22 April 2014
EMA/CHMP/169875/2014
Procedure Management and Business Support Division

Committee for Medicinal Products for Human Use (CHMP)

Agenda of meeting to be held on 22-25 April 2014

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

22 April 2014, 15:00 – 19:30, room 3A

23 April 2014, 08:30 – 19:30, room 3A

24 April 2014, 08:30 – 19:30, room 3A

25 April 2014, 08:30 – 13:00, room 3A

Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present following a request for access to documents under Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

Health & Safety Information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential and therefore not disclosed. With regards to therapeutic indications listed against products it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. The procedures discussed by the CHMP are on-going and therefore are considered

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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 applicant details are published as this information is already publicly available. Of note, this agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

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

AGENDA (EMA/CHMP/169875/2014) and Annex to CHMP agenda of the CHMP plenary session to be held 22-25 April 2014	
TIMESCHEDULE of the CHMP plenary session to be held 22-25 April 2014	
MINUTES (EMA/CHMP/189248/2014) of the CHMP plenary session held 17-20 March 2014	
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 22-25 April 2014	*See April 2014 minutes (to be published post May 2014 CHMP meeting)*
Draft Agenda *of May 2014 CHMP* meeting	

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1 ORAL EXPLANATIONS

1.1 Pre-authorisation Procedure Oral Explanations

(EMEA/H/C/002633), Orphan, (tobramycin), Applicant: PARI Pharma GmbH, (treatment of chronic pulmonary infection) List of Outstanding Issues adopted in October 2013 and March 2014. List of Questions adopted in February 2013. • Similarity Assessment Report: Adopted by written procedure on 2nd April 2014	Opinion or possible oral explanation to be held on Thursday 24 April 2014 at 9.00 See also 2.1 Opinions- New full applications

1.2 Re-examination Procedure Oral Explanation

No items

1.3 Post-authorisation Procedure Oral explanation

Pradaxa (EMEA/H/C/000829/II/0048/G) (Dabigatran Etexilate Mesilate), MAH: Boehringer Ingelheim International GmbH, (dabigatran etexilate), Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis, "Extension of indications to two new related indications: • Treatment of acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and prevention of related death (a VTEt) • Prevention of recurrent deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and related death (s VTEp)" Request for Supplementary Information adopted in September 2013.	Oral explanation to be held on Tuesday 22 April 2014 at 16.00. See also 4.1 Type II variations – extension of indications; Opinions

1.4 Referral Procedures Oral Explanations

Caustinerf arsenical® and Yranicid arsenical® and associated names, paste for dental use (oral formulations) (EMEA/H/A-31/1382) (lidocaine, ephedrine, arsenic trioxide), SEPTODONT and A.T.O. ZIZINE, Rapporteur: Alar Irs, Co-Rapporteur: Joseph Emmerich, Article 31 triggered by the ANSM for ephedrine hydrochloride, lidocaine and arsenous anhydride containing medicinal products for topical use, based on genotoxicity data. List of Outstanding Issues adopted in February 2014.	Oral explanation to be held on Wednesday 23 April 2014 at 11.00. See also 12.6 Community Interests- Referral under Article 31
Estradiol (topical use) (EMEA/H/A-31/1336) Re-examination Rapporteur: Arantxa Sancho, Re-examination Co-Rapporteur: Milena Stain, Review of the benefit-risk balance of medicinal products containing estradiol for intravaginal administration and administration on the skin of the vulva due to observed high systemic absorption which may lead to safety issues.	Possible oral explanation to be held on Wednesday 23 April 2014 at 14.00. See also 12.7 Re-examination Procedure under Article 32(4) of Directive 2001/83/EC

2 NEW APPLICATIONS

2.1 Opinions – New full applications

(EMEA/H/C/002643), (trametinib), (treatment of unresectable or metastatic melanoma with a BRAF V600 mutation) Oral explanation held in March 2014. List of Outstanding Issues adopted in November 2013. List of Questions adopted in June 2013.	
(EMEA/H/C/002633), Orphan, (tobramycin), Applicant: PARI Pharma GmbH, (treatment of chronic pulmonary infection) List of Outstanding Issues adopted in October 2013 and March 2014. List of Questions adopted in February 2013.	Opinion or possible oral explanation to be held on Thursday April 2014 at 9.00. See also 1.1 Pre-authorisation Procedure Oral Explanations

2.2 Day 180 List of outstanding issues – New full applications

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

(EMEA/H/C/002799), Orphan,
(obinutuzumab), Applicant: Roche Registration Ltd (treatment of chronic lymphocytic leukaemia)
List of Questions adopted in September 2013.

