23 January 2014
EMA/CHMP/6103/2013
Committee for Medicinal Products for Human Use (CHMP)

Committee for Medicinal Products for Human Use (CHMP)

CHMP minutes of the meeting held on 16-19 December 2013

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

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. All decisions taken at this meeting (relating to adoption of Opinions, Lists of Questions, Lists of Outstanding Issues, etc.) were made in presence of a quorum of members – i.e. 22 or more members were present in the room.

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 product name and applicant details are published as this information is already publicly available. 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

For adoption

AGENDA (EMA/723655/2013) and Annex to CHMP agenda of the CHMP plenary to be held 16-19 December 2013.	The agenda and annex were adopted.
TIMESCHEDULE (EMA/735317/2013) of the CHMP plenary to be held 16-19 December 2013.	The timeschedule was adopted.
MINUTES /(EMA/CHMP/738707/2013) of the CHMP plenary held on 18-21 November 2013.	The CHMP minutes of the plenary held on 18-21 November 2013 were adopted.
MINUTES (EMA/CHMP/780238/2013) of the CHMP ORGAM meeting held on 9 December 2013.	The minutes of the CHMP ORGAM meeting held on 9 December 2013 were adopted together with all decisions taken at that meeting.

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 to be held 16-19 December 2013.	The pre-meeting list was noted.
Draft Agenda of CHMP plenary to be held on 20-23 January 2014 CHMP	The draft agenda was noted.

1. ORAL EXPLANATIONS

1.1. Pre-authorisation Procedure Oral Explanations

(EMEA/H/C/002817)
(serelaxin), (treatment of acute heart failure)
List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 2013.
The chair of the Scientific Advisory Group Cardiovascular (SAG) reported on the meeting that took place on 9 December 2013. An Oral explanation was held on Monday 16 December 2013 at 14.00. After the Oral Explanation the Committee discussed the available data. The opinion is scheduled for January 2014.

Translarna (EMEA/H/C/002720), Orphan
Applicant: PTC Therapeutics Limited, (ataluren), (treatment of Duchenne muscular dystrophy)
List of Outstanding Issues adopted in September 2013. List of Questions adopted in March 2013.
The chair of the Scientific Advisory Group Neurology reported on the meeting held on 5 December 2013. An Oral Explanation was held on Tuesday 17 December 2013 at 9.00. After the Oral Explanation the Committee discussed the available data. The opinion is scheduled for January 2014.

(EMEA/H/C/002546)
(Laquinimod Sodium), (treatment of multiple sclerosis)
List of Outstanding Issues adopted in July 2013 and November 2013. List of Questions adopted in November 2012.
The chair of the SWP reported on the discussion held on 3 December 2013. An Oral Explanation was held on Tuesday 17 December 2013 at 14.00. The Committee discussed the available data. The opinion is scheduled for January 2014.

(EMEA/H/W/002652)
(misoprostol), (treatment of Post Partum Haemorrhage)
List of Outstanding Issues adopted in October 2013, May 2013. List of Questions adopted in December 2012.
The Committee agreed that no Oral Explanation was needed at this time as all outstanding issues had been addressed.
This Article 58 CHMP scientific opinion issued by the CHMP, in collaboration with WHO is scheduled for January 2014. This medicinal product is intended exclusively for markets outside the European Community.

(EMEA/H/C/002713)
(lurasidone), (treatment of schizophrenia)
List of Outstanding Issues adopted in July 2013, List of Questions adopted in February 2013.
The Committee agreed that no Oral Explanation was needed at this time.
See also section 2.2 List of Outstanding Issues.

Masiviera (EMEA/H/C/002659), Orphan
Applicant: AB Science, (masitinib), (treatment of non resectable locally advanced or metastatic pancreatic cancer)
List of Outstanding Issues adopted in September 2013. List of Questions adopted in January 2013.
An Oral Explanation was held on Wednesday 18 December 2013 at 14.00. After the Oral Explanation the Committee discussed the available data. The opinion is scheduled for January 2014.

1.2. Referral Procedures Oral Explanations

Valebo 70 mg tablets and 1 microgram capsule (EMEA/H/A-29(4)/1364)
(alendronic acid and alfacacidol) Teva Pharma B.V, Rapporteur: Harald Enzmann, Co-rapporteur: Concepcion Prieto Yerro Decentralised Procedure number: DE/H/3436/01/DC.
Referral procedure due to disagreements regarding the demonstration of the role of alfacalcidol in the reduction in the fall rate. List of Questions adopted in March 2013. List of Outstanding Issues adopted in July 2013.
The Committee agreed that no Oral Explanation was needed at this time.
See also section 12.4. Disagreement between Member States on application for medicinal product - Referral under Article 29(4) of Directive 2001/83/EC.

Estradiol (topical use) (EMEA/H/A-31/1336)
Rapporteur: Martina Weise, Co-Rapporteur: Hubert Leufkens
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.
List of Questions adopted in June 2012, November 2012, February 2013, March 2013 and November 2013. Oral Explanations were held in March and November 2013.
An additional Oral Explanation with Dr A. Wolff was held on Monday 16 December 2013 at 17.00.
See also section 12.6 Community Interests - Referral under Article 31 of Directive 2001/83/EC.

Methysergide containing products (EMEA/H/A-31/1335)
Rapporteur: Joseph Emmerich, Co-Rapporteur: Rafe Suvarna
Review of the benefit-risk balance of methysergide containing products due to safety concerns related to fibrotic risks. List of Questions adopted in May 2012. List of Outstanding Issues adopted in December 2012 and May 2013. SAG meeting held on 5 September 2013.
The Committee agreed that no Oral Explanation was needed at this time.
See also section 12.6 Community Interests - Referral under Article 31 of Directive 2001/83/EC.

2. NEW APPLICATIONS

2.1. Opinions – New full applications

Cometriq (EMEA/H/C/002640), Orphan
Applicant: TMC Pharma Services Ltd, (cabozantinib), (treatment of medullary thyroid carcinoma)
New active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted in October 2013, July 2013. List of Questions adopted in March 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 conditional marketing authorisation by consensus, together with the CHMP Assessment report and Translation timetable.
Furthermore, the CHMP considered that cabozantinib is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to restricted medical prescription.
The summary of opinion was circulated for information.

Mirvaso (EMEA/H/C/002642)

Applicant: Galderma International, (brimonidine), (treatment of facial erythema of rosacea)
Known active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 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.

