12 December 2014
EMA/CHMP/722409/2014
Procedure Management and Business Support Division

Committee for medicinal products for human use (CHMP)

Agenda of meeting to be held on 15-18 December 2014

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

15 December 2014, 13:00 – 19:30, room 3A

16 December 2014, 08:30 – 19:30, room 3A

17 December 2014, 08:30 – 19:30, room 3A

18 December 2014, 08:30 – 16:00, 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 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.

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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/CHMP/722409/2014 rev.3) and Annex to CHMP agenda of the CHMP plenary session to be held on 15-18 December 2014	
Timeschedule (EMA/CHMP/754937/2014 rev.2) of the CHMP plenary session to be held on 15-18 December 2014	
Minutes (EMA/741182/2014) of the CHMP plenary session held on 17-20 November 2014	
ToD / Minutes (EMA/764768/2014) of the ORGAM meeting held on 8 December 2014	

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 on 15-18 December 2014.	*See December 2014 Minutes (to be published post January 2015 CHMP meeting)*
Draft Agenda of CHMP meeting to be held on 19-22 January 2015.	

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1. Oral explanations

1.1. Pre-authorisation procedure oral explanations

Vantobra (EMEA/H/C/002633) (Tobramycin), Applicant: PARI Pharma GmbH, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	Possible Oral explanation on Tuesday 16 December 2014 at 14.00.
(EMEA/H/C/003780), (liraglutide), (treatment of obesity) List of Outstanding Issues adopted on 23.10.2014. List of Questions adopted on 22.05.2014.	Oral explanation on Tuesday 16 December 2014 at 11.00
(EMEA/H/C/002066), (ciclosporin), (treatment of keratitis) List of Outstanding Issues adopted on 25.09.2014. List of Questions adopted on 25.04.2014. • List of experts to ad hoc expert group meetings held on 4 December 2014: **Adopted by written procedure** • Report from the ad hoc expert group meetings to held on 4 December 2014: **For discussion**	Oral explanation to be held on Wednesday 17 December 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 explanation

No items

2. Initial full applications

2.1. Initial full applications; Opinions

(EMEA/H/C/004006), (clopidogrel), (prevention of myocardial infarction and acute coronary syndrome
Myocardial infarction, ischaemic stroke, peripheral arterial disease, acute coronary syndrome, prevention of atherothrombotic and thromboembolic events in atrial fibrillation
Myocardial infarction, ischaemic stroke, peripheral arterial disease, acute coronary syndrome, prevention of atherothrombotic and thromboembolic events in atrial fibrillation
Myocardial infarction, ischaemic stroke, peripheral arterial disease, acute coronary syndrome, prevention of atherothrombotic and thromboembolic events in atrial fibrillation.)
List of Outstanding Issues adopted on 20.11.2014

List of Questions adopted on 25.09.2014.

(EMEA/H/C/002450), Orphan, ATMP, (ex vivo autologous corneal epithelial cells including stem cells), Applicant: Chiesi Farmaceutici S.p.A., (treatment of limbal stem cell deficiency)
List of Outstanding Issues adopted on 23.10.2014.
List of Questions adopted on 25.07.2013.

- BWP Report: **For adoption**

(EMEA/H/C/003687), (naltrexone / bupropion), (indicated for the management of obesity)
List of Outstanding Issues adopted on 23.10.2014, 24.07.2014.
List of Questions adopted on 20.02.2014.

(EMEA/H/C/002789), Orphan, (levofloxacin), Applicant: Aptalis Pharma SAS, (indicated for chronic pulmonary infections)
List of Outstanding Issues adopted on 20.11.2014, 25.09.2014.
List of Questions adopted on 25.04.2014.

(EMEA/H/C/003968), (sevelamer), (indicated for control of hyperphosphataemia)
List of Questions adopted on 25.09.2014.

(EMEA/H/C/002396), (safinamide), (treatment of Parkinson's disease (PD))
List of Outstanding Issues adopted on 25.09.2014.
List of Questions adopted on 25.04.2014.

(EMEA/H/C/002840), (dalbavancin), (treatment of tissue infections (cSSTI))
List of Outstanding Issues adopted on 25.09.2014.
List of Questions adopted on 25.04.2014.

2.2. Initial full applications; Day 180 List of outstanding issues –

(EMEA/H/C/002772), Orphan, (dasiprotimut-t), Applicant: Biovest Europe Ltd, (treatment of non-Hodgkin's lymphoma (FL))
List of Questions adopted on 25.04.2014.