- BWP Report: **For adoption**

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

2.3 Day 120 List of Questions – New full applications

(EMEA/H/C/003768)
(daclatasvir), (treatment of chronic hepatitis C virus (HCV))

(EMEA/H/C/002772) Orphan
(dasiprotimut-t), Applicant: Biovest Europe Ltd, (treatment of non-Hodgkin's lymphoma (FL))

- BWP Report: **For adoption**

(EMEA/H/C/003773)
(cangrelor), (indicated for the reduction of thrombotic cardiovascular events (including stent thrombosis) in adult patients with coronary artery disease undergoing percutaneous coronary intervention (PCI). Also indicated to maintain P2Y12 inhibition in adult patients with acute coronary syndromes or in patients with stents who are at increased risk for thrombotic events (such as stent thrombosis) when oral P2Y12 therapy is interrupted due to surgery)

(EMEA/H/C/003750), Orphan, ATMP,
(substance to be reviewed) allogenic human heterologous liver cells), (treatment of urea cycle disorders (UCD))

- BWP Report: **For adoption**

(EMEA/H/C/002739)
(human alpha1-proteinase inhibitor), (treatment to slow the underlying destruction of lung tissue)

- BWP Report: **For adoption**

(EMEA/H/C/002066)
(ciclosporin), (treatment of dry eye disease in adult patients with severe keratitis that does not improve despite treatment with tear substitutes)

(EMEA/H/C/002788), Orphan,
(tolvaptan), Applicant: Otsuka Pharmaceutical Europe Ltd, (treatment of autosomal dominant polycystic kidney disease (ADPKD))

(EMEA/H/C/003800), Orphan
(ketoconazole), Applicant: Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare, (treatment of Cushing's syndrome)

(EMEA/H/C/002789), Orphan
(levofloxacin), Applicant: Aptalis Pharma SAS, (indicated for long term management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis (CF) aged 12 years and older)

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

(EMEA/H/C/002396)
(safinamide), (treatment of Parkinson's disease (PD))

(EMEA/H/C/002661), Orphan
(recombinant l-asparaginase), Applicant: medac Gesellschaft fuer klinische Spezialpraeparate mbH, (combination therapy for B/T cell lymphoblastic leukaemia (ALL) or B/T cell lymphoblastic lymphoma (LBL))

- CHMP similarity assessment report: **For adoption**
- BWP Report: **For adoption**

(EMEA/H/C/003787)
(tadalafil), (treatment of erectile dysfunction in adult males)

(EMEA/H/C/002800), Orphan, (dinutuximab), (treatment of high-risk neuroblastoma)

- BWP Report: **For adoption**

(EMEA/H/C/002840)
(dalbavancin), (treatment of complicated skin and soft tissue infections (cSSTI))

(EMEA/H/C/002814)
(vorapaxar), (indicated for the reduction of atherothrombotic events)

2.4 Update on on-going new applications for Centralised Procedures

(EMEA/H/C/003906), Orphan
(ketoconazole), Applicant: Laboratoire HRA Pharma, (treatment of Cushing's syndrome)

- Similarity Assessment report: **For adoption**

(EMEA/H/C/002418), Orphan
(Dexamethasone Acetate), LABORATOIRES CTRS BOULOGNE BILLANCOURT, (treatment of symptomatic multiple myeloma)
List of Outstanding Issues adopted in September 2013 and February 2014.
List of Questions adopted in May 2013.

- Letter from the applicant dated 16 April 2014 requesting a clock stop for the submission of responses to the 2nd Day 180 CHMP List of Outstanding Issue: **For discussion**

(EMEA/H/C/003771)
(Nonacog Gamma), (treatment of haemophilia B)

- Letter from the applicant dated 15 April 2014 requesting a clock stop for the submission of responses to Day 120 List of Questions adopted in March 2014: **For information**

(EMEA/H/C/002647)
(insulin degludec / liraglutide), (treatment of type 2 diabetes mellitus)
List of Outstanding Issues adopted in March 2014.
List of Questions adopted in October 2013.

