16 December 2013
EMA/CHMP/723655/2013 Rev.3

Committee for Medicinal Products for Human Use (CHMP)

Agenda of December 2013 meeting

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

16 December 2013, 09:00 – 19:30, room 3A

17 December 2013, 08:30 – 19:30, room 3A

18 December 2013, 08:30 – 19:30, room 3A

19 December 2013, 08:30 – 13:00, room 3A

Declaration on conflict of interest

In accordance with the Agency's revised policy and procedure on the handling of conflicts of interests, participants in this meeting are 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 will take 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.

Health & Safety Information

In accordance with the Agency's Health and Safety policy, delegates are to be briefed on health & safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in this agenda is considered commercially confidential 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

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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 will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available.For orphan medicinal products the product name and the applicant are published as this information is already publicly available. Documents mentioned in the agenda 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 agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

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

For adoption

AGENDA (EMA/723655/2013) and Annex to CHMP agenda of the CHMP plenary session to be held 16-19 December 2013	
TIMESCHEDULE (EMA/735317/2013) of the CHMP plenary session to be held 16-19 December 2013	
MINUTES /(EMA/CHMP/738707/2013) of the CHMP plenary session held 18-21 November 2013	
MINUTES (EMA/CHMP/780238/2013) of the CHMP ORGAM meeting held on 9 December 2013	

For information

PRE-MEETING LIST of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 16-19 December 2013.	*See December 2013 minutes (to be published post January 2014 CHMP meeting)*
Draft Agenda of January 2014 CHMP meeting	

1. ORAL EXPLANATIONS

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. • Report from Scientific Advisory group Cardiovascular (SAG) meeting : **For discussion**	Oral explanation to be held on Monday 16 December 2013 at 14.00.
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. • Report from SAG Neurology meeting : **For discussion**	Oral explanation to be held on Tuesday 17 December 2013 at 9.00.
(EMEA/H/C/002546) (Laquinimod Sodium), (treatment of multiple sclerosis) List of Outstanding Issues adopted in July 2013. • Report from Safety Working Party (SWP) meeting: **For discussion**	Oral explanation to be held on Tuesday 17 December 2013 at 14.00. See also 2.1 Opinions – New full applications
(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.	Possible Oral explanation.
(EMEA/H/C/002713) (lurasidone), (treatment of schizophrenia) List of Outstanding Issues adopted in July 2013. List of Questions adopted in February 2013.	Possible Oral explanation to be held on Wednesday 18 December 2013 at 09.00.
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.	Oral explanation to be held on Wednesday 18 December 2013 at 14.00

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.	Oral explanation to be held on Tuesday 17 December 2013 at 11.00. See also section 12.4. Disagreement between Member States on application for medicinal product under Article 29(4)
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 explanation held in November 2013	Possible Oral Explanation to be held on Monday 16 December 2013 at 11.00. 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.	Possible Oral explanation on Tuesday 17 December 2013 at 16.00. 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)
List of Outstanding Issues adopted in October 2013, July 2013.
List of Questions adopted in March 2013.

(EMEA/H/C/002642)
(brimonidine), (treatment of facial erythema of rosacea)
List of Outstanding Issues adopted in October 2013.
List of Questions adopted in May 2013.

(EMEA/H/C/002546)
(laquinimod), (treatment of multiple sclerosis)
List of Outstanding Issues adopted in November 2013, July 2013.
List of Questions adopted in November 2012.

(EMEA/H/C/002553)
(florbetaben (18f)), (detection of β-amyloid in the brain)
List of Outstanding Issues adopted in October 2013.
List of Questions adopted in May 2013.

SIRTURO (EMEA/H/C/002614), Orphan
Applicant: Janssen-Cilag International N.V.,
(bedaquiline), (treatment of pulmonary tuberculosis)
List of Outstanding Issues adopted in September 2013, June 2013.
List of Questions adopted in January 2013.

(EMEA/H/C/002738)
(travoprost), (treatment of ocular hypertension or open-angle glaucoma)
List of Outstanding Issues adopted in October 2013.
List of Questions adopted in May 2013.

(EMEA/H/W/003838)
(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))

Winfuran (EMEA/H/C/002683), Orphan
Applicant: Toray Europe Limited, (nalfurafine), (treatment of uraemic pruritus)
List of Outstanding Issues adopted in July 2013.
List of Questions adopted in November 2012.
Oral explanation was held in November 2013.