Neuraceq (EMEA/H/C/002553)

Applicant: Piramal Imaging GmbH, (florbetaben (18f)), (detection of β-amyloid in the brain)
New active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 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.
Furthermore, the CHMP considered that florbetaben (18F) is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to restricted medical prescription.
The summary of opinion was circulated for information.

SIRTURO (EMEA/H/C/002614), Orphan

Applicant: Janssen-Cilag International N.V., (bedaquiline), (treatment of pulmonary tuberculosis)
New active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted in September 2013, June 2013. List of Questions adopted in January 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.
Furthermore, the CHMP considered that bedaquiline is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to restricted medical prescription.
The summary of opinion was circulated for information.

IZBA (EMEA/H/C/002738)

Applicant: Alcon Laboratories (UK) Ltd, (travoprost), (treatment of ocular hypertension or open-angle glaucoma)

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

List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 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.

Tritanrix HB (EMEA/H/W/003838)

Applicant: GlaxoSmithKline Biologicals S.A., (diphtheria (d), tetanus (t), pertussis (whole cell) (pw) and hepatitis b (rdna) (hbv) vaccine (adsorbed)), (indicated for active immunisation against diphtheria, tetanus, pertussis and hepatitis B (HBV))

Article 58 of Regulation (EC) No 726/2004 (by analogy to Article 10c of Directive No 2001/83/EC)

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

The Committee adopted a positive CHMP Scientific Opinion in accordance with Article 58 of Regulation (EC) No 726/2004 by consensus, together with the CHMP Assessment report.

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.

This medicinal product Tritanrix HB is exclusively intended for markets outside the European Union.

Winfuran (EMEA/H/C/002683), Orphan

Applicant: Toray Europe Limited, (nalfurafine), (treatment of uraemic pruritus)

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

List of Outstanding Issues adopted in July 2013. List of Questions adopted in November 2012.

Oral explanation held in November 2013.

The Committee concluded that the main concern in this application was that the benefits of Winfuran in the treatment of uraemic pruritus had not been sufficiently demonstrated. The main study failed to show that Winfuran was more effective than placebo at relieving itching. Although an additional analysis showed a modest benefit in a subpopulation of patients with a severe form of uraemic pruritus, the CHMP considered that the clinical relevance had not been shown. Therefore, at this point in time, the CHMP was of the opinion that the benefits of Winfuran did not outweigh its risks and recommended that it be refused marketing authorisation.

The Committee adopted a negative opinion by majority (26 negative out of 28), together with the Assessment Report.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Romaldas Mačiulaitis, Natalja Karpova) was appended to the opinion.

The refusal question-and-answer document was circulated for information.

The applicant did not request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

2.2. Day 180 List of outstanding issues – New full applications

(EMEA/H/C/002348)

(budesonide / formoterol), (treatment of asthma and COPD)
List of Questions adopted in July 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/003717)

(oseltamivir)
(1) Treatment of influenza in patients one year of age and older who present with symptoms typical of influenza, when influenza virus is circulating in the community.
2) Treatment of infants less than 1 year of age during a pandemic influenza outbreak.
3) Post-exposure prevention in individuals 1 year of age or older following contact with a clinically diagnosed influenza case when influenza virus is circulating in the community.
4) Post-exposure prevention of influenza in infants less than 1 year of age during a pandemic influenza outbreak.
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.

(EMEA/H/C/002621)

(propranolol), (treatment of proliferating infantile haemangioma)
List of Questions adopted in July 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/002713)

(lurasidone), (treatment of schizophrenia)
List of Outstanding Issues adopted in July 2013. List of Questions adopted in February 2013.
The Committee agreed that no Oral Explanation was needed at this time.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a 2nd List of Outstanding Issues with a specific timetable.

(EMEA/H/C/002085)

(tilmanocept), (used in the delineation and localisation of lymph nodes)
List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 2013.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a 2nd List of Outstanding Issues with a specific timetable.

(EMEA/H/C/002677)

(empagliflozin), (treatment of type 2 diabetes mellitus)
List of Questions adopted in July 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/002782)
(vedolizumab), (treatment of Ulcerative Colitis and Crohn's Disease)
List of Questions adopted in July 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.

Vimizim (EMEA/H/C/002779), Orphan
Applicant: BioMarin Europe Ltd, (recombinant human n-acetylgalactosamine-6-sulfatase (rhgalns)), (treatment of mucopolysaccharidosis type IV)
List of Questions adopted in September 2013.
***Note**: The ANSM in France granted authorisation of a compassionate use of Vimizim in treatment of mucopolysaccharidosis type IV on 14 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.
The BWP report was adopted.

(EMEA/H/C/002557)
(flutemetamol f-18), (indicated for the visual detection of amyloid-beta neuritic plaques in the brain)
List of Questions adopted in April 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/002656)
(canagliflozin / metformin), (treatment of type 2 diabetes mellitus)
List of Questions adopted in July 2013.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP discussed the PRAC recommendation.
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/002806)
(busulfan), (conditioning prior to conventional haematopoietic progenitor cell transplantation (HPCT))
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 similarity Assessment Report.

(EMEA/H/C/002272)
(clopidogrel / acetylsalicylic acid), (indicated for the prevention 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/002347)

(PERFLUBUTANE), (ultrasound imaging agent indicated for the detection of coronary artery disease (CAD)),

The CHMP agreed to the request by the applicant for a clock stop extension of time frame to respond to the List of Outstanding Issues adopted in November 2013, with a specific timetable.

(EMEA/H/C/002705),

(MIXTURE OF POLYNUCLEAR IRON(III)-OXYHYDROXIDE, SUCROSE AND STARCHES), (indicated for the control of serum phosphorus levels in patients with end-stage renal disease (ESRD)),

The CHMP noted the additional information.

Cerdelga (EMEA/H/C/003724), Orphan

(Eliglustat), Genzyme Europe BV, (treatment of Gaucher disease type 1)

The CHMP adopted the similarity Assessment Report.

2.5. Products in the Decision Making Phase

Cholic Acid FGK (EMEA/H/C/002081), Orphan

(CHOLIC ACID), Applicant: FGK Representative Service GmbH, (treatment of inborn errors of primary bile acid synthesis),

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

The CHMP addressed the additional information. The Committee agreed to revise the CHMP opinion documents.

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

RoActemra (EMEA/H/C/000955/X/0030)

MAH: Roche Registration Ltd, (tocilizumab), Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC Co-Rapporteur: Julia Pallos,

Extension application to register a new route of administration "subcutaneous" use, a new pharmaceutical form "solution for injection", a new strength "162 mg" and two new presentations "pre-filled pen" and "pre-filled syringe"

List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 2013.

