17 February 2014
EMA/CHMP/723655/2014
Procedure Management and Business Support Division

Committee for Medicinal Products for Human Use (CHMP)

Agenda of meeting to be held on 17-20 February 2014

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

17 February 2014, 13:00 – 19:30, room 3A

18 February 2014, 08:30 – 19:30, room 3A

19 February 2014, 08:30 – 19:30, room 3A

20 February 2014, 08:30 – 15:00, 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 confidential. Additional details on some of these procedures will be published in the CHMP meeting

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

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

AGENDA (EMA/CHMP/723655/2014) and Annex to CHMP agenda of the CHMP plenary session to be held 17-20 February 2014: **For adoption**	
AGENDA (EMA/CHMP/55710/2014) of ORGAM meeting to be held within the CHMP plenary session of February 2014: **For adoption**	
TIMESCHEDULE of the CHMP plenary session to be held 17-20 February 2014: **For adoption**	
MINUTES (EMA/CHMP/59462/2014) of the CHMP plenary and session held 20-23 January 2014: **For adoption**	
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 on 17-20 February 2014: **For information**	*See February 2014 minutes (to be published post March 2014 CHMP meeting)*
Draft Agenda of CHMP plenary to be held on 17-20 March 2014 CHMP: **For information**	

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1 ORAL EXPLANATIONS

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Folcepri (EMEA/H/C/002570), Orphan, (etarfolatide), Applicant: Endocyte Europe, B.V., (indicated for single photon emission computed tomography (SPECT) imaging) List of Outstanding Issues adopted in November 2013. List of Questions adopted in March 2013.	Possible Oral explanation to be held on Tuesday 18 February 2014 at 14.00.
Neocepri (EMEA/H/C/002773), Orphan, (folic acid), Applicant: Endocyte Europe, B.V., (indicated for the enhancement of etarfolatide single photon emission computed tomography (SPECT) image quality) List of Outstanding Issues adopted in November 2013. List of Questions adopted in March 2013.	Possible Oral explanation to be held on Tuesday 18 February 2014 at 14.00.
Vynfinit (EMEA/H/C/002571), Orphan, (vintafolide), Applicant: Endocyte Europe, B.V., (treatment of platinum resistant ovarian cancer (PROC)) List of Outstanding Issues adopted in November 2013. List of Questions adopted in March 2013.	Possible Oral explanation to be held on Tuesday 18 February 2014 at 14.00.
(EMEA/H/C/002782), (vedolizumab), (treatment of Ulcerative Colitis and Crohn's Disease) List of Outstanding Issues adopted in December 2013. List of Questions adopted in July 2013.	Possible Oral Explanation to be held on Tuesday 18 February 2014 at 9:00.

1.2 Re-examination procedure oral explanation

No items

1.3 Post-authorisation procedure oral explanation

No items

1.4 Referral procedure oral explanations

Protelos (EMEA/H/C/000560) (Strontium Ranelate), Les Laboratoires Servier, Rapporteur: Bengt Ljungberg, Co-Rapporteur: Andrea Laslop, (treatment of osteoporosis) PRAC outcome at January 2014 PRAC meeting. Oral explanation held in January 2014.	Possible Oral explanation to be held on Wednesday 19 February 2014 at 11.00. See also 12.1 Procedure for Centrally Authorised products under Article 20 Council Regulation (EC) No 726/2004
Osseor (EMEA/H/C/000561) (Strontium Ranelate), Les Laboratoires Servier, Rapporteur: Bengt Ljungberg, Co-Rapporteur: Andrea Laslop, (treatment of osteoporosis). PRAC outcome at January 2014 PRAC meeting. Oral explanation held in January 2014.	Possible Oral explanation to be held on Wednesday 19 February 2014 at 11.00. See also 12.1 Procedure for Centrally Authorised products under Article 20 Council Regulation (EC) No 726/2004

2 NEW APPLICATIONS

2.1 Opinions – New full applications

(EMEA/H/C/002751), (umeclidinium bromide/vilanterol), (treatment of chronic obstructive pulmonary disease (COPD)) List of Outstanding Issues adopted in November 2013, September 2013. List of Questions adopted in May 2013.
(EMEA/H/C/003754), (umeclidinium bromide/vilanterol), (treatment of chronic obstructive pulmonary disease (COPD)) List of Outstanding Issues adopted in November 2013, September 2013. List of Questions adopted in May 2013.
(EMEA/H/C/002348), (budesonide/formoterol), (treatment of asthma and COPD) List of Outstanding Issues adopted in December 2013. List of Questions adopted in July 2013.