- Preliminary List of experts to SAG CVS : **For adoption**

(EMEA/H/C/002817) (serelaxin)

- List of Questions to SAG CVS : **For adoption**
- List of experts for SAG CVS: **For adoption**

(EMEA/H/C/002548), Orphan
(afamelanotide), Applicant: Clinuvel (UK) Limited, (treatment of phototoxicity in adult patients with erythropoietic protoporphyria (EPP))
List of Outstanding Issues adopted in March 2013. List of Questions adopted in July 2012.

- List of Questions to experts for ad-hoc meeting: **For adoption**

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

- List of Questions to SAG Oncology: **For adoption**

2.5 Products in the Decision Making Phase

Masican (EMEA/H/C/002670), Orphan
(MASITINIB), Applicant: AB Science, Rapporteur: Jens Ersbøll, Co-Rapporteur: Greg Markey, (treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST))Negative Opinion adopted in March 2014

- Request from the European Commission for clarification in relation to the Opinion adopted by the CHMP for Masican at its March 2014 meeting: **For discussion**

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

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

No items

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

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

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

Humalog (EMEA/H/C/000088/X/0125),
(insulin lispro), MAH: Eli Lilly Nederland B.V., Rapporteur: Robert James Hemmings, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, "To add a new strength (200 U/ml KwikPen presentation)."

Liprolog (EMEA/H/C/000393/X/0092),
(insulin lispro), MAH: Eli Lilly Nederland B.V., Informed Consent of Humalog, Rapporteur: Robert James Hemmings, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, "To add a new strength (200 U/ml KwikPen presentation)."

Zoledronic acid Teva (EMEA/H/C/002439/X/0008), (zoledronic acid), MAH: Teva Pharma B.V., Generic of Zometa, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PTL: Irene Garcia Bravo, "Line extension to include a new pharmaceutical form, solution for infusion which has three new presentations."

3.4 Update on on-going 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 - Type II variation; Extension of indication

Gilenya (EMEA/H/C/002202/II/0021), (fingolimod), MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, "To modify the indication section 4.1 of Gilenya to extend the patient population from patients with high disease activity despite treatment with a beta-interferon (IFN) to patients with high disease activity despite treatment with a disease modifying therapy (DMT)." Request for Supplementary Information adopted in October 2013 and April 2014.	
Invega (EMEA/H/C/000746/II/0037), (paliperidone), MAH: Janssen-Cilag International N.V., Rapporteur: Filip Josephson, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue, PRAC Co-Rapporteur: Martin Huber, "Extension of indication to add the treatment of schizophrenia in adolescents 12 years and older." Request for Supplementary Information adopted in December 2013, June 2013.	
Javlor (EMEA/H/C/000983/II/0011), (vinflunine ditartrate), MAH: Pierre Fabre Médicament, Rapporteur: Greg Markey, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Julie Williams, "Extension of Indication: in combination with capecitabine for the treatment of adult patients with locally advanced or metastatic breast cancer previously treated with or resistant to an anthracycline and who are taxane resistant." Request for Supplementary Information adopted in September 2013.	

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

Nexavar (EMEA/H/C/000690/II/0035), Orphan
(sorafenib), MAH: Bayer Pharma AG, Rapporteur: Filip Josephson, Co-Rapporteur: Dinah Duarte, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of indication to include treatment of differentiated thyroid carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated. The Package Leaflet is updated accordingly. The product information is also revised in line with QRD version 9.0. In addition the MAH took the opportunity to update the details of the local representatives in the package leaflet."
Request for Supplementary Information adopted in October 2013

Pradaxa (EMEA/H/C/000829/II/0048/G)
(Dabigatran Etexilate Mesilate), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis, "Extension of indications to two new related indications:
• Treatment of acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and prevention of related death (a VTEt)
• Prevention of recurrent deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and related death (s VTEp)"
Request for Supplementary Information adopted in September 2013.

Prezista (EMEA/H/C/000707/II/0063), (darunavir), MAH: Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Sabine Straus, "Update of section 4.1 of the SmPC for the 100mg/ml oral suspension and the 400mg, 800mg film-coated tablets with information on the use of darunavir with cobicistat as pharmacokinetic enhancer. Consequential changes have been introduced in the SmPC and the PL of all formulations. Update of the Annex II with a correction to the address of one of the manufacturers responsible for batch release. Update of the PL with the local representatives' contact information for France, Romania, Ireland and Cyprus."