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.

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

Noxafil (EMEA/H/C/000610/X/0028)

MAH: Merck Sharp & Dohme Limited, (posaconazole), Rapporteur: Rafe Suvarna, PRAC Rapporteur: Julia Dunne, To add a new pharmaceutical form: gastroresistant tablets 100 mg.

List of Questions adopted in July 2013.

The Committee was reminded of the status of this application and its remaining outstanding issues. The issues remaining related to clinical aspects regarding the proposed dose of 300mg as the most appropriate dose for the entire target population or not. In addition the safety database for patients with high exposure is very limited and the MAH should submit proposals for measures to generate further exposure related safety data in the treatment and prophylaxis population. Finally due to the known food effect, proposals should be submitted to collect further data on exposures when food status is known.

The Committee adopted a List of Outstanding Issues with specific timetable.

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

Isentress (EMEA/H/C/000860/X/0044/G)

MAH: Merck Sharp & Dohme Limited, (raltegravir), 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 (Quality Review of Documents) QRD version 9.3.

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

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 Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

3.4. Update on pending Extension application according to Annex I of Reg. 1234/2008

No items

4. TYPE II VARIATIONS - Extension of indication procedures

4.1. Opinions or Requests for Supplementary information (RSI) - Type II variation; Extension of indication

Avastin (EMEA/H/C/000582/II/0063)

MAH: Roche Registration Ltd, (bevacizumab), Rapporteur: Jens Ersbøll, Co-Rapporteur: Ingunn Hagen Westgaard, PRAC Rapporteur: Doris Stenver, Extension of indication to include the use of

Avastin in combination with chemotherapy (paclitaxel, topotecan or pegylated liposomal doxorubicin) in patients with recurrent, platinum-resistant epithelial ovarian, primary peritoneal, or fallopian tube carcinoma.
The Committee discussed the issues identified in this application which related to several aspects of the clinical safety and efficacy. Indeed limitations of an open-label study and the lack of independent review of data were pointed out. In addition concerns were raised regarding the wording of the indication and the lack of efficacy of Avastin in the limited number of patients with previous anti-angiogenic therapy. Finally the review of safety was hampered by a very high discontinuation rate. The matter is further complicated by several considerable deficiencies (lack of collection of data with regard to dose-interruptions, dose-modifications, and laboratory parameters) which should be investigated further.
The Committee adopted a Request for Supplementary Information with a specific timetable.
The BWP report was adopted.

Halaven (EMEA/H/C/002084/II/0011)
MAH: Eisai Europe Ltd., (eribulin), Rapporteur: Bengt Ljungberg, Co-Rapporteur: Jens Ersbøll, Extension of indication of Halaven 0.44 mg/ml solution for injection to earlier lines of metastatic breast cancer . Changes have been made to SmPC sections 4.1, 4.8, and 5.1. The Package leaflet has been updated accordingly. Furthermore the product information has been updated in line with the latest version of QRD template (version 9). Request for Supplementary Information adopted in July 2013.
The Committee discussed the issues identified in this application and noted that the post hoc non-inferiority analysis on the overall survival performed after the study did not meet its primary endpoints. The Committee discussed whether the non-inferiority analysis could be accepted.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Invega (EMEA/H/C/000746/II/0037)
MAH: Janssen-Cilag International N.V., (paliperidone), Rapporteur: Bengt Ljungberg, 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 12 years and older. Request for Supplementary Information adopted in June 2013.
The Committee discussed the issues identified in this application, especially relating to the efficacy and safety data for patients below 15 years of age. The CHMP considered that the efficacy in subjects under 15 years had not been established based on the submitted data.The Committee adopted a Request for Supplementary Information with a specific timetable.

Jentadueto (EMEA/H/C/002279/II/0012)
MAH: Boehringer Ingelheim International GmbH, (linagliptin / metformin), Rapporteur: Pieter de Graeff, PRAC Rapporteur: Menno van der Elst, Extension of indication for the use of Jentadueto as combination therapy with insulin in adult patients with type 2 diabetes when insulin and metformin do not provide adequate glycaemic control. The package leaflet has been updated accordingly. Request for Supplementary Information adopted in October 2013.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive Opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendation. The summary of opinion was circulated for information.

NovoThirteen (EMEA/H/C/002284/II/0002)
MAH: Novo Nordisk A/S, (catridecacog), Rapporteur: Joseph Emmerich, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Evelyne Falip, Update of section 4.1 of the SmPC to include the treatment of bleeding in children with congenital factor XIII A-subunit deficiency below 6 years of age. The package leaflet has been updated accordingly. Request for Supplementary Information adopted in September 2013.
The Committee was reminded of the status of this application and its identified issues which related to several clinical aspects and still required further clarifications by the applicant.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Stivarga (EMEA/H/C/002573/II/0001)
MAH: Bayer Pharma AG, (regorafenib), Rapporteur: Pieter de Graeff, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, , Extension of indication to include treatment of patients with gastrointestinal stromal tumours (GIST) who have been previously treated with 2 tyrosine kinase inhibitors. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC were proposed to be updated. The Package leaflet has been updated accordingly.
The Committee discussed the issues identified in this application, mainly on the lack of compelling biomarker analysis and an overall survival analysis.
The Committee adopted a Request for Supplementary Information with a specific timetable.

4.2. Update on ongoing Type II variation - Extension of indications

RoActemra (EMEA/H/C/000955/II/0032)
(TOCILIZUMAB), Applicant: Roche Registration Ltd, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, 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 rheumatoid arthritis (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.
The CHMP agreed to the request made by the MAH for a clock stop extension to respond to the Request for Supplementary Information adopted in November 2013.

Avastin (EMEA/H/C/000582/II/0059)
(BEVACIZUMAB), Applicant: Roche Registration Ltd, Rapporteur: Jens Ersbøll, Co-Rapporteur: Ingunn Hagen Westgaard, Update of section 4.1 of the SmPC in order to extend the indication of Avastin in combination with radiotherapy and temozolomide for the treatment of adult patients with newly diagnosed glioblastoma. Related changes were proposed to SmPC sections 4.2, 4.5, 4.8 and 5.1. The Package Leaflet was proposed to be updated accordingly. Furthermore, the MAH took the opportunity to make some editorial changes in the SmPC and the PL. Request for Supplementary Information adopted in June and November 2013.
The CHMP adopted a list of experts for a future SAG Oncology meeting.

