23 February 2015
EMA/CHMP/48163/2015
Procedure Management and Business Support Division

Committee for medicinal products for human use (CHMP)

Agenda of meeting to be held on 23-26 February 2015

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

23 February 2015, 13:00 – 19:30, room 2A

24 February 2015, 08:30 – 19:30, room 2A

25 February 2015, 08:30 – 19:30, room 2A

26 February 2015, 08:30 – 14:00, room 2A

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. Of note, this agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

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

For adoption

Agenda (EMA/CHMP/48163/2015 rev. 4) and Annex to CHMP agenda of the CHMP plenary session to be held 23-26 February 2015
Timeschedule (EMA/CHMP/83005/2015 rev.3) of the CHMP plenary session to be held 23-26 February 2015
Minutes (EMA/CHMP/68245/2015 rev.0) of the CHMP plenary session held 19-22 January 2015

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 23-26 February 2015	*See February 2015 Minutes (to be published post March 2015 CHMP meeting)*
Membership announcement The Committee is asked to note that Ingunn Hagen Westgaard is no longer Norwegian CHMP alternate. The Committee is asked to note that Ivana Pankuchová was nominated as the CHMP Alternate from Slovakia, replacing Jana Klimesová in this role.	
Draft Agenda of CHMP meeting to be held on 23-26 March 2015.	

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(EMEA/H/C/002629), (edoxaban), (prevention of stroke; embolism and treatment of venous thromboembolism) List of Outstanding Issues adopted on 20.11.2014. List of Questions adopted on 26.06.2014.	Oral explanation to be held on Tuesday 24 February 2015 at 11.00.

1.2. Re-examination procedure oral explanation

1.3. Post-authorisation procedure oral explanation

1.4. Referral procedure oral explanation

2. Initial full applications

2.1. Initial full applications; Opinions

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List of Questions adopted on 25.04.2014.

(EMEA/H/C/003910), (pegfilgrastim), (treatment of neutropenia)
Request for Supplementary Information adopted on 20.11.2014.

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

(EMEA/H/C/003803), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
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(EMEA/H/C/003899), (aripiprazole), (treatment of schizophrenia and prevention of manic episodes in bipolar I disorder)
List of Questions adopted on 20.11.2014.

(EMEA/H/C/003870), Orphan, (tasimelteon), Applicant: Vanda Pharmaceuticals Ltd., (treatment of Non-24-Hour Sleep-Wake Disorder)
List of Questions adopted on 25.09.2014.

(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))
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(EMEA/H/C/002749), (lutetium, isotope of mass 177), (used only for the radiolabelling of carrier molecules)
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(EMEA/H/C/003962), (pregabalin), (treatment of neuropathic pain, epilepsy and generalised anxiety disorder (GAD))
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(EMEA/H/C/003834), Orphan, (idebenone), Applicant: Santhera Pharmaceuticals (Deutschland) GmbH, (treatment of Leber's Hereditary Optic Neuropathy (LHON))
List of Questions adopted on 25.09.2014.

2.3. Initial full applications; Day 120 List of Questions

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

- BWP Report: **For adoption**

(EMEA/H/C/003788), (pemetrexed), (treatment of malignant pleural mesothelioma and non-small cell lung cancer)

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- BWP Report: **For adoption**

(EMEA/H/C/003938), (betulae cortex dry extract (5-10 : 1); extraction solvent: n-heptane 95% (w/w)), (treatment of partial thickness wounds)

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- BWP Report: **For adoption**

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

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obesity)
Fixed combination application (Article 10b of Directive No 2001/83/EC). Opinion adopted on 18.12.2014.

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

Optisulin (EMEA/H/C/000309/X/0079/G), (insulin glargine), MAH: Sanofi-aventis Deutschland GmbH, Duplicate of Lantus, Rapporteur: Pieter de Graeff, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "To extend MA of Optisulin to register additional strength 300 U/ml, grouped with type IA variation to vary the invented name from Optisulin to Toujeo".
List of Questions adopted on 25.09.2014.

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 Outstanding Issues adopted on 18.12.2014.
List of Questions adopted on 24.07.2014.

JETREA (EMEA/H/C/002381/X/0013), (ocriplasmin), MAH: ThromboGenics NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "to introduce a ready-to-use (RTU) formulation with adjusted fill volume for Jetrea 0.375 mg/0.3 mL"
List of Questions adopted on 20.11.2014.