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.

(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.

(EMEA/H/C/002621)
(propranolol), (treatment of proliferating infantile haemangioma)
List of Questions adopted in July 2013.

(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.

(EMEA/H/C/002677) (empagliflozin), (treatment of type II diabetes mellitus) List of Questions adopted in July 2013.	
(EMEA/H/C/002782) (vedolizumab), (treatment of Ulcerative Colitis and Crohn's Disease) List of Questions adopted in July 2013.	
Vimizim (EMEA/H/C/002779), Orphan Applicant: BioMarin Europe Ltd, (recombinant human n-acetylgalactosamine-6-sulfatase (rhgalns)), (treatment of mucopolysaccharidosis) List of Questions adopted in September 2013.	Note: The ANSM in France granted authorisation of a compassionate use of Vimizim in treatment of mucopolysaccharidosis on 14 November 2013.
(EMEA/H/C/002557) (flutemetamol f-18), (indicated for the visual detection of amyloid-beta neuritic plaques in the brains) List of Questions adopted in April 2013.	
(EMEA/H/C/002656) (canagliflozin / metformin), (treatment of type 2 diabetes mellitus) List of Questions adopted in July 2013.	

2.3. Day 120 List of Questions – New full applications

(EMEA/H/C/002806) (busulfan), (conditioning prior to conventional haematopoietic progenitor cell transplantation (HPCT)) • Similarity Assessment report: **For adoption**	
(EMEA/H/C/002272) (clopidogrel / acetylsalicylic acid), (indicated for the prevention of atherothrombotic events)	

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)),

- Letter from the applicant dated 3 December 2013 requesting extension of time frame to respond to the List of Outstanding Issues adopted in November 2013 : **For discussion**

(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 renaldisease (ESRD)),

- Additional information

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),

- Additional information

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.

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.

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.

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.

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.

Halaven (EMEA/H/C/002084/II/0011)

MAH: Eisai Europe Ltd., (eribulin), Rapporteur: Bengt Ljungberg, Co-Rapporteur: Jens Ersbøll, This application concerns an extension of the 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.

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.

Jentadueto (EMEA/H/C/002279/II/0012)
MAH: Boehringer Ingelheim International GmbH, (linagliptin / metformin), Rapporteur: Pieter de Graeff, PRAC Rapporteur: Menno van der Elst, , The MAH applied for a an extension of the indication for the combination therapy with insulin in adult patients with type 2 diabetes when insulin and metformin do not provide adequate glycaemic control. Consequently, the MAH proposed the update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC. The Package Leaflet has been updated accordingly. Request for Supplementary Information adopted in October 2013.

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.

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.

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.

- Letter from the MAH requesting an additional clock stop to respond to the Request for Supplementary Information adopted in November 2013: **For discussion**

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.

- List of experts for the SAG Oncology meeting : **For adoption**

Vfend (EMEA/H/C/000387/II/0097)

(VORICONAZOLE), Applicant: Pfizer Limited, Rapporteur: Hans 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.

- List of experts for the SAG anti-infectives meeting : **For adoption**

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. Consequential changes to sections 1 and 4 of the PL.

- Assessment Report of similarity of Kalydeco versus Bronchitol: **For adoption**

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.

- Letter from the MAH dated 6 December 2013 requesting an extension of the timeframe for the provision of the responses to the CHMP Request for Supplementary Information : **For 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))
Negative Opinion adopted in November 2013.

- Letter from the applicant dated 28 November 2013 requesting a re-examination of the Opinion adopted in November 2013 and consultation of SAG: **For information**
- Appointment of Re-examination (Co)Rapporteur: **For discussion**
- Draft timetable: **For information**

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.

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. Signal for orlistat on "Pharmacokinetic drug interaction (at absorption) with highly active antiretroviral therapy (HAART) leading to loss of HAART efficacy. • PKWP Report: **For adoption**	Follow-up from October 2013.
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 List of Outstanding Issues adopted in November 2013.	

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)

- Letter from the MAH informing of a voluntary withdrawal of the product by February 2014 due to commercial reasons: **For information**

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

Erivedge (EMEA/H/C/002602)

(Vismodegib), Roche Registration Ltd, Rapporteur: Kristina Dunder, Co-Rapporteur: Pierre Demolis, (treatment of advanced basal cell carcinoma),

- DHPC regarding issue of defective label which partially affects readability: **For information**

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.