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

Rienso (EMEA/H/C/002215/II/0008), (ferumoxytol), MAH: Takeda Pharma A/S, Rapporteur: Harald Enzmann, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Martin Huber, "Extension of indication: all cause iron deficiency anaemia when oral therapy is ineffective or inappropriate or where there is a need for rapid iron repletion
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were proposed to be updated. The Package Leaflet was proposed to be updated accordingly. The MAH took the opportunity to propose minor editorial changes to the SmPC and to propose the update of the Product Information in line with the latest version of the QRD template (9.0)"
Request for Supplementary Information adopted in October 2013.

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

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

WS0523
Gardasil-EMEA/H/C/000703/WS0523/0047
Silgard-EMEA/H/C/000732/WS0523/0045
(human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)), MAH: Merck Sharp & Dohme Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Pierre Demolis, "Extension of indication to include prevention of premalignant anal lesions and anal cancer."

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

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

- Letter from the MAH informing of the decision to withdraw this application: **For information**

5 ANCILLARY MEDICINAL SUBSTANCES IN MEDICAL DEVICES

5.1 Opinions/ List of outstanding issues / List of Questions

(EMEA/H/D/002769),
(thrombin), (indicated in surgical procedures)
List of Questions adopted in September 2013.

- Day 180 List of Outstanding Issues: **For adoption**
- BWP Report: **For adoption**

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

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

- Timetable: **For information**
- List of experts to SAG Oncology: **For adoption**

Nerventra (EMEA/H/C/002546)
Applicant: Teva Pharma GmbH, (laquinimod),
(treatment of multiple sclerosis)
Negative Opinion adopted in January

- List of experts to SAG CVS : **For information**
- Revised timetable: **For adoption**

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.

(veruprevir (ABT-450), ritonavir, ombitasvir (ABT-267))(treatment of genotype 1 and 4 chronic hepatitis C),

- Request for accelerated assessment Briefing note and Rapporteurs' recommendation: **For adoption**

(dasabuvir (ABT-333))(treatment of genotype 1 chronic hepatitis C),

- Request for accelerated assessment Briefing note and Rapporteurs' recommendation: **For adoption**

11 POST-AUTHORISATION ISSUES

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

Herceptin (EMEA/H/C/000278)
(trastuzumab), MAH: Roche Registration Ltd, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Greg Markey, (treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)), Falsification of Herceptin 150 mg powder for concentrate for solution for infusion

- DHPC: **For information**
- EMA Press Release: **For information**

Pradaxa (EMEA/H/C/000829/ LEG 042)
(Dabigatran Etexilate Mesilate), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis, (prevention of venous thromboembolic events).

- Request for Supplementary Information: **For adoption**

Tamiflu (EMEA/H/C/000402)
(Oseltamivir Phosphate), MAH: Roche Registration Ltd, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Bruno Sepodes, (treatment and prevention of influenza),
Cochrane Review

12 REFERRAL PROCEDURES

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

No items

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

No items

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

No items

12.4 Disagreement between Member States on application for medicinal product (Potential serious risk to Public Health) –under Article 29(4) of Directive 2001/83/EC

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

- Final List of expert to SAG Psychiatry: **For adoption**

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

Amoxil (EMEA/H/A-30/1372)
(amoxicillin), MAH: GlaxoSmithKline**,** Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro,
List of Questions adopted in July 2013

- List of Outstanding Issues / Opinion: **For adoption**

Plendil (EMA/H/A-30/1385)
(felodipine), Astra Zeneca group of companies and associated companies, Rapporteur: Alar Irs, Co-Rapporteur: Martina Weise,
The Committee started a harmonisation exercise for Plendil and associated names. The review was triggered by the European Commission, due to the need of harmonisation of the Summary of Product Characteristics across Member States.
List of Questions adopted in November 2013.

- List of Outstanding Issues / Opinion: **For adoption**

Nasonex (EMEA/H/A-30/1374)
(mometasone), nasal spray suspension, MAH: Merck Sharp & Dohme, Rapporteur: Kristina Dunder, Co-Rapporteur: David Lyons,
Nasonex was included in the list of products for SmPC harmonisation, drawn up by the CMDh, in accordance with Article 30(2) of Directive 2001/83/EC.