- DHPC: **For discussion**

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

Somavert (EMEA/H/C/000409/X/0072), (pegvisomant), MAH: Pfizer Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Arnaud Batz, "Addition of 25 mg and 30 mg powder and solvent for solution for injection."
List of Questions adopted on 25.09.2014

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

Instanyl (EMEA/H/C/000959/X/0030/G), (fentanyl / fentanyl citrate), MAH: Takeda Pharma A/S, Rapporteur: Pierre Demolis, Co-Rapporteur: Martina Weise, "Annex I_2.(c) To add the new strength of 400 micrograms/dose in a multi-dose nasal spray in pack size of 10's, 20's, 30's & 40 doses.
Type II cat. B.II.e.4.b) To replace the current multi-dose nasal spray by a new improved child resistant multi-dose nasal spray.
3 X Type IB cat. B.II.e.5.d) To add a new pack size of 30 doses for each current strength (50 micrograms/dose, 100 micrograms/dose & 200 micrograms/dose).
Type IA cat. B.II.d.1.a) – To tighten the assay release limit of the multi-dose finished product to 98.0%-102.0%.
Type IA cat. B.II.f.1.a) 1. – To reduce the shelf life of all strengths of the multi-dose finished product to 24 months.
Additionally, the Applicant took the opportunity to include an editorial change, as to change the wording of the specification footnote regarding the droplet size distribution test from "The test is performed by the vendor on every pumping system batch" to "The test is performed at release of the pumping system"."

Kalydeco (EMEA/H/C/002494/X/0034/G), Orphan, (ivacaftor), MAH: Vertex Pharmaceuticals (U.K.) Ltd., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia, Line extension application to add a new strength and a new pharmaceutical form (50mg and 75mg granules), grouped with a type II variation C.1.4.

Pyramax (EMEA/H/W/002319/X/0008/G), (pyronaridine / pyronaridine phosphate / artesunate), MAH: Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Arnaud Batz, "Line Extension to add a new paediatric formulation PYRAMAX 60 mg/20 mg Granules for Oral Suspension.
The PI for Pyramax 180 mg/60 mg Film Coated Tablets has also been updated with data submitted for the line extension."

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

Mabthera (EMEA/H/C/000165/X/0101/G), (rituximab), MAH: Roche Registration Ltd, Rapporteur: Christian Schneider, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Doris Stenver, , "Grouping of:
Line extension to add a new strength 1600 mg solution for subcutaneous injection, a new indication is proposed for this strength (different from 1400mg strength).
Type II variation to update the product information of the existing strengths as a consequence to the line extension application
Type II variation to update the RMP"

- Similarity assessment: **For adoption**
- BWP Report: **For adoption**

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 -

Adenuric (EMEA/H/C/000777/II/0037), (febuxostat), MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, , "Update of sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC for the 120 mg strength further to the introduction of a new indication for prevention and treatment of hyperuricaemia in adult patients undergoing chemotherapy for haematologic malignancies at intermediate to high risk of Tumor Lysis Syndrome (TLS). The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 20.11.2014.

Avastin (EMEA/H/C/000582/II/0072), (bevacizumab), MAH: Roche Registration Ltd, Rapporteur: Christian Schneider, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Doris Stenver, "Extension of indication for the use of Avastin in combination with paclitaxel and cisplatin or paclitaxel and topotecan in patient with persistent, recurrent, or metastatic carcinoma of the cervix. Consequently, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC and the Package Leaflet are proposed to be updated."
Request for Supplementary Information adopted on 22.01.2015, 25.09.2014.

Esmya (EMEA/H/C/002041/II/0028), (ulipristal), MAH: Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.1 of the SmPC with subsequent updates to sections 4.2, 4.4, 4.8 and 5.1 in order to extend the current indication to long term (repeated intermittent) treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 20.11.2014.

Humira (EMEA/H/C/000481/II/0134), (adalimumab), MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga, “Extension of Indication to add treatment of chronic plaque psoriasis in children and adolescents from 4 years of age, based on data from study M04-717 ‘A multicentre, randomised, double-dummy, double-blind study evaluating two doses of adalimumab versus methotrexate in paediatric subjects with chronic plaque psoriasis.’ As a consequence sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH proposed minor editorial changes in the SmPC and Package Leaflet. A revised RMP version 11.2 was included as part of this application.” Request for Supplementary Information adopted on 23.10.2014.	
Humira (EMEA/H/C/000481/II/0137), (adalimumab), MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga, “This application seeks to add paediatric indication to section 4.1 of the SmPC for all presentations of Humira: Humira is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients, including treatment of inflammatory lesions and prevention of worsening of abscesses and draining fistulas. Consequential changes are proposed for sections 4.2, 4.4, 4.8, 5.1 and 5.2. Changes reflecting the additions to the SmPC are proposed for sections 1 and 3 of the Package Leaflet.”	