(EMEA/H/C/003890), (budesonide/formoterol), (treatment of asthma and COPD)	
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(EMEA/H/C/002809) (umeclidinium bromide), (treatment of symptoms in adult patients with chronic obstructive pulmonary disease (COPD)) List of Outstanding Issues adopted in January 2014. List of Questions adopted in September 2013.	
(EMEA/H/C/002621), (propranolol), (treatment of proliferating infantile haemangioma) List of Outstanding Issues adopted in December 2013. List of Questions adopted in July 2013.	
(EMEA/H/C/003880), (pregabalin), (treatment of peripheral and central neuropathic pain)	
(EMEA/H/C/003875) (indacaterol / glycopyrronium bromide), (bronchodilator treatment to relieve symptoms in adult treatment of chronic obstructive pulmonary disease (COPD))	
Vimizim (EMEA/H/C/002779), Orphan, (recombinant human n-acetylgalactosamine-6-sulfatase (rhgalns)), Applicant: BioMarin Europe Ltd, (treatment of mucopolysaccharidosis) List of Outstanding Issues adopted in December 2013. List of Questions adopted in September 2013.	
(EMEA/H/C/002656) (canagliflozin /metformin), (treatment of type 2 diabetes mellitus) List of Outstanding Issues adopted in December 2013. List of Questions adopted in July 2013.	

2.2 Day 180 List of outstanding issues – New full applications

(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 Outstanding Issues adopted in December 2013.
List of Questions adopted in September 2013.

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

2.3 Day 120 List of questions – New full applications

(EMEA/H/C/002825), (dulaglutide),
(treatment of adults with type 2 diabetes mellitus)

Cerdelga (EMEA/H/C/003724), Orphan,
(eliglustat), Applicant: Genzyme Europe BV,
(treatment of Gaucher disease type 1)

(EMEA/H/C/002819),
(darunavir /cobicistat), (treatment of patients with human immunodeficiency virus (HIV-1) in:
1. antiretroviral therapy (ART) naïve adults.
2. ART-experienced adults with no darunavir resistance associated mutations (DRV-RAMs) and who have plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 100 cells x 106/l)

(EMEA/H/C/003687)(naltrexone/bupropion),
(indicated for the management of obesity)

(EMEA/H/C/002569)
(nintedanib), (treatment of non-small cell lung cancer (NSCLC)).

2.4 Update on on-going new applications for Centralised Procedures

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

- Assessment report of similarity : **For adoption**

(EMEA/H/C/003843)
(idelalisib), (treatment of patients with relapsed chronic lymphocytic leukaemia (CLL) and refractory indolent non-Hodgkin lymphoma (iNHL))

- Assessment Report of similarity : **For adoption**

(EMEA/H/C/002593)
(Colecalciferol, Strontium Ranelate), (treatment of osteoporosis)

- Letter from the applicant dated 27 January 2014 requesting an additional clock stop for the provision of the responses to the Day 180 List of Outstanding Issues: **For information**

(EMEA/H/C/002756)
(Colecalciferol, Strontium Ranelate), (treatment of osteoporosis)

2.5 Products in the Decision Making Phase

Tecfidera (EMEA/H/C/002601)
(dimethyl fumarate), Biogen Idec Ltd., (treatment of multiple sclerosis)

- Update by European Commission : **For 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

Noxafil (EMEA/H/C/000610/X/0028) (posaconazole), MAH: Merck Sharp & Dohme Limited, Rapporteur: Rafe Suvarna, PRAC Rapporteur: Rafe Suvarna, "To add a new pharmaceutical form: gastroresistant tablets 100 mg" List of Outstanding Issues adopted in December 2013. List of Questions adopted in July 2013.