Vfend (EMEA/H/C/000387/II/0097)
(VORICONAZOLE), Applicant: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur:

Pierre Demolis, 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.
The CHMP adopted a list of experts for a future SAG anti-infectives meeting.
The Committee agreed to the request from the MAH for an additional clock-stop to submit responses to the Request for Supplementary Information adopted in October 2013.

Kalydeco (EMEA/H/C/0002494/II/0009)
(IVACAFTOR), Applicant: Vertex Pharmaceuticals (U.K.) Ltd., CHMP Rapporteur: Concepcion Prieto Yerro, CHMP 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. The Package Leaflet is updated accordingly.
The Committee adopted the similarity Assessment Report.

XGEVA (EMEA/H/C/002173/II/0016)
(DENOSUMAB), Applicant: Amgen Europe B.V., Rapporteur: Bengt Ljungberg, Co-Rapporteur: Jan Mueller-Berghaus, Extension of indication to add treatment of giant cell tumour of bone in adults or skeletally mature adolescents. As a consequence, it is proposed to update sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and to update the Package Leaflet accordingly. Request for supplementary information adopted in March and September 2013.
The CHMP agreed to the request made by the MAH for a clock stop extension to respond to the CHMP Request for Supplementary Information adopted in September 2013.

Rienso (EMEA/H/C/002215/II/0008)
(FERUMOXYTOL), Applicant: Takeda Pharma A/S, Rapporteur: Harald Enzmann, Co-Rapporteur: Romaldas Mačiulaitis, 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).
The CHMP agreed to the request made by the MAH for a clock stop extension to respond to the CHMP Request for Supplementary Information.

5. ANCILLARY MEDICINAL SUBSTANCES IN MEDICAL DEVICES

5.1. 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
Masican (EMEA/H/C/002670), Orphan

(MASITINIB), Applicant: AB Science, (treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST))
New active substance (Article 8(3) of Directive No 2001/83/EC). Negative Opinion adopted in November 2013.
The Committee addressed the letter from the applicant dated 28 November 2013 requesting a re-examination of the Opinion adopted in November 2013 and consultation of a SAG.
The Committee appointed re-examination Rapporteur and re-examination Co-Rapporteur.
PRAC re-examination Rapporteurs were also appointed.

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

No items

8. WITHDRAWAL OF APPLICATION

No items

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.

11. POST-AUTHORISATION ISSUES

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

Abraxane (EMEA/H/C/000778)

(Paclitaxel Albumin), CELGENE EUROPE LIMITED, Rapporteur: Pieter de Graeff, Co-Rapporteur: Ingunn Hagen Westgaard,(treatment of metastatic breast cancer)
Quality defect: Follow-up from November 2013.
The CHMP was updated on the situation regarding the appearance of visible strands in the final infusion suspension and with the agreed recommendation to visually inspect the suspension and in case of visual strands to use a filter to remove the precipitates. The CHMP agreed to the wording of the Direct Healthcare Professional Communication (DHPC) letter and the communication plan.

Response from Pharmacokinetic Working Party (PKWP) on the orlistat/HIV medicines interactions

During the October 2013 meeting, the PKWP input has been sought on the issue of a potential drug-drug interaction between orlistat and the HIV medicines. Further discussions on this issue will take place and the parallel assessment of a signal for orlistat on “Pharmacokinetic drug interaction (at absorption) with highly active antiretroviral therapy (HAART) leading to loss of HAART efficacy.
The PKWP Report was adopted and the Committee noted that Rapporteurs should take this into consideration.

ellaOne (EMEA/H/C/001027/R/0025)
MAH: Laboratoire HRA Pharma, SA, (ulipristal acetate), Rapporteur: Pieter de Graeff, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, Renewal procedure
Request for Supplementary Information adopted in November 2013.
Back in November 2013, within this renewal procedure, the CHMP considered that based on the review of all data, the benefit-risk balance of EllaOne remained favourable and therefore recommended the renewal of the marketing authorisation subject to some questions being addressed.
In addition a discussion was held on emergency contraceptives with regard to the issue of reduced efficacy in women with a higher body weight or higher BMI. Consequently, an additional question was asked to which the MAH responded.
The Committee adopted a 2nd Request for Supplementary Information regarding additional data analysis
The CHMP also agreed to the request by the MAH for a extension of the clock stop for variation II/21 with a specific timetable.

Increlex (EMEA/H/C/000704), Orphan
(Mecasermin), Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, (treatment of growth failure)
The Committee was made aware of the resolution of the shortage and agreed to the wording of a DHPC letter regarding the re-supply.

Rotarix (EMEA/H/C/000639), (Human Rotavirus, Live Attenuated), GlaxoSmithKline Biologicals S.A., Rapporteur: Daniel Brasseur, Co-Rapporteur: Karsten Bruins Slot, (prevention of gastro-enteritis caused by Rotavirus of types G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8],prevention of gastro-enteritis caused by Rotavirus of types G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8])
RotaTeq (EMEA/H/C/000669), (Serotype G1,Serotype G2,Serotype G3,Serotype G4,Serotype P1), Sanofi Pasteur MSD, SNC, Rapporteur: Greg Markey, Co-Rapporteur: Kristina Dunder, (prevention of gastroenteritis in infants due to rotavirus of serotypes G1P1[8], G2P[4], G3P1[8], G4P1[8], and G9P1[8])
Assessment of responses from MAHs following the July 2013 CHMP request concerning new data from US and Australia on intussusception with rotavirus vaccines.
The CHMP agreed to the proposed harmonised SmPC wording and variations are expected to be submitted by the MAHs.

Doribax (EMEA/H/C/000891)
(Doripenem Monohydrate), Janssen-Cilag International N.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Alar Irs, (treatment of nosocomial pneumonia, complicated intra-abdominal infections and complicated urinary tract infections)
The CHMP addressed the draft DHPC and communication plan from the MAH informing of a voluntary recall of the product in February/March 2014 and subsequent withdrawal of the MA due to commercial reasons. The CHMP considered that it was not in the position to further comment on the document and expressed regret that such a decision was taken by the company considering the loss of this antibiotic within the EU.
In view of planned managed access programmes, the CHMP considered that the MAH may wish to contact Member States individually in which this is intended to be set up.

Epoetins – Legally binding measure (LEG) – risk of tumour growth progression and increased mortality in cancer patients
Aranesp- LEG 89
NeoRecormon - LEG 51
Silapo/Retacrit - LEG 38/LEG 38
Abseamed/Binocrit/Epoetin Alfa Hexal -LEG 28/LEG 27/LEG 28
Eporatio/Biopoin - LEG 20/LEG 20
Eprex/Erypo –MRP
Rapporteur: Pierre Demolis
The CHMP agreed to the PRAC recommendation (see PRAC December Minutes section 10.3).