Imbruvica (EMEA/H/C/003791/II/0001), Orphan, (ibrutinib), MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, Co-Rapporteur: Christian Schneider, PRAC Rapporteur: Julie Williams, “Extension of indication for Imbruvica for the treatment of adult patients with Waldenström Macroglobulinaemia (WM). Consequently, changes are proposed to sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and to the Package Leaflet in order to incorporate all information relevant to the WM indication. In addition, some minor editorial corrections have been made in the SmPC.”

Kalydeco (EMEA/H/C/002494/II/0027), Orphan, (ivacaftor), MAH: Vertex Pharmaceuticals (U.K.) Ltd., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia, “Extension of indication for Kalydeco to include the treatment of cystic fibrosis in patients aged 18 years and older who have a R117H mutation in the CFTR gene. Consequently, changes are proposed to sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and to the Package Leaflet.” Request for Supplementary Information adopted on 23.10.2014.

Kuvan (EMEA/H/C/000943/II/0033), Orphan, (sapropterin), MAH: Merck Serono Europe Limited, Rapporteur: Patrick Salmon, Co-Rapporteur: Daniel Brasseur, “Extension of indication for the 'treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of 4 years of age and over with phenylketonuria (PKU) who have shown to be responsive to such treatment' to include the paediatric population under 4 years old. Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated accordingly.”

REVOLADE (EMEA/H/C/001110/II/0020), (eltrombopag), MAH: GlaxoSmithKline Trading Services, Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas, “Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add a new indication on the treatment of adult patients with severe aplastic anaemia (SAA) who have had an insufficient response to immunosuppressive therapy. The package leaflet is updated accordingly. In addition, the MAH has corrected the acronym used for full blood counts (FBC) in the SmPC, Annex II and PL.”	
Simponi (EMEA/H/C/000992/II/0061), (golimumab), MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add a new therapeutic indication for non-radiographic axial spondyloarthritis. The Package Leaflet is updated accordingly.”	
Soliris (EMEA/H/C/000791/II/0066), Orphan, (eculizumab), MAH: Alexion Europe SAS, Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pierre Demolis, “Update of sections 4.1 and 5.1 of the SmPC with an extension of the indication in patients with Paroxysmal nocturnal haemoglobinuria (PNH) regardless of their history of transfusion. The PL has been updated accordingly. In addition, some minor corrections are proposed in Section 5.1 of the SmPC and in the PL.” Request for Supplementary Information adopted on 20.11.2014, 24.07.2014.	

Sustiva (EMEA/H/C/000249/II/0126/G), (efavirenz), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Margarida GuimarãesGrouped variation consisting of two consequential variations. A type II variation to extend the therapeutic indication to include children 3 months of age to less than 3 year of age and weighing at least 3.5kg. A type IB, consequential to this update, to remove the Oral Solution pharmaceutical form for Sustiva (efavirenz) and as such upgrade the already approved “capsule sprinkle” dosing method as primary means of dosing for young patients and those that cannot swallow capsules and/or tablets”
Request for Supplementary Information adopted on 23.10.2014, 22.05.2014.

Vectibix (EMEA/H/C/000741/II/0065), (panitumumab), MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings, Co-Rapporteur: Karsten Bruins Slot, “Update of section 4.1 to extend the indication for Vectibix in the treatment of adult patients with wild-type RAS metastatic colorectal cancer (mCRC) to include use in the first-line setting in combination with FOLFIRI. Subsequently the section 5.1 is being updated to include clinical data supporting the extended indication.”

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

Revlimid (EMEA/H/C/000717/II/0079), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Arnaud Batz, "Extension of Indication to add treatment of adult patients with relapsed and/ or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. A revised version of the RMP (version 25.0) was provided as part of this application."

- CHMP assessment of similarity : **For adoption**

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 18.12.2014, 25.09.2014.
List of Questions adopted on 23.01.2014.

- Opinion: **For adoption**
- BWP Report: **For adoption**

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

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

8. Withdrawal of full initial application

Ketoconazole AID-SCFM (EMEA/H/C/003800), Orphan
(ketoconazole), Applicant: Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare, (treatment of Cushing's syndrome)
Well-established use application (Article 10a of Directive No 2001/83/EC).