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

Imatinib Actavis
(EMEA/H/C/002594/X/0003)

(imatinib), MAH: Actavis Group PTC ehf, Generic, Generic of Glivec, Rapporteur: Reynir Arngrímsson, PRAC Rapporteur: Dolores Montero Corominas, "Line extension to add a new strength, 400mg hard capsule for the following extended set of indications already authorised for the reference product Glivec: Imatinib Actavis is indicated for the treatment of

- paediatric patients with newly diagnosed Philadelphia chromosome (bcr -abl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment.
- paediatric patients with Ph+ CML in chronic phase after failure of interferon -alpha therapy, or in accelerated phase or blast crisis.
- adult patients with Ph+ CML in blast crisis.
- adult patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ CML in blast crisis ALL) integrated with chemotherapy.
- adult patients with relapsed or refractory Ph+ ALL as monotherapy.
- adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements.
- adult patients with advanced hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukaemia (CEL) with FIP1L1-PDGFRα rearrangement.

The effect of imatinib on the outcome of bone marrow transplantation has not been determined.
Imatinib Actavis is indicated for

- the treatment of adult patients with unresectable dermatofibrosarcoma protuberans (DFSP) and adult patients with recurrent and/or metastatic DFSP who are not eligible for surgery."

List of Questions adopted in November 2013.

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

Synagis (EMEA/H/C/000257/X/0095), (palivizumab), MAH: AbbVie Ltd., Rapporteur: Jens Heisterberg, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Line Michan, "Introduction of a new pharmaceutical form: 100 mg/ml solution for injection presented in vials containing 0.5 ml and 1 ml."

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

No items

3.5 Extension application according to Annex I of Reg. 1234/2008- Products in the Decision Making Phase

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".
Positive Opinion adopted by consensus on 19 December 2013. Letter from the MAH dated 20 December 2013. List of Questions to the MAH adopted on 23 January 2014.

- Rapporteur's and Co-Rapporteur's joint assessment report on the MAH's responses to the List of Questions dated 7 February 2014: **For information**
- Revised Opinion and assessment report: **For adoption**
- Letter from the MAH dated 11 February 2014 informing of the withdrawal of the prefilled pen formulation**: For information**

4 TYPE II VARIATIONS - Extension of indication procedures

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

Baraclude (EMEA/H/C/000623/II/0041)
(entecavir), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Kristina Dunder, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Qun-Ying Yue, "Extension of indication to include treatment of chronic HBV infection in paediatric patients from 2 to <18 years of age with compensated liver disease and evidence of active viral replication and persistently elevated serum ALT levels"

Eliquis (EMEA/H/C/002148/II/0014/G)
(apixaban), MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Pieter de Graeff, Co-Rapporteur: Robert James Hemmings, "Grouping of 2 variations including a type II Extension of indication to include treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurrent DVT and PE in adults and a type IA to add a new pack size of 28 film coated tablets for Eliquis 5mg strength."

Enbrel (EMEA/H/C/000262/II/0167)
(etanercept), MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, "Extension of indication for treatment of adults with severe non-radiographic axial spondyloarthritis (nr-AxSpA)"

Eylea (EMEA/H/C/002392/II/0009)
(aflibercept), MAH: Bayer Pharma AG, Rapporteur: Pierre Demolis, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Evelyne Falip, "Extension of indication for treatment of adult patients with diabetic macular oedema. Consequential updates were proposed for SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2. SmPC section 4.8 was furthermore updated to introduce a single table of adverse drug reactions."

Gilenya (EMEA/H/C/002202/II/0021)
(fingolimod), MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, Co-Rapporteur: Bengt Ljungberg, "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.