- BWP Report: **For adoption**

(EMEA/H/C/003852), (human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed)), , (treatment of HPV diseases)
List of Questions adopted on 24.07.2014.

- BWP Report: **For adoption**

(EMEA/H/C/003750), Orphan, ATMP, (allogenic human heterologous liver cells), Applicant: Cytonet GmbH&Co KG, (treatment of urea cycle disorders (UCD))
List of Questions adopted on 25.04.2014.

- BWP Report: **For adoption**

(EMEA/H/C/003819), (ceritinib), (treatment of non-small cell lung cancer (NSCLC)
treatment of anaplastic lymphomakinase (ALK)-positive locally advanced or metastatic non-small cell lung cancer (NSCLC))
List of Questions adopted on 24.07.2014.

2.3. Initial full applications; Day 120 List of Questions

(EMEA/H/C/004021), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)

(EMEA/H/C/002734), Orphan, (isavuconazole), Applicant: Basilea Medical Ltd, (treatment of aspergillosis and mucormycosis)

(EMEA/H/C/004024), (pregabalin), (treatment of neuropathic pain, epilepsy and generalised anxiety disorder (GAD))

(EMEA/H/C/003962), (pregabalin), (treatment of neuropathic pain, epilepsy and generalised anxiety disorder (GAD))

(EMEA/H/C/004078), (pregabalin), (treatment of epilepsy and generalised anxiety disorder (GAD))

(EMEA/H/C/004010), (pregabalin), (treatment of neuropathic pain, epilepsy and generalised anxiety disorder)

(EMEA/H/C/004070), (pregabalin), (treatment of epilepsy and generalised anxiety disorder (GAD))

(EMEA/H/C/003900), (pregabalin), (treatment of epilepsy and Generalised Anxiety Disorder (GAD))

(EMEA/H/C/003772), (ceftolozane / tazobactam), (treatment of intra-abdominal urinary tract infections)

2.4. Update on on-going initial full applications for Centralised procedure

(EMEA/H/C/003769), Orphan, (mercaptamine hydrochloride), Applicant: Orphan Europe S.A.R.L., (treatment of cystinosis)

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

(EMEA/H/C/003727), Orphan, (lenvatinib), Applicant: Eisai Ltd, (Treatment of papillary thyroid cancer
Treatment of follicular thyroid cancer)

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

(EMEA/H/C/003731), Orphan, (blinatumomab), Applicant: Amgen Europe B.V., (for the treatment of adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia)

- Assessment report on similarity **For adoption**
- BWP Report: **For adoption**

(EMEA/H/C/003702), (phenylephrine hydrochloride / ketorolac trometamol), (maintenance of intraoperative mydriasis, prevention of intraoperative miosis and reduction of acute postoperative ocular pain in intraocular lens replacement (ILR) in adults)
List of Outstanding Issues adopted on 22.05.2014.
List of Questions adopted on 23.01.2014.

- List of experts to ad hoc expert group meetings held on 4 December 2014: **Adopted by written procedure**
- Report from the ad hoc expert group meetings held on 4 December 2014: **For discussion**
- QWP Report: **For discussion**

(EMEA/H/C/002739), (human alpha1-proteinase inhibitor), (treatment of lung tissue) List of Outstanding Issues adopted on 20 November 2014. List of Questions adopted on 25.04.2014. • List of experts for the ad hoc expert group meeting : **For adoption**	
(EMEA/H/C/003800), Orphan (ketoconazole), Applicant: Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare, (treatment of Cushing's syndrome) Day 120 List of Questions adopted in April 2014.Letter from the applicant received 11 December 2014 requesting further extension of clock stop to respond to Day 120 List of Questions : **For discussion**	

2.5. Products in the Decision Making Phase

Vantobra (EMEA/H/C/002633) (Tobramycin), Applicant: PARI Pharma GmbH, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	Possible Oral explanation on Tuesday 16 December 2014 at 14.00.

3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

3.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinions

Oprymea (EMEA/H/C/000941/X/0017), (pramipexole), MAH: Krka d.d. Novo mesto, Generic of Sifrol, Rapporteur: Jens Heisterberg, PRAC Rapporteur: Doris Stenver, "To add new strengths 2.62 mg and 3.15 mg prolonged-release tablets." List of Questions adopted on 25.09.2014.

