involvement	
Greg Markey	United Kingdom	Full involvement	
Sol Ruiz	Co-opted	Full involvement	
Robert James Hemmings	Co-opted	Full involvement	
Jean-Louis Robert	Co-opted	Full involvement	
Jan Mueller-Berghaus	Co-opted	Full involvement	
Hubert Leufkens	Co-opted	Full involvement	

CHMP Alternate	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
Milena Stain	Austria	Full involvement	
Bart Van der Schueren	Belgium	Full involvement	
Ana Dugonjić	Croatia	Full involvement	
Georgios Savva	Cyprus	Full involvement	
Radka Montoniová	Czech Republic	Full involvement	
Jens Ersbøll	Denmark	Full involvement	
Joseph Emmerich	France	No participation in final deliberations and voting on:	Pradaxa (EMEA/H/C/000829/II/0048/G) (Dabigatran Etexilate Mesilate)
			Pradaxa (EMEA/H/C/000829/ LEG 042) (Dabigatran Etexilate Mesilate)
			(EMEA/H/C/002814) (vorapaxar)
			(EMEA/H/C/003773) (cangrelor)
			(EMEA/H/C/002272) (clopidogrel/acetylsalicylic acid)
Martina Weise	Germany	Full involvement	
George Aislaitner	Greece	Full involvement	
Melinda Sobor	Hungary	Full involvement	
Reynir Arngrímsson	Iceland	Full involvement	*Replacing CHMP member*
Patrick Salmon	Ireland	Full involvement	

CHMP Alternate	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
Daniela Melchiorri	Italy	Full involvement	*Replacing CHMP member*
Natalja Karpova	Latvia	Full involvement	
Johann Lodewijk Hillege	Netherlands	Full involvement	
Ingunn Hagen Westgaard	Norway	Full involvement	
Dinah Duarte	Portugal	Full involvement	
Jana Klimasová	Slovakia	Full involvement	
Arantxa Sancho-Lopez	Spain	Full involvement	
Filip Josephson	Sweden	Full involvement	
Rafe Suvarna	United Kingdom	Full involvement	

EUROPEAN COMMISSION	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
	European Commission	Full involvement	

CHMP Expert *	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
* Experts were only evaluated against the product they have been invited to talk about.			
Christophe Focke	Belgium	Full involvement	
Marie Louise Schougaard Christiansen	Denmark	Full involvement	
Kristina Bech Jensen	Denmark	Full involvement	
Ljiljana Milosevic-Kapetanovic	France	Full involvement	
Vincent Gazin	France	Full involvement	
Sophie Negellen	France	Full involvement	
Alexandre Moreau	France	Full involvement	
Sylvain Gueho	France	Full involvement	
Sabine Mayrhofer	Germany	Full involvement	
Mair Powell	United Kingdom	Full involvement	
Yolanda Barbachano	United Kingdom	Full involvement	
Paul Marshall	United Kingdom	Full involvement	
Kofi Owusu	United Kingdom	Full involvement	
Emmanouil Zouridakis	United Kingdom	Full involvement	

CHMP Expert	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
Angeliki Siapkara	United Kingdom	Full involvement	

CHMP Expert by phone *	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
* Experts were only evaluated against the product they have been invited to talk about.			
Kevin Cunningham	Ireland		
Peter Kiely	Ireland		
Massimo Cirillo	Italy		
Hendrik Kommerie	Netherlands		
Lies (Elizabeth) Van Vlijmen	Netherlands		
Jan Willem van der Laan	Netherlands		
Leon van Aerts	Netherlands		
Graham Carroll	United Kingdom		
David Churchward	United Kingdom		
Elizabeth Baker	United Kingdom		
Paul Hargreaves	United Kingdom		
Jon Sisson	United Kingdom		

CHMP Expert by phone *	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/* *substance*
Barbara Bannister	United Kingdom		

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)*

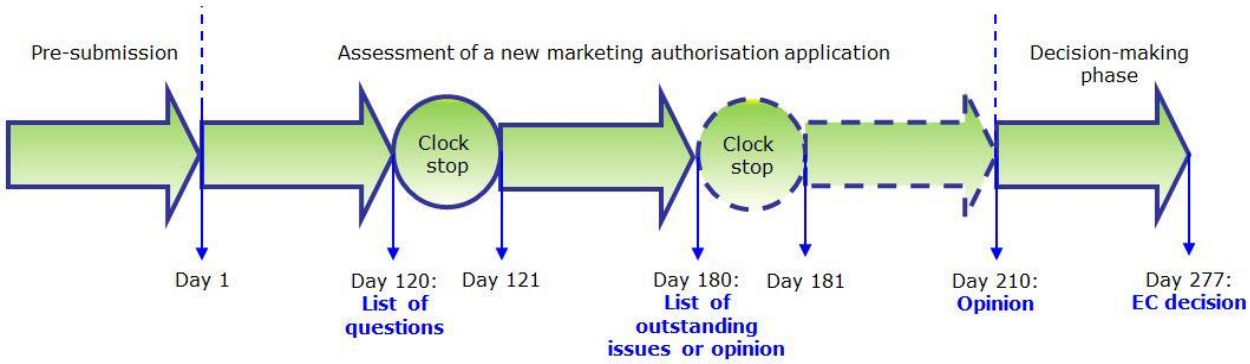
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section 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.