Ozurdex (EMEA/H/C/001140/II/0015)
(dexamethasone), MAH: Allergan Pharmaceuticals Ireland, Rapporteur: Greg Markey, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Julie Williams, "Update of SmPC section 4.1 to add a new indication for treatment of adult patients with diabetic macular oedema. Consequential updates were proposed for SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2. In addition, the MAH proposed to reduce and consolidate the current HCP leaflet, which is provided as tear off section after the PL.
The MAH also used this opportunity to implement QRD version 9.0."
Request for Supplementary Information adopted in October 2013.

Pegasys (EMEA/H/C/000395/II/0073)
(peginterferon alfa-2a), MAH: Roche Registration Ltd, Rapporteur: Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Qun-Ying Yue, "Update of the SmPC to include the use of HCV NS3/4A protease inhibitors for the treatment of HCV genotype 1. Section 4.1 is updated and cross reference to the SmPC's of the HCVNS3/4A protease inhibitors is made throughout the SmPC."

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

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. Request for Supplementary information adopted in December 2013

- Letter from the MAH requesting an additional clock stop to respond to the request for supplementary information adopted in December 2013: **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

Reasanz (EMEA/H/C/002817)
(serelaxin), Applicant: Novartis Europharm Ltd, (treatment of acute heart failure)

- Letter from the applicant dated 28 January 2014 requesting a re-examination of the opinion adopted in January 2014: **For information**
- Appointment of re-examination Rapporteurs: **For discussion**
- Timetable: **For information**

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

- Letter from the applicant dated 28 January 2014 requesting a re-examination of the opinion adopted in January 2014: **For information**
- Appointment of re-examination Rapporteurs: **For discussion**
- Timetable: **For information**

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

- Letter from the applicant dated 24 January 2014 requesting a re-examination of the Opinion adopted in January 2014 and consultation of SAG Oncology: **For information**
- Appointment of re-examination Rapporteurs: **For discussion**
- Timetable: **For information**

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.

- List of questions to SAG-Oncology meeting : **For adoption**
- List of experts to SAG-Oncology meeting : **For adoption**

Nerventra (EMEA/H/C/002546)
(laquinimod), Applicant: Teva Pharma GmbH, (treatment of multiple sclerosis)
Negative Opinion adopted in January 2014.

- Letter from the applicant dated 4 February 2014 requesting a re-examination of the Opinion adopted in January 2014 and consultation of SAG: **For information**
- Appointment of re-examination Rapporteurs: **For discussion**
- 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

HEPLISAV (EMEA/H/C/002603)
(Hepatitis B Surface Antigen), Applicant: Dynavax International B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Daniel Brasseur, (indicated for active immunisation of adults against hepatitis B virus (HBV) infection)

- Letter from the Applicant dated 10 February 2014 informing of the decision to withdraw the marketing authorisation application: **For information**

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.

Ketoconazole Lab HRA Pharma (H0003906), Orphan
(Ketoconazole), Laboratoire HRA Pharma, (treatment of Cushing's syndrome),

- Letter from the company requesting an Accelerated Assessment: **For information**
- Briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment: **For adoption**

(H0003850)
(sofosbuvir/ledipasvir), (treatment of chronic genotype 1 HCV infection in adults),

- Briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment: **For adoption**

11 POST-AUTHORISATION ISSUES

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

SonoVue (EMEA/H/C/000303/II/0025),
(sulphur hexafluoride), MAH: Bracco International B.V., Rapporteur: Pierre Demolis,
"Update of section 4.3 of the SmPC to delete the contraindications for use in patients with acute coronary syndrome or clinically unstable ischaemic cardiac disease and to insert these patient
populations into section 4.4 Special warnings and precautions for use, with editing of the wording as appropriate. The package leaflet was updated accordingly. Furthermore, the MAH took this opportunity to bring the PI in line with the latest QRD template version 9."
Request for Supplementary Information adopted in December 2013, October 2013.