Erivedge (EMEA/H/C/002602)
(Vismodegib), Roche Registration Ltd, Rapporteur: Kristina Dunder, Co-Rapporteur: Pierre Demolis, (treatment of advanced basal cell carcinoma)
The Committee addressed the DHPC letter regarding issue of defective label which partially affects readability.

Cimzia (EMEA/H/C/001037/II/0035/G)
MAH: UCB Pharma SA, (certolizumab pegol), Rapporteur: Kristina Dunder, Introduction of additional presentations which combine the prefilled syringe used in the currently authorised Cimzia presentations with an automatic injection device (autoinjector). The primary container closure system remains unchanged. In addition, minor editorial changes are introduced in the product information of the currently approved presentations in alignment with the product information for the new presentations.
The CHMP agreed to the request by the applicant for a clock stop to respond to the Request for Supplementary Information adopted in December 2013.

Rienso (EMEA/H/C/002215)

(Ferumoxytol), Takeda Pharma A/S, Rapporteur: Harald Enzmann, Co-Rapporteur: Romaldas Mačiulaitis, (treatment of iron deficiency with chronic kidney disease (CKD)). In October 2013, a DHPC letter was circulated with important information concerning all intravenous (IV) iron products approved/marketed in the European Union. This communication arose from a European review by the CHMP of their benefits versus risks following concerns about the risk of serious hypersensitivity reactions. The review resulted in new recommendations for managing the risk of allergic reactions associated with all IV iron-containing medicines.

Rienso (Ferumoxytol) is an IV iron product, but was not included in the above review as it was not yet authorised in the European Union at the time the review started. It was therefore agreed at the CHMP that the outcome of the referral would be applied upon finalisation. Currently this is being done via ongoing type IB variation and a DHPC is to be circulated accordingly.

12. REFERRAL PROCEDURES

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

KOGENATE Bayer (EMEA/H/C/000275/A-20/0150)

(Octocog Alfa), Bayer Pharma AG , Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Bengt Ljungberg, (treatment of haemophilia A)

Review of the benefit-risk balance following a notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, following procedural steps of Article 31 of Directive 2001/83/EC, based on pharmacovigilance data.

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

Helixate NexGen (EMEA/H/C/000276/A-20/0143)

(Octocog Alfa), Bayer Pharma AG , Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Bengt Ljungberg, (treatment of haemophilia A)

Review of the benefit-risk balance following a notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, following procedural steps of Article 31 of Directive 2001/83/EC, based on pharmacovigilance data.

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

Iclusig (EMEA/H/C/002695/A-20/0003), Orphan

(Ponatinib Hydrochloride), ARIAD Pharma Ltd, Rapporteur: Greg Markey, Co-Rapporteur: Bengt Ljungberg, (treatment of chronic myeloid leukaemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL)), PRAC Rapporteur: Julia Dunne, PRAC Co-Rapporteur: Ulla Wändel Liminga.

Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, based on pharmacovigilance data. The CHMP noted the start of referral at the PRAC in December 2013.

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

Nanotop 0.5mg (EMEA/H/29/1386)

(human albumin, denatured [NanoHSA], Rotop Pharmaka AG, Rapporteur: Harald Henzmann, Co-Rapporteurs: Kristina Dunder,

Referral procedure due to disagreement regarding quality and efficacy of the product.

MRP: DE/H/3731/001/MR

The CHMP assessed additional supportive data from additional batches of Nanotop with that of Nanocoll provided by the company, which demonstrated acceptably, that the particles size distribution for the studied size ranges as well as the batch variability for Nanotop, is in the same range as for Nanocoll.

Based on the evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that particle size distribution for the studied size range, as well as the batch variability, are similar for Nanotop and Nanocoll. The CHMP therefore considered that Nanotop is comparable to Nanocoll, and therefore an impact on clinical efficacy is not expected. It recommended that Nanotop be granted marketing authorisation in the concerned Member States.

The Committee adopted an opinion by consensus, recommending that the objections raised by Sweden should not prevent the granting of a marketing authorisation.

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

Tibolona Aristo 2.5 mg tablets (EMEA/H/A-29/1389)
(tibolone) Aristo Pharma GmbH, Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Harald Enzmann, Mutual recognition procedure number: ES/H/0223/001/DC
The Committee was reminded of the status of this referral.
The Committee discussed GCP findings on the managing of the study samples and whether clarification from the MAH was required, which would result in reverting back the short procedure to a normal timetable. After discussion an orientation was sought on whether the members were sufficiently informed to conclude the referral in December and a positive trend was observed (20 out of 32 votes in favour for a positive opinion in December).
Based on evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that bioequivalence to the reference medicinal product has been shown. The company had supplied additional evidence to indicate that the study samples had been stored and maintained under adequate temperature conditions, further supported by the concentrations recorded in the bioequivalence study. The CHMP therefore concluded that the benefits of Tibocina outweigh its risks and recommended that the marketing authorisations be granted in the concerned Member States.
The Committee adopted an opinion by majority (21 positive out of 33 votes), recommending that the objections raised by Germany should not prevent the granting of the marketing authorisations.
The divergent position (Daniel Brasseur, Harald Enzmann, Jacqueline Genoux-Hames, Alar Irs, Andrea Laslop, David Lyons, Outi Mäki-Ikola, Ivana Mikačić, Aikaterini Moraiti, Jan Mueller-Berghaus, Jean-Louis Robert, Ondřej Slanař and Karsten Bruins Slot) was appended to the opinion.
The Icelandic and Norwegian Members were not in agreement with the CHMP recommendation.
The CHMP noted the EMA communication document.

Tibocina 2.5 mg tablets (EMEA/H/A-29/1390) (tibolone) Aristo Pharma GmbH, Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Harald Enzmann, Mutual recognition procedure number: ES/H/0224/001/DC.
The Committee was reminded of the status of this referral. After discussion an orientation was sought on whether the members were sufficiently informed to conclude the referral in December and a positive trend was observed (20 out of 32 votes in favour for a positive opinion in December).
Based on evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that bioequivalence to the reference medicinal product has been shown. The company had supplied additional evidence to indicate that the study samples had been stored and maintained under adequate temperature conditions, further supported by the concentrations recorded in the bioequivalence study.
The CHMP therefore concluded that the benefits of Tibocina outweigh its risks and recommended that the marketing authorisations be granted in the concerned Member States.
The Committee adopted an opinion by majority (21 positive out of 33 votes) recommending that the objections raised by Germany should not prevent the granting of the marketing authorisations.
The divergent position (Daniel Brasseur, Harald Enzmann, Jacqueline Genoux-Hames, Alar Irs, Andrea Laslop, David Lyons, Outi Mäki-Ikola, Ivana Mikačić, Aikaterini Moraiti, Jan Mueller-Berghaus, Jean-Louis Robert, Ondřej Slanař and Karsten Bruins Slot) was appended to the opinion.
The Icelandic and Norwegian Members were not in agreement with the CHMP recommendation.
The CHMP noted the EMA communication document.