3.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 List of outstanding issues

Orfadin (EMEA/H/C/000555/X/0042), Orphan, (nitisinone), MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, "To add a new strength 20 mg capsule, hard."
List of Questions adopted on 24.07.2014.

Revlimid (EMEA/H/C/000717/X/0073/G), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Arnaud Batz, "To add indication for the continuous treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant. A line extension application to add the following strength: 20 mg (21 capsules pack)"
List of Questions adopted on 24.07.2014.

3.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of Questions

No items

3.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No items

4. Type II variations - Extension of indication procedures according to Annex I of Commission Regulation (EC) No 1234/2008

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

Aloxi (EMEA/H/C/000563/II/0038), (palonosetron), MAH: Helsinn Birex Pharmaceuticals Ltd., Rapporteur: Patrick Salmon, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Almath Spooner, "Extension of the therapeutic indication for paediatric patients 1 month of age and older for the prevention of nausea and vomiting associated with moderately and highly emetogenic cancer chemotherapy for the IV formulation, based on the paediatric studies PALO-10-14 and PALO-10-20 and update of sections 5.1 and 5.2 of the Aloxi Oral formulation to reflect those studies. The MAH took the opportunity of this variation to update the Aloxi product information annexes in line with Version 9 of the QRD template."
Request for Supplementary Information adopted on 25.09.2014.

Fycompa (EMEA/H/C/002434/II/0016), (perampanel), MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams, "Extension of indication as adjunctive treatment of Primary Generalised Tonic-Clonic seizures in patients with epilepsy aged 12 years and older. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to propose minor changes to PL and update the contact details of the Maltese local representative."

Perjeta (EMEA/H/C/002547/II/0010), (pertuzumab), MAH: Roche Registration Ltd, Rapporteur: Christian Schneider, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver, “The MAH is submitting a type II 90 day variation application to extend the use of Perjeta in combination with trastuzumab and docetaxel as part of a neoadjuvant treatment for patients with locally advanced, inflammatory or early stage HER2-positive breast cancer suitable for neoadjuvant therapy (tumours > 2 cm in diameter).

The submission is based primarily on the results of two randomized Phase II studies, NEOSPHERE (WO20697) and TRYPHAENA (BO22280).

The Perjeta annexes have been updated in the concerned sections as outlined in the table below and in the SmPC track change version in Module 1.3.1. The section 4.8 Undesirable effects of the SmPC (and the section 4 of the PIL accordingly) has been revised and includes now a pooled safety analysis across the studies CLEOPATRA, the pivotal study in metastatic breast cancer, and the two neoadjuvant studies NEOSPHERE and TRYPHAENA. A “Note to the Reviewer” providing further explanations on the pooled safety analysis is also included in the track change SmPC version in Module 1.3.1.”

Pyramax (EMEA/H/W/002319/II/0002), (pyronaridine / pyronaridine phosphate / artesunate), MAH: Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Arnaud Batz, "To amend SmPC section 4.1 (Therapeutic Indications) to remove restrictions on repeated course of treatment in any individual and use only in areas of low transmission with evidence of artesmisinin resistance, based on further clinical experience. Consequent changes in SmPC sections 4.2 (Posology), 4.4 (Special warnings and precautions), 4.8 (Undesirable effects) and the PL are also included.
A recommended change is made to SmPC Section 4.2 (Posology) in relation to dosing in mild to moderate renal impairment.
A minor editorial adjustment is proposed to SmPC section 5.1 (Pharmacodynamic properties)."
Request for Supplementary Information adopted on 26.06.2014.

Resolor (EMEA/H/C/001012/II/0034), (prucalopride), MAH: Shire Pharmaceuticals Ireland Ltd., Rapporteur: Greg Markey, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Rafe Suvarna, "This type II variation (category C.I.6) is provided on the basis of the completion of the clinical study SPD555-302. Following a meeting with the Resolor Rapporteur on 11 March 2014 it was agreed that the results of SPD555-302 would be provided to the EMA for assessment no later than 30 September 2014.
The conduct and conclusion of study SPD555-302 was completed as a Post Approval Commitment (FUM 004 (MEA 004.2)) - To perform an efficacy study in males.
Based on the results from study SPD555-302, the MAH has submitted this type II variation to extend the indication for Resolor into the male population. The results of study SPD555-302 will be reflected in the Annex (a clean and track change version of the Resolor SmPC and PIL are provided for review). Throughout section 5.1 (Pharmacodynamic properties) of the SmPC the MAH has replaced the name of the active "prucalopride" with "Resolor" for consistency and accuracy in this section.