PSUR procedures (PRAC recommendation for variation) for CHMP opinion in February 2014:

Pegasys (EMEA/H/C/000395/PSU 050)
(Peginterferon Alfa-2a), MAH: Roche Registration Ltd, Rapporteur: Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Qun-Ying Yue,

EMEA/H/C/PSUSA/00010007/201307
(PSUSA: PSUR single assessment procedures, referring to CAPs, NAPs products)

CAPS:
Rebetol (EMEA/H/C/000246) (Ribavirin), MAH: Merck Sharp & Dohme Limited, Rapporteur: Joseph Emmerich,
Ribavirin Mylan (EMEA/H/C/001185) (Ribavirin), MAH: Generics (UK) Limited, Rapporteur: Greg Markey
Ribavirin Teva (EMEA/H/C/001018) (Ribavirin), MAH: Teva Pharma B.V., Rapporteur: Greg Markey
Ribavirin Teva Pharma BV (EMEA/H/C/001064) (Ribavirin), MAH: Teva Pharma B.V., Rapporteur: Greg Markey

NAPS:
Ribavirin CT -CT Arzneimittel GmbH Ribavirin 200mg capsules JSC Olainfarm
Ribavirin Normon - Laboratorios Normon S.A.
Copegus - Roche registration Limited
Ribavirin NL/H/2303/001/DC – Valeant
Ribavirin Zentiva – Zentiva
PRAC Rapporteur: Isabelle Robine

Onduarp (EMEA/H/C/002118)
(Amlodipine Besilate,Telmisartan), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Harald Enzmann, Co-Rapporteur: Alar Irs, (treatment of essential hypertension), Informed consent application (Article 10c of Directive No 2001/83/EC)

- Letter from the MAH dated 20 December 2013 informing of voluntary withdrawal of Marketing Authorisation for commercial reasons: **For information**

Firazyr (EMEA/H/C/000899/II/0024/G), Orphan, (icatibant), MAH: Shire Orphan Therapies GmbH, Rapporteur: Kristina Dunder, "Extension of indication for the treatment of ACE-inhibitor induced angioedema: update to sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8 and 5.1 of the SmPC and consequential changes to sections 1, 2 and 3 of the Package Leaflet. - Update to section 5.1 of the SmPC to include the results of the open-label extension phase of study FAST-3 (HGT-FIR-054). In addition the MAH has taken the opportunity to make minor editorial changes throughout the Package Information." In addition, the MAH has submitted a request for one additional year of Market Exclusivity with this grouping application in Module 1.5.3. Request for Supplementary Information adopted in November 2013, March 2013. • Letter from the MAH dated 14 February 2014 informing of the decision to withdraw the type II variation: **For information**	

12 REFERRAL PROCEDURES

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

Protelos (EMEA/H/C/000560) (Strontium Ranelate), Les Laboratoires Servier, Rapporteur: Bengt Ljungberg, Co-Rapporteur: Andrea Laslop, (treatment of osteoporosis) PRAC outcome at January 2014 PRAC meeting. Oral explanation held in January 2014. • Opinion: **For adoption**	Possible Oral explanation to be held on Wednesday 19 February 2014 at 11.00. See also 1.4 Referral procedure oral explanations
Osseor (EMEA/H/C/000561) (Strontium Ranelate), Les Laboratoires Servier, Rapporteur: Bengt Ljungberg, Co-Rapporteur: Andrea Laslop, (treatment of osteoporosis). PRAC outcome at January 2014 PRAC meeting. Oral explanation held in January 2014. • Opinion: **For adoption**	Possible Oral explanation to be held on Wednesday19 February 2014 at 11.00. See also 1.4 Referral procedure oral explanations

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

Polymyxin-based products (EMEA/H/A-5(3)/1384)
(colistin, colistimethate), Rapporteur: Robert Hemmings, Co-Rapporteur: Martina Weise, Review of the module 3 (quality) and the Eur. Pharm. Monograph. Article 5(3) triggered by the EMA Executive Director
List of Questions adopted in September 2013.

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

See also section 12.6 Community Interests - Referral under Article 31

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

Seasonique film coated tablets (EMEA/H/A-29(4)/1392)
(levonogestrel 150 µg and Ethinylestradiol 30 µg / 10 µg), MAH: Teva Pharma B.V (NL), RMS: FR, CMS: AT, BE, DE, IT, PL, RO, SI ,SK, Procedure number: FR/H/0516/001/DC,

Article 29(4) triggered due to disagreement with regard to the demonstration of contraceptive effectiveness and treatment compliance.