Valebo 70 mg tablets and 1 microgram capsule (EMEA/H/A-29(4)/1364)
(alendronic acid and alfacacidol) Teva Pharma B.V, Rapporteur: Harald Enzmann, Co-rapporteur: Concepcion Prieto Yerro, , Decentralised Procedure number: DE/H/3436/01/DC.

Referral procedure due to disagreements regarding the demonstration of the role of alfacalcidol in the reduction in the fall rate. List of Questions adopted in March 2013. List of Outstanding Issues adopted in July 2013.
The Committee agreed that no Oral Explanation was needed at this time (see also section 1. Oral Explanations). After discussion orientations were sought on proposed SmPC wording and whether to include a statement on the reduction of risk of falls in the elderly in section 5.1 and a split view was observed (16 out of 30 votes supporting the inclusion). In a second orientation a trend in favour of deleting the part of the indication in 4.1. referring to the reduction in the fall rate was observed (23 out of 30 votes in favour of the deletion).
Based on evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that Valebo should be granted marketing authorisation in all concerned Member States for the treatment of postmenopausal women with osteoporosis. However, although alfacalcidol has been shown in some clinical studies to reduce the risk of falls in older people, the Committee considered that this information should be included under section 5.1 of the summary of product characteristics (and not in section 4.1) and section 1 of the package leaflet.
The CHMP adopted an opinion by majority (26 positive out of 32 votes) together with the Assessment Report.
The divergent position (David Lyons, Sol Ruiz, Nela Vilceanu, Kristina Dunder, Conception Prieto Yerro and Romaldas Mačiulaitis) was appended to the opinion.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The CHMP noted the EMA communication document.

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 Committee agreed to the request of a month clock stop extension for responses to the List of Outstanding issues and adopted a revised timetable: Responses to list of outstanding issues: 12.02.2014; Restart of the procedure: 18.02.2014; Assessment report: 05.03.2014; Comments from CHMP: 10.03.2014; List of outstanding issues or CHMP opinion: March 2014 CHMP

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

Ikorel / Dancor and associated names (EMEA/H/A-30/1380)
Rapporteur: Pierre Demolis, Co-Rapporteur: Pieter de Graeff, (nicorandil), Sanofi-Aventis group of companies and associated companies, Merck group of companies and associated companies.
The Committee started a harmonisation exercise for Ikorel and associated names and Dancor and associated names. The review was triggered by the European Commission, due to the need of harmonisation of the Product Information across Member States.
The CHMP adopted a specific timetable: Start of procedure: 19.12.2013; Responses to list of questions: 27.06.2014; Restart of the procedure: 18.07.2014; Assessment report: 10.09.2014; Comments from CHMP: 15.09.2014; List of outstanding issues or CHMP opinion: September 2014 CHMP.

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

Methysergide containing products (EMEA/H/A-31/1335)

Rapporteur: Joseph Emmerich, Co-Rapporteur: Rafe Suvarna

Review of the benefit-risk balance of methysergide containing products due to safety concerns related to fibrotic risks. List of Questions adopted in May 2012. List of Outstanding Issues adopted in December 2012 and May 2013. SAG meeting held on 5 September 2013.

During the December meeting, the CHMP discussed further outstanding issues which should be addressed by the companies. The Committee agreed that no Oral Explanation was needed at this time.

See also section 1. Oral Explanations

The CHMP adopted a 4th List of Outstanding Issues with a specific timetable: Responses by MAHs: 17.01.2014; Restart of the procedure: 27.01.2014; Joint assessment report: 07.02.2014; Comments from CHMP: 11.02.2014; Oral Explanation/CHMP Opinion: February 2014 CHMP

Estradiol (topical use) (EMEA/H/A-31/1336)

Rapporteur: Martina Weise, Co-Rapporteur: Hubert Leufkens,

Medicinal products containing estradiol for intravaginal administration and administration on the skin of the vulva.

Review of the benefit-risk balance of estradiol for intravaginal administration and administration on the skin of the vulva due to observed high systemic absorption which may lead to safety issues. List of Questions adopted in June 2012, November 2012, February 2013, March 2013 and November 2013. An Oral explanation was held in November 2013.

See also section 1. Oral explanations

The Committee noted a new proposal for the wording of the indication by the MAH: *Treatment of vaginal atrophy due to oestrogen deficiency in postmenopausal women* and discussed different wordings for the indication as well as for other sections in the SmPC.

After discussion orientations on the wording of the indications were sought:

1) Treatment of vaginal atrophy due to oestrogen deficiency in postmenopausal women.

A negative trend was observed (5 positive out of 32 votes).

2) Treatment of vaginal atrophy due to oestrogen deficiency in postmenopausal women when hormone-free topical treatments have failed.

A negative trend was observed (13 positive out of 32 votes).

3) Treatment of vaginal atrophy due to oestrogen deficiency in postmenopausal women when at least one lower dose topical oestrogen treatment has failed.

A positive trend by consensus was observed.

After liaison with the MAH the Committee was informed that the MAH did not accept the proposed SmPC changes and the cancellation of the Oral Explanation.

An Oral Explanation with Dr A. Wolff was held on Monday 16 December 2013 at 17.00.

After the Oral Explanation orientations on the three indications were sought again and the above trends were in principle confirmed.

The Committee adopted a final opinion by consensus together with the Assessment Report. The Committee recommended the variation to the terms of the Marketing Authorisations for the 0.01 % w/w estradiol containing medicinal products for topical use and the variation to the terms of the Marketing Authorisations for the 0.005 % w/w estradiol /0.4 % w/w prednisolone containing medicinal products for topical use.

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

The CHMP noted the EMA public health communication.