In support of the proposed update to the Resolor SmPC a Phase 1 Study (SPD555-104) to Investigate the Absorption, Metabolism, and Excretion of [14C] Prucalopride Succinate Following a Single Oral Dose in Healthy Male Subjects has also been provided with this variation. In support of the proposed amendment to section 4.1 (Therapeutic indications) of the SmPC the MAH also intends to apply for extended data/market exclusivity Under Article 14 (11) of Regulation (EC) No 726/2004 or Article 10 (1) fourth subparagraph of Directive 2001/83/EC. The Marketing Authorisation Holder (MAH) hereby applies for an additional 1 year of marketing protection and supporting documentation is thus provided in module 1.5.3. An updated Risk Management Plan (RMP) (version 12) is also provided with this submission. The updated RMP is provided following the finalisation of study SPD555-302 for the male population and also following a request from the Rapporteur during the assessment of the PSUR 007 (EMEA/H/C/1012/ PSU 021) to include the important potential risk "Increase in prolactin levels". Separate to the update of the Resolor Annex with an update to the therapeutic indication, the MAH also proposes changes to section 6 of the Patient Information Leaflet with the revision of the contact details (address and/or telephone numbers for the local representatives in Belgium and Italy." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004).	
Tresiba (EMEA/H/C/002498/II/0011), (insulin degludec), MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Extension of the indication in children aged from 1 to 18 years. Update to sections 4.1, 4.2, 4.8 and 5.1 of the SmPC. The PL is updated accordingly. In addition, update of the Section 2 of the PL in line with the existing information in Section 4.2 of the SmPC." Request for Supplementary Information adopted on 25.09.2014.	

Velcade (EMEA/H/C/000539/II/0072), (bortezomib), MAH: Janssen-Cilag International N.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Carmela Macchiarulo, "Extension of indication for the use of VELCADE in combination with rituximab, cyclophosphamide, doxorubicin and prednisone for the treatment of adult patients with previously untreated mantle cell lymphoma. Consequently, the MAH proposed updates of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC and the Package Leaflet."
Request for Supplementary Information adopted on 25.09.2014.

- Updated similarity assessment report against Torisel and Imbruvica: **For adoption**

Voncento (EMEA/H/C/002493/II/0008/G), (human coagulation factor viii / human von willebrand factor), MAH: CSL Behring GmbH, Rapporteur: Pieter de Graeff, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Sabine Straus, "Extension of indication to include prophylactic treatment of patients with VWD. In addition the MAH is providing data to support treatment of paediatric patients with VWD."

Xiapex (EMEA/H/C/002048/II/0044), (collagenase clostridium histolyticum), MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Martina Weise, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Martin Huber, "Update of the SmPC with a new indication in the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity. The PL is updated accordingly."
Request for Supplementary Information adopted on 25.09.2014.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

4.2. Update on on-going type II variation; extension of indications

No items

5. Ancillary medicinal substances in medical devices

5.1. Ancillary medicinal substances in medical devices - Opinions/ List of outstanding issues / List of Questions

(EMEA/H/D/003740), (human serum albumin), (the storage, manipulation, in-vitro culture and transfer of human gametes)
List of Outstanding Issues adopted on 25.09.2014.
List of Questions adopted on 23.01.2014.

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

(EMEA/H/D/002831), (insulin-like growth factor-i (igf-i) segment), (hard-to-heal wounds, primarily venous leg ulcers)

List of Questions adopted on 23.01.2014. List of Outstanding Issues adopted on 25.09.2014.

Revised timetable: **for adoption**

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6. Re-examination procedure (new applications) under Article 9(2) of Regulation no 726/2004

No items

7. Re-examination procedure (Type II variations) under Article Article 16 of Commission Regulation (EC) No 1234/2008 and 9(2) of Regulation (EC) No 726/2004

No items

8. Withdrawal of full new 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.

(H0003790), Orphan
(carfilzomib) Applicant: Amgen Europe B.V., (indicated for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies that included bortezomib (a proteasome inhibitor) and an immunomodulatory agent, or for whom such treatments are not appropriate),

- Request for an accelerated assessment dated 25 November 2014**: For information**
- Rapporteurs' accelerated assessment briefing note: **For adoption**

11. Post-authorisation issues

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

Tyverb (EMEA/H/C/000795/II/0037), (lapatinib), MAH: Glaxo Group Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.1 of the SmPC with information on lapatinib effect on CNS metastasis further to comparative data on the incidence of CNS metastases from studies EGF108919 (COMPLETE), EGF105485 (TEACH) and EGF106708 (ALTTO) (SOB 002.4). Annex II is also updated further to the fulfilment of the specific obligation."

Tyverb (EMEA/H/C/000795/II/0038), (lapatinib), MAH: Glaxo Group Ltd, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC further to disease-free survival (DFS) results from hormone receptor-positive patients in the adjuvant EGF106708 (ALTTO) study (REC 037)."

INOmax (EMEA/H/C/000337)
(Nitric Oxide), MAH: Linde Healthcare AB, Rapporteur: Robert James Hemmings, Co-Rapporteur: Daniel Brasseur, (treatment of hypoxic respiratory failure in newborns), Complete application (stand-alone) - Council Directive 81/851/EEC

- DHPC: **For adoption by written procedure**
- Communication plan: **For adoption by written procedure**

Eperzan (EMEA/H/C/002735/II/0009), (albiglutide), MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, "Update of section 4.8 with information on appendicitis / pancreatitis. The PL is updated accordingly. In addition, the MAH took the opportunity to correct some information in Sections 5.1 and 6.6 of the SmPC, the Annex III.A and the Package Leaflet." Request for Supplementary Information adopted on 23.10.2014.

Xarelto (EMEA/H/C/000944/II/0033), (rivaroxaban), MAH: Bayer Pharma AG, Rapporteur: Kristina Dunder, , "Section 4.2 and 5.1: After approval of the Xarelto in 2008, a prospective, randomized, open-label, parallel-group, active
controlled phase IIIb study (X-VERT) was performed to compare Xarelto® with vitamin K antagonists (VKA) for the prevention of cardiovascular events in patients with non-valvular atrial fibrillation undergoing cardioversion. Based on the results of this X-VERT study, the applicant therefore proposes to update the information in the indication SPAF in the section 4.2 and to describe the results of this X-VERT study in section 5.1 of the SmPC." Request for Supplementary Information adopted on 25.09.2014.

Docetaxel Accord (EMEA/H/C/002539)
(Docetaxel), MAH: Accord Healthcare Ltd, Rapporteur: Filip Josephson, (Article 10(1) of Directive No 2001/83/EC).

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

Polymyxin-based products (EMEA/H/A-5(3)/1384)
(colistin, colistimethate), Rapporteur: Robert James Hemmings, Co-Rapporteur: Martina Weise, Review of the module 3 (quality) and European Pharmacopeia monograph. Triggered by the EMA Executive Director.

- Revised timetable: **For adoption**
- Consultation of the QWP: **For adoption**

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

No items

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

No items

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

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097),
Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff,
FUM related to the updated 3rd annual cumulative safety reviews on nephrogenic systemic fibrosis (NSF) with regards to Omniscan: GE HealthCare

GVK Biosciences (EMEA/H/A-31/1408)
Rapporteur: Harald Enzmann, Co-Rapporteur: Christian Schneider,
Article 31 procedure triggered by the European Commission concerning GVK Biosciences Private Limited (GVK Bio), Swarna Jayanthi commercial complex, Ameerpet, Hyderabad 500 038, India
Oral explanation held in October and November 2014.

Procedure status update: **for discussion**

Adrenaline auto injectors (EMEA/H/A-31/1398)
Rapporteur: Alars Irs, Co-Rapporteur: Robert Hemmings,
Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients.

- Revised timetable: **For adoption**
- List of experts for the ad hoc expert group meeting: **For adoption**
- Agenda of the ad hoc expert group meeting: **For information**

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 1-4 December 2014: **For information**	
List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for December 2014: **For adoption**	
Early Notification System: December 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 Innovation Task Force: For information

15.2. Briefing meetings (Innovation Task Force)

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

ITF Briefing Meeting
ITF Briefing Meeting

15.3. Eligibility to EMA scientific services

No items

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

No items

15.5. Nanomedicine activities

No items

16. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 1-4 December 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 15-17 December 2014: **For information**

CMDh question to CHMP (PKWP) regarding potential risk of longer half-life of acitretin,

- Feedback from the teleconference between the Chairs of CHMP, PKWP and SWP and the DK assessor held on 2 December 2014: **For discussion**
- Questions from CMDh to PKWP and SWP on a possible extension of the post-treatment pregnancy prevention period after use of acitretin: **For adoption**

Reply letter from PDCO about the request from CMDh to CHMP and PDCO regarding Guidance on the development of parenteral nutrition in the paediatric population: **For adoption**

18. Other Committees

18.1. Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 9-10 December 2014: **For information**

18.2. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 24-25 November 2014: **For information**

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2014 PDCO: **For information**

Report from the PDCO meeting held on12-14 December 2014: **For information**

18.4. Committee for Advanced Therapies (CAT)

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

19. Invented name issues

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

20. Any other business

Initiative to enhance early dialogue with applicants to foster better development of products	
Reminder to committee members to submit e-DoI version 2 by 30 Jan 2015	
Benefit-risk communication to medicines users How can regulators best meet the information needs of patients and healthcare professionals? Workshop (held 2013-2014) report (EMA/581546/2014): **For information**	
Benefit-Risk Effects Table Guidance: **For discussion**	
Update Multinational Teams Scheme – Extended to CHMP/CAT Rapporteurships (not only Co-Rapporteurships): **For information**	Follow up from December ORGAM. Extension of Multinational Teams Scheme to rapporteurships, starts from January 2015 on and applies only for the initial MAA assessment.
PSUR repository implementation plan: **For discussion**	
Outcome of presidency CHMP meeting in Rome • Action items: **For agreement**	
Presidency CHMP meeting in the first half of year 2015 under the Latvian EU presidency: **For discussion**	
FDA final rule on changes to pregnancy and lactation labeling information for prescription drug and biological products: **For discussion**	
Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues (EMEA/CHMP/BMWP/42832/2005 Rev1): **For adoption and release for implementation**	
Update on Risk Management Process: **For discussion**	
Follow-up on general aspects regarding SmPC labelling (indication wording): **For discussion**	
Process for agreement of Working Parties' Work Programmes 2015: **For discussion**	

Answers to the requests for scientific advice on the impact on public health and animal health of the use of antibiotics in animals (EMA/381884/2014): **For adoption** • Overview of comments received on 'Answers to the request for scientific advice on the impact on public health and animal health of the use of antibiotics in animals' (EMA/381884/2014): **For information**	
Draft Guidance with applicants on responses to questions received from EMA Scientific Committees during the evaluation within the centralised procedure: **For adoption**	
Appointment of CHMP representatives to the CAT	The current members (Sol Ruiz, Romaldas Maciulaitis, Bruno Sepodes, John Borg, Jean-Louis Robert) confirmed their willingness to continue the cross Committee membership to the CAT. The CHMP should renominate these 5 members for another 3-year mandate.

List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 15-18 December 2014 meeting.

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)*

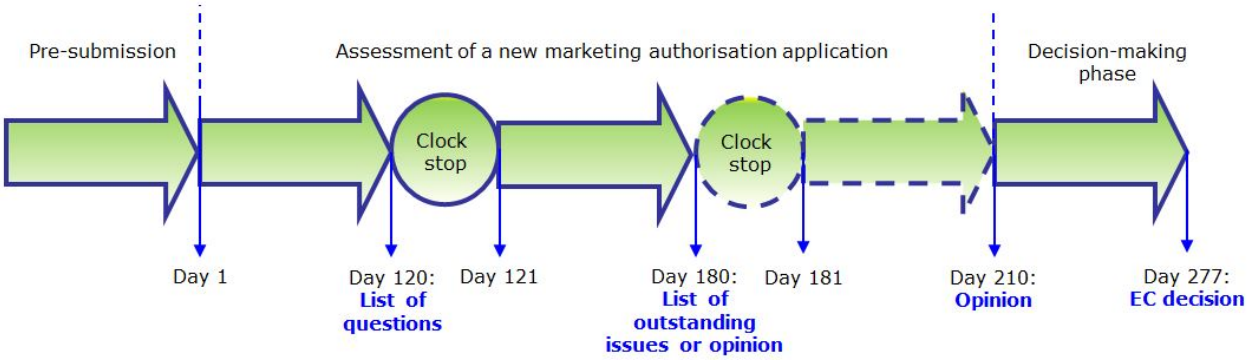
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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