- Revised timetable: **For adoption by written procedure**

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

Caustinerf arsenical® and Yranicid arsenical® and associated names, paste for dental use (oral formulations) (EMEA/H/A-31/1382)
(lidocaine, ephedrine, arsenic trioxide), SEPTODONT and A.T.O. ZIZINE, Rapporteur: Alar Irs, Co-Rapporteur: Joseph Emmerich,
Article 31 triggered by the ANSM for ephedrine hydrochloride, lidocaine and arsenous anhydride containing medicinal products for topical use, based on genotoxicity data.
List of Outstanding Issues adopted in February 2014.

- Opinion: **For adoption**

Oral explanation to be held on Wednesday 23 April 2014 at 11.00.
See 1.4. Referral Procedures Oral Explanations

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097) Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff, • FUM related to the 3rd annual cumulative safety reviews on nephrogenic systemic fibrosis (NSF): Omniscan (GE HealthCare) third monthly update and interim analysis report submission as requested by CHMP in November 2013 and assessment report: **For adoption** • Inspection report: **For adoption**	
Adrenaline auto injectors (EMEA/H/A-31/1398) Rapporteur: To be appointed, Co-Rapporteur: To be appointed Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients. • Notification from MHRA dated 2 April 2014: **For information** • Appointment of (Co) Rapporteur: **For discussion** • List of questions: **For adoption** • Timetable: **For adoption**	

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

Estradiol (topical use) (EMEA/H/A-31/1336) Re-examination Rapporteur: Arantxa Sancho, Re-examination Co-Rapporteur and Milena Stain, Review of the benefit-risk balance of medicinal products containing estradiol for intravaginal administration and administration on the skin of the vulva due to observed high systemic absorption which may lead to safety issues • Re-examination Opinion: **For adoption**	Re-examination Opinion Oral explanation to be held on Wednesday 23 April 2014 at 11.00. See 1.4. Referral Procedures Oral Explanations

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,

- Assessment reports of 3-years cumulative analysis of photosensitivity reactions including photo allergy reactions together with a report of the effectiveness of risks minimisation measures (submissions received on 14 November 2013 as well as, for the patch formulation, submissions received on 13 November 2013, 29 November 2013 (including minutes and report of the Expert Panel meeting held on 11 November 2013), 24th February 2014 (containing upcoming publication entitled 'Serious photocontact dermatitis induced by topical ketoprofen depends on formulation') and 6th March 2014)
- Assessment reports of the 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 (PASS pilot study) (submissions received on 14 November 2013)
- Requests of 2-months extension for submission of responses from EG S.p.A., Menarini and Sanofi for ketoprofen FUM art.107 (following outcomes of the March 2014 CHMP meeting): **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

Crestor and associated names (EMEA/H/A-29-PAE/1378)
MAH: AstraZeneca, (rosuvastatin), Rapporteur: Pieter de Graeff, Co-Rapporteur: Radka Montoniová,
Application to extend the age range of the existing paediatric indication [hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments is inadequate] from patients aged 10 to 17 to patients aged 6 to 17 years.

- Opinion: **For adoption**

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 7-10 April 2014: **For information**

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2014: **For adoption**

Early Notification System:
April 2014 Early Notification System on Envisaged CHMP Recommendations for Regulatory Action (based on Identified Safety Concerns) Accompanied by Communication to the General Public: **For information**

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 Programme 2014-2015: **For adoption**	

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

No items

15.2 Briefing meetings (Innovation Task Force)

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

ITF Briefing Meeting: **For information**

15.3 Eligibility to EMA scientific services

No items

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

Update on CHMP opinion under Art. 57 (1)P of Regulation (EC) No 726/2004: **For information**

15.5 Nanomedicines activities

No items

16 SCIENTIFIC ADVICE WORKING PARTY (SAWP)

Report from the SAWP meeting held on 31 March-3 April 2014 Table of conclusions: **For information**	
Scientific advice letters:	*Disclosure of information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.*

17 SATELLITE GROUPS

17.1 Coordination Group for Mutual Recognition and Decentralised Procedures

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures Human (CMDh) on the meeting held on 21-23 April 2014: **For information**	
Letter to CHMP on Classification of levothyroxine and data requirements for levothyroxine applications **Levothyroxine 50 microgram /5ml and 100 microgram/5 ml oral solutions** Data requirements for Art 10a (well-established used) levothyroxine applications and whether levothyroxine should be considered as a narrow therapeutic index drug(NTID) or critical dose drug (CDD) Letter from Chair of CMDh: **for information** List of questions from CMDh to be addressed by CHMP WPs/expert group: **for agreement**	