PRAC outcome at December PRAC meeting.

- Opinion: **For adoption**

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.

PRAC outcome at December PRAC meeting.

- Opinion: **For adoption**

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.

Start of referral procedure at December 2013 PRAC

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.

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

- Opinion: **For adoption**

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,

Referral procedure due to concerns on bioequivalence of the generic product.

- Opinion: **For adoption**

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. Referral procedure due to concerns on bioequivalence of the generic product. • Opinion: **For adoption**	
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. • Opinion: **For adoption**	Oral explanation to be held on Tuesday 17 December 2013 at 11.00. See also section 1. Oral explanations

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. Letter from the European Commission notifying of the official referral under article 30: **For information**	Start of procedure

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. • Opinion: **For adoption**	Oral explanation on Tuesday 17 December 2013 at 16.00. See also section 1. Oral explanations
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. Oral explanation was held in November 2013	Oral Explanation to be held on Monday 16 December 2013 at 16.00. See also section 1. Oral explanations

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 Montoniova,
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).

- Timetable for assessment: **For adoption**

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**

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for December 2013: **for adoption**

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**

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.*

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 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.
Services for combination therapy (co-packaged regimen) Request for CHMP scientific recommendation on eligibility to the Agency's scientific services.

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

Request for CHMP opinion under Art. 57 (1)P of Regulation (EC) No 726/2004

Opinion: **For adoption**

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**	
Election of chair of the Scientific Advice Working Party: **For adoption** Candidate: Robert Hemmings	
Scientific advice letters:	*Disclosure of information related to scientific advice letters cannot be released 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 2013: **For information**

17.2. OTHER COMMITTEES

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.

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.

Paediatric Committee (PDCO)

PIPs reaching D30 at 19-20 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**

Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 12-13 December 2013: **For information**

18. INVENTED NAME ISSUES

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

19. ANY OTHER BUSINESS

Reflection paper on Orphan Similarity assessment: **For discussion and adoption**

Guideline on the investigation of subgroups in confirmatory clinical trials (Biostatistics Working Party): **For discussion**

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**

Cardiovascular Working Party (CVS WP) response to the CHMP List of Questions regarding the impact of the 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**	Follow–up from November 2013.
Minutes of the CHMP Informal meeting held in Vilnius (29-30 October 2013): **For adoption** Topics identified for follow-up Topic leaders	
Nomination of a new Member for Guideline Consistency Group.	
Nomination of CHMP member as EU expert in the ICH Expert Working Group top develop a Concept Paper for updating the ICH Guideline E11 on Paediatric Drug Development: **For discussion**	
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**	
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**	

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)*

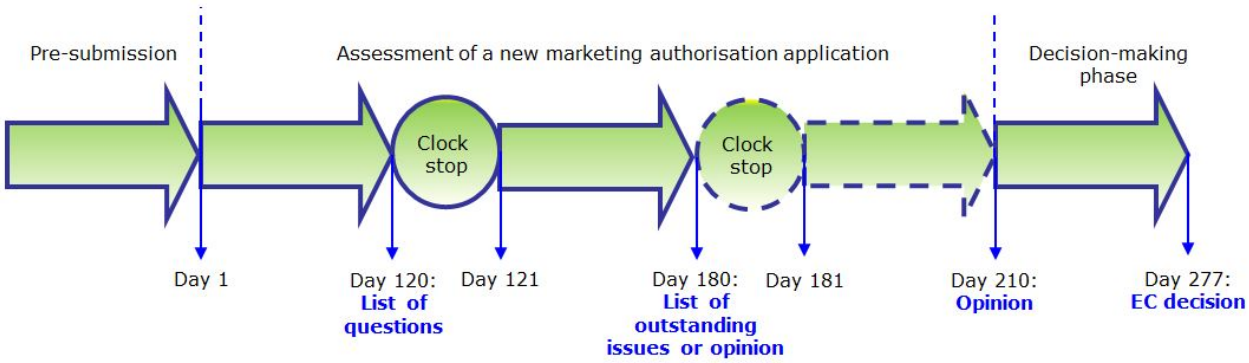
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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