- Letter from ANSM dated 3 February 2014 notifying of an official referral under article 29 and its grounds: **For information**
- Appointment of (Co) Rapporteur): **For discussion**
- Timetable: **For adoption**

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

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.

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

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

Caustinerf arsenical® and Yranicid arsenical®, 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 and published literature.

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

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) first monthly update and interim analysis report submission as requested by CHMP in November 2013 and assessment report: **For adoption**

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**	
Polymyxin-based products (EMEA/H/A-31/1383) (colistin, colistimethate), Rapporteur: Robert Hemmings, Co-Rapporteur: Joseph Emmerich, To carry out a full benefit-risk review and update and harmonise the product information. Triggered by European Commission List of Questions adopted in September 2013. • List of Outstanding Issues: **For adoption**	See also section 12.2 Requests for CHMP Opinion under Article 5(3)

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

No items

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

No items

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

No items

12.11 Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) No 1234/2008)

No items

13 PHARMACOVIGILANCE ISSUES

Summary of recommendations and advice of

PRAC meeting held on 3-6 February 2014: **For information**	
List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for February 2014: **For adoption**	
Early Notification System: February 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.*

14.3 Pharmacovigilance Inspections

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

14.4 GLP Inspections

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

15 INNOVATION TASK FORCE

15.1 Minutes of ITF: For information

15.2 Briefing meetings (Innovation Task Force)

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

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

No items

15.5 Nanomedicines activities

No items

16 SCIENTIFIC ADVICE WORKING PARTY (SAWP)

Report from the SAWP meeting held 3-5 February 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 17-19 February 2014: **For information**	

18 OTHER COMMITTEES

18.1 Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 4-5 February 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 27-28 January 2014: **For information**	To be sent in the Post-mail.

18.3 Paediatric Committee (PDCO)

PIPs reaching D30 at February 2014 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on 12-14 February 2014: **For information**	

18.4 Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 13-14 February 2014 **For information**

19 INVENTED NAME ISSUES

Table of Decisions of the NRG meeting held on 29 January 2014: **For adoption**

20 ANY OTHER BUSINESS

Election of CHMP Co-opted member at the February 2014 CHMP meeting: **For adoption**

Election of BWP Chair: **For adoption**

Calculation of voting quorum and majority vote: **For information**

Presentation on the Move to Churchill Place: **For information**

Multinational assessment teams: **For discussion**

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)*

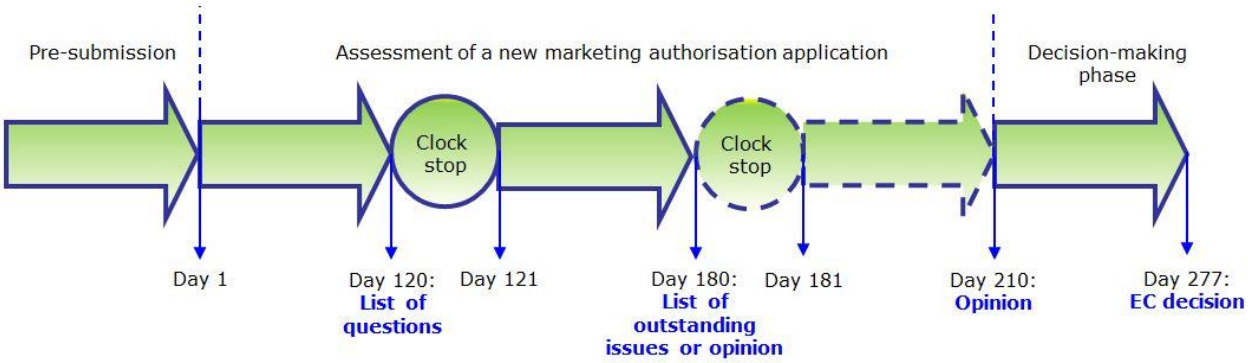
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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