18 OTHER COMMITTEES

18.1 Committee for Orphan Medicinal Products (COMP)

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

18.2 Committee for Herbal Medicinal Products (HMPC)

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

18.3 Paediatric Committee (PDCO)

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

18.4 Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 15-16 April 2014: **For information**

19 INVENTED NAME ISSUES

No items

20 ANY OTHER BUSINESS

Election of BWP Vice Chair
Presentation by EC on the Delegated Regulation on Post-Authorisation Efficacy Studies (PAES)
EMA presentation on implementation steps on PAES
Guideline on treatment of Juvenile Idiopathic Arthritis (EMA/CPMP/422/04): **For adoption for 6-months public consultation**
Guideline on non-clinical and clinical development of similar biological medicinal products containing recombinant human insulin and insulin analogues (EMEA/CHMP/BMWP/32775/2005_Rev. 1): **For adoption for 3-months public consultation** (2nd consultation).
Guideline on process validation for the manufacture of biotechnology-derived active substances and data to be provided in the regulatory submission (EMA/CHMP/BWP/187338/2014): **For adoption for 6-month public consultation**
Guideline on Influenza Vaccines Quality Module (EMA/CHMP/BWP/310834/2012): **For adoption** • Overview of comments: **For information**

Concept paper on Viral safety of blood products with respect to hepatitis E (EMA/CHMP/BWP/78086/2014): **For adoption for 3-month public consultation**
Guideline on non-clinical local tolerance testing of medicinal products (EMA/CHMP/SWP/187944/2014 Rev. 1): **For 3-month public consultation**
Questions and answers on the withdrawal of the 'Guideline on pharmacokinetics and metabolic studies in the safety evaluation of new medicinal products in animals (3BS11A)' (EMA/CHMP/SWP/191104/2014): **For adoption**
Draft Minutes SWP Meeting on 11-12 February (EMA/CHMP/SWP/131453/2014): **For information**
Revised SWP Work plan 2014 (EMA/CHMP/SWP/743862/2013): **For adoption**
ToD/Minutes of the BSWP plenary meeting held on 6-7 March 2014 (EMA/141899/2014): **For information**
Survey results from "Alliance for Safe Biologic Medicines" on prescribing habits and knowledge of biosimilar medicines: **For information** • INN / naming topic and WHO activities • ADRs reporting
2014 initial MAAs submission planning update: **For discussion**
Class labelling for antiretroviral medicinal products regarding mitochondrial dysfunction, lactic acidosis and lipodystrophy. Update on regulatory framework
Draft guideline on literature monitoring: **For information**

Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 1)*

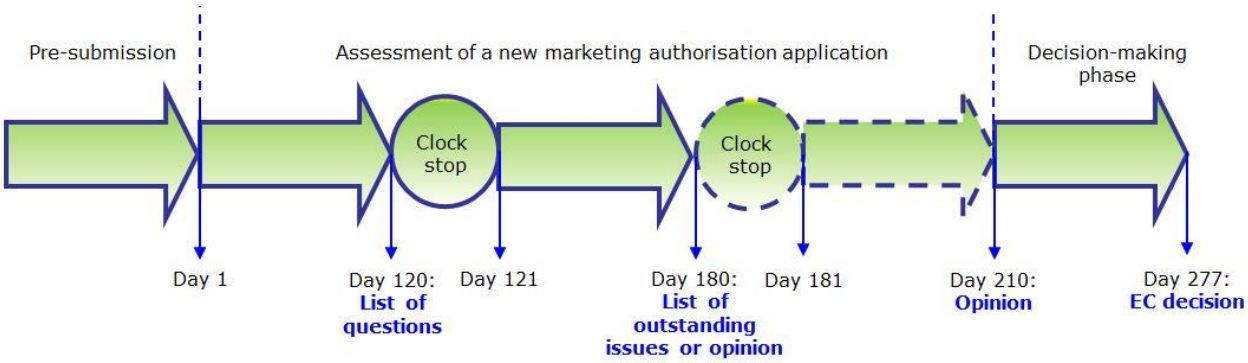
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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

New applications *(section 2)*

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

Section 2.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 2.2 (**Day 180 List of outstanding issues**) and 2.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 2.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 2.5, **products in the decision making phase**.

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

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 4)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 3. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 5)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 6)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section 7)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 8)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 9)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 10)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 11)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 12)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 13)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 14)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 15)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 16)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 17)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 18)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.