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

No items

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,
Surveillance study of photocontact dermatitis leading to hospitalization in Europe with a special focus on topical ketoprofen and other topical NSAIDs, including evaluation of severe photosensitivity reactions (condition of the marketing authorisations).
The CHMP adopted a specific timetable for assessment of the 3-years cumulative analysis of photosensitivity reactions including photoallergy reactions (submissions received on 14 November 2013): Start: 18.02.2014; Assessment Report: 05.03.2014; Comments from CHMP: 10.03.2014; CHMP conclusion: March 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

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 2-5 December 2013: **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 submission of Periodic Safety Update Reports (EURD list) for December 2013: **For adoption**	The EURD list was adopted.
Early Notification System: December 2013 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

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

14.3. Pharmacovigilance Inspections

Pharmacovigilance Inspection reports: **for information**	*Disclosure of information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections.*
Risk-based programme for routine pharmacovigilance inspections of MAHs connected with human centrally authorised products: **for adoption**	Confidential PhV inspection programme (2nd revision for 2013).
PhV Inspections, PRAC advice: **for adoption**	

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.

15.3. Eligibility to EMA scientific services

Services for combination therapy (co-packaged regimen) Request for CHMP scientific recommendation on eligibility to the Agency's scientific services. • Report: **For adoption**	The CHMP adopted the report.

Services for combination therapy (co-packaged regimen) Request for CHMP scientific recommendation on eligibility to the Agency's scientific services. • Report: **For adoption**	The Committee noted the report.

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

• Opinion: **For adoption**	The CHMP adopted the opinion by consensus.

15.5. Nanomedicines activities

16. SCIENTIFIC ADVICE WORKING PARTY (SAWP)

Report from the SAWP meeting held on 27-29 November 2013. • Table of conclusions: **For information**	The Committee noted the report.
Election of chair of the Scientific Advice Working Party: **For adoption** Candidate: Robert Hemmings	The CHMP elected Robert James Hemmings as SAWP chair.
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 / OTHER COMMITTEES

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 16-19 December 201: **For information**	The Committee noted the report.

18. OTHER COMMITTEES

18.1. Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 10-11 December 2013: **For information**	To be sent in the Post-mail.

18.2. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 11-12 November 2013: **For information**	To be sent in the Post-mail.

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at 20-19 December 2013 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on 4-6 December 2013: **For information**	The Committee noted the report.

18.4. Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 12-13 December 2013: **For information**	The Committee noted the report.

19. INVENTED NAME ISSUES

Table of Decisions of the NRG meeting held on 14 November 2013 (EMA/713139/2013): **For adoption**	The Committee adopted the Table of Decisions of the NRG meeting held on 14 November 2013.

20. ANY OTHER BUSINESS

Reflection paper on Orphan Similarity assessment: **For discussion**	The members were informed about the reflection paper on orphan similarity. Further discussion expected at the January 2014 CHMP meeting.
Guideline on the investigation of subgroups in confirmatory clinical trials (Biostatistics Working Party): **For information**	The members were informed about the draft guideline on the investigation of subgroups in confirmatory clinical trials. Further discussion and adoption for public consultation expected at the January 2014 CHMP meeting.
Guideline on clinical investigation of medicinal products in the treatment of lipid disorders (EMA/CHMP/748108/2013): **For adoption** Overview of comments received (EMA/CHMP/748246/2013): **For adoption**	The CHMP adopted the guideline and the overview of comments received
Cardiovascular Working Party (CVS WP) response to the CHMP List of Questions regarding the impact of the ACCOAST study on of antiplatelet medicinal products: **For adoption** CVS WP response to the CHMP List of Questions regarding simplified universal indication wording in 4.1 for Type 2 Diabetes medicinal products: **For adoption**	The CHMP adopted the CVS WP proposal that no changes should be made to the SmPC of antiplatelet medicinal products. Based on the split view of the CVS WP, the CHMP agreed to consult specialist organisations on this matter and a relevant set of questions to be asked should be prepared.
Minutes of the CHMP Informal meeting held in Vilnius (29-30 October 2013): **For adoption** Topics identified for follow-up Topic leaders	Postponed to January 2014 CHMP

Nomination of a new Member for Guideline Consistency Group.	Pierre Demolis and Jan Muller-Berghaus were appointed as new members to the Guideline Consistency Group.
Nomination of CHMP member as EU expert in the ICH Expert Working Group to develop a Concept Paper for updating the ICH Guideline E11 on Paediatric Drug Development: **For discussion**	The CHMP nominated Daniel Brasseur as EU expert and noted that the PDCO chair would also be approached as potential additional EU expert for the revision of this concept paper.
Concept paper on revision of the Points to Consider on Pharmacokinetics and Pharmacodynamics in the Development of Antibacterial Medicinal Products (CHMP/EWP/2655/99) and conversion to a CHMP guideline: **For adoption for 2-month public consultation**	The CHMP agreed that a member of the Pharmacokinetics Working Party should also be involved in the creation of the relevant CHMP guideline. The concept paper was adopted for 2-month public consultation.
BMWP response to the recent position statement from the European Crohn's and Colitis Organisation (ECCO) in the Journal of Crohn's and Colitis regarding the use of biosimilars in the treatment of Inflammatory bowel disease: **For adoption**	The CHMP adopted the BMWP response.
Renin-angiotensin system (RAS)-acting agents and the planned SAG CVS: **For adoption**	The CHMP noted the PRAC List of Questions to the experts and agreed to convene a Cardiovascular SAG meeting for the Art. 31 procedure on RAS-acting agents. The CHMP also decided that while all MAHs can follow the open parts of the SAG meeting, presentations from the MAHs are not foreseen. MAHs who still want to present to the SAG CVS should group themselves to make use of the single 2-hour timeslot allocated for MAH presentation.
Joint CVMP/CHMP ad-hoc expert group on the application of 3Rs Draft concept paper on review and update of EMA guideline to implement best practice with regards to 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products: For adoption for 3-months public consultation Need to develop a concept paper for developing	The CHMP adopted the draft concept paper for 3-month public consultation.

a guideline to support product specific validation of 3Rs tests used for batch release purposes of biologicals. • Revised workplan: **For adoption**	The revised work plan was adopted.
Questions to the IDWP on the use of antiviral agents to prevent transmission of HBV: **For adoption**	The CHMP adopted the List of Questions to the IDWP.
CHMP sub-group on revision of the Guideline on Fixed dose combinations Proposal for definition of criteria applicable for clinical development of fixed dose combinations (FDCs): **For information**	The CHMP discussed the update and agreed to have one month reflection.