- Letter from the applicant dated 20 February 2015 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)

IV Zanamivir (EMEA/H/K/002288 procedure OTH004)
(zanamivir), MAH: Glaxo Group Ltd., (treatment of pandemic A(H1N1)v infection or infection due to seasonal influenza A or B virus)
This is an application to update the Conditions of Use document for Zanamivir injection (10mg/mL) compassionate use supplies under Article 83(4) of Regulation (EC) 726/2004.

- Opinion: **For adoption**

10. Pre-submission issues

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

(H0003986)
(Idarucizumab), (indicated in adults treated with dabigatran etexilate when rapid reversal of the anticoagulant effects of dabigatran is required:
• life-threatening or uncontrolled bleeding
• emergency surgery/procedures),

- Request for an accelerated review: **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.

Brintellix (EMEA/H/C/002717/II/0004), (vortioxetine), MAH: H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC with information on the effect of vortioxetine on cognitive dysfunction in Major Depressive Disorder."
Request for Supplementary Information adopted on 20.11.2014.

- Opinion / Request for Supplementary information: **For adoption**

Herceptin (EMEA/H/C/000278/II/0089/G), (trastuzumab), MAH: Roche Registration Ltd, Rapporteur: Jan Mueller-Berghaus, "As requested by the CHMP during the assessment of the variation II-076 and based on the mega population pharmacokinetic analysis, update of section 4.2 (for Herceptin IV only), 4.4, 4.6 and 5.2 to include the key findings.
Update of section 4.5 to include the outcomes of the H4613g/GO01305 study and the updated population pharmacokinetic analysis of PK data from BO22227/HannaH study."

- Opinion / Request for Supplementary information: **For adoption**

Revlimid (EMEA/H/C/000717/II/0076), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, "Update of section 4.4 of the SmPC with a new warning regarding an increased risk of mortality with the use of Revlimid in patients with chronic lymphocytic leukemia (CLL). The package leaflet is updated accordingly."
Request for Supplementary Information adopted on 18.12.2014, 20.11.2014, 26.06.2014.

- Opinion / Request for Supplementary information: **For adoption**

WS0689/G
TECFIDERA-
EMEA/H/C/002601/WS0689/0011/G
NAPs included in WS: Fumaderm, Fumaderm Intial (fumarate containing products), MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 of the SmPC in order to add a recommendation to consider interruption of treatment in patients with low lymphocyte counts (<0.5 x 109/L) persisting for more than six months and to monitor lymphocyte counts until recovery. Update of section 4.8 of the SmPC with information on observed low lymphocyte counts in clinical studies with tecfidera and PML (Progressive multifocal leukoencephalopathy) occurrence in the setting of severe and prolonged lymphopenia. Furthermore, the due dates of two commitments as part of the RMP have been revised."

Pradaxa (EMEA/H/C/000829/ LEG 043 and LEG2 043.1
dabigatran etexilate), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Torbjorn Callreus,

- PRAC Advice: **For discussion**
- CHMP Recommendation: **For adoption**

12. Referral procedures

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

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.

- Opinion: **For adoption**

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

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

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 on 25.07.2013. List of Outstanding Issues adopted 23.10.2014, 25.04.2014.

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

Cymevene IV and associated names (EMEA/H/A-30/1406) (ganciclovir), F. Hoffmann-La Roche
Rapporteur: Rugile Pivliene, Co-Rapporteur: Alar Irs, , List of Questions adopted on 25.09.2014.

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

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

Adrenaline auto injectors (EMEA/H/A-31/1398)
Rapporteur: Alar Irs, Co-Rapporteur: Robert James Hemmings,
Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients. List of Outstanding Issues adopted on 25.09.2014.

- Minutes of the ad-hoc expert group meeting held on 23 January 2015: **For**

discussion

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

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

12.8. Procedure under Article 107(2) of Directive 2001/83/EC

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

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

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)

13. Pharmacovigilance issues

Summary of recommendations and advice of PRAC meeting held on 9-12 February 2015: **For information**

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for February 2015: **For adoption**

Early Notification System:
February 2015 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

For information

ITF Briefing Meeting

For discussion

ITF Briefing Meeting

For discussion

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

Request from EC for EMA scientific Opinion under Art. 57 (1)P of Regulation (EC) No 726/2004

- Final report: **For adoption**

15.4. Nanomedicines activities

16. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on January 2015. 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 23-25 February 2015: **For information**

18. Other Committees

18.1. Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 10-11 February 2015: **For information**

18.2. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 27-30 January 2015: **For information**

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2015 PDCO: **For**

information

Report from the PDCO meeting held