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)*

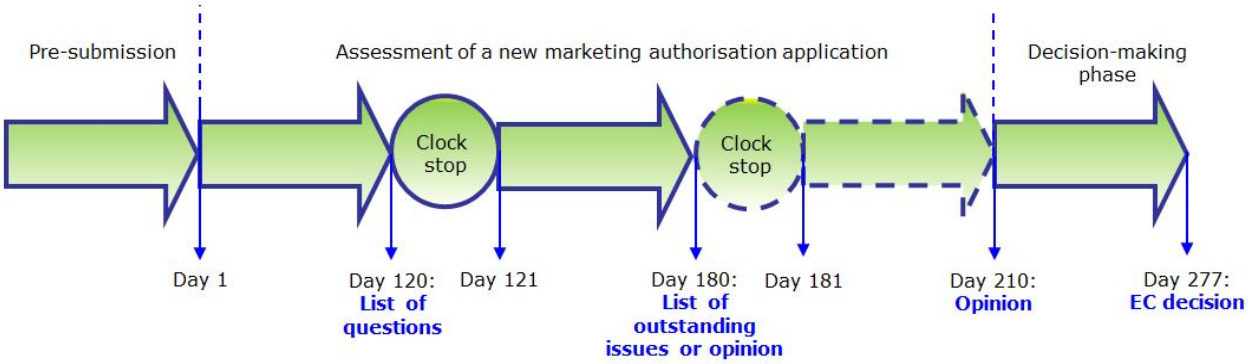
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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

List of participants: *including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 16-19 December 2013 meeeting.*

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	
Emilia Mavrokordatou	Cyprus	Full involvement	
Ondrej Slanar	Czech Republic	No participation in discussions, final deliberations and voting on:	(EMEA/H/C/002656) (canagliflozin / metformin)
			Jentadueto (EMEA/H/C/002279/II/0012) (linagliptin / metformin)
			(EMEA/H/C/002677) (empagliflozin)
			(EMEA/H/C/002713) (lurasidone)
			Ketoprofen formulation for topical use (EMEA/H/A-107/1259) (Ketum)
			Methysergide containing products (EMEA/H/A-31/1335)
			Noxafil (EMEA/H/C/000610/X/0028) (posaconazole),
			IZBA (EMEA/H/C/002738) (travoprost)
			Atripla (EMEA/H/C/000797) (Efavirenz, Emtricitabine, Tenofovir Disoproxil Fumarate), Stocrin (EMEA/H/C/000250) (Efavirenz), Sustiva (EMEA/H/C/000249) (Efavirenz)

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
Jens Heisterberg	Denmark	No participation in final deliberations and voting on:	(EMEA/H/C/002713) (lurasidone) Invega (EMEA/H/C/000746/II/0037) (paliperidone)
Alar Irs	Estonia	Full involvement	
Outi Maki-Ikola	Finland	No participation in discussions, final deliberations and voting on:	(previously Serelaxin) (EMEA/H/C/002817)
			(EMEA/H/C/002705), (MIXTURE OF POLYNUCLEAR IRON(III)-OXYHYDROXIDE, SUCROSE AND STARCHES)
			Epoetins - Aranesp- LEG 89
			Rienso (EMEA/H/C/002215/II/0008) (ferumoxytol),
			XGEVA (EMEA/H/C/002173/II/0016) (denosumab)
Pierre Demolis	France	Full involvement	
Harald Enzmann	Germany	Full involvement	
Jan Mueller-Berghaus	Co-opted	Full involvement	
Aikaterini Moraiti	Greece	Full involvement	
Agnes Gyurasics	Hungary	Full involvement	
Kolbeinn Gudmundsson	Iceland	Full involvement	
David Lyons	Ireland	Full involvement	
Juris Pokrotnieks	Latvia	No participation in discussions, final deliberations and voting on:	(previously Vedolizumab Takeda) (EMEA/H/C/002782) (vedolizumab)

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	
Jean-Louis Robert	Co-opted	Full involvement	
John Joseph Borg	Malta	Full involvement	
Pieter de Graeff	Netherlands	Full involvement	
Hubert Leufkens	Co-opted	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	
Concepcion Prieto Yerro	Spain	Full involvement	
Sol Ruiz	Co-opted	Full involvement	
Tomas Salmonson	Chair	Full involvement	
Kristina Dunder	Sweden	Full involvement	
Greg Markey	United Kingdom	Full involvement	
Robert James Hemmings	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	
Radka Montoniová	Czech Republic	Full involvement	
Jens Ersbøll	Denmark	Full involvement	
Joseph Emmerich	France	Full involvement	
Martina Weise	Germany	Full involvement	
Chrysoula Ntaousani	Greece	Full involvement	
Patrick Salmon	Ireland	Full involvement	
Daniela Melchiorri	Italy	Full involvement	
Natalja Karpova	Latvia	Full involvement	
Johann Lodewijk Hillege	Netherlands	Full involvement	
Aldona Paluchowska	Poland	Full involvement	
Dinah Duarte	Portugal	Full involvement	
Jana Klimasová	Slovakia	Full involvement	
Nevenka Trsinar	Slovenia	Full involvement	
Arantxa Sancho-Lopez	Spain	Full involvement	
Bengt Ljungberg	Sweden	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
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
Dagmar Stara	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.			
Sabine Mayrhofer	Germany	Full involvement	
Dominique Masset	France	Full involvement	
Ljiljana Milosevic-Kapetanovic	France	Full involvement	
Mette Madsen	Denmark	Full involvement	
Catherine Deguines	France	Full involvement	
Jan Willem van der Laan	Netherlands	Full involvement	
Patrick Vrijlandt	Netherlands	Full involvement	
Christophe Focke	Belgium	Full involvement	
Ana Alonso Gutierrez	Spain	Full involvement	
Giuseppe Rosano	Italy	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.			
Macarena Rodriguez Mendizabal	Spain	Full involvement	
Marion Haberkamp	Germany	Full involvement	
Roland Froetschl	Germany	Full involvement	
Susanne Steinecker	Germany	Full involvement	
Beate Ziegeler	Germany	Full involvement	
Kathryn Ord	UK	Full involvement	
Annie Eyre-Brook	UK	Full involvement	
Melanie Conteh	UK	Full involvement	
Jean-Hugues Trouvin	France	Full involvement	
Anjana M Aggarwal	UK	Full involvement	
Abi Moran	UK	Full involvement	
Ulla Wändel-Liminga	Sweden	Full involvement	
Sigrid Klaar	Sweden	Full involvement	
Bertil Jonsson			
Leigh Henderson	UK	Full involvement	
Sara Galluzzo	Italy	Full involvement	
Serge Bakchine	France	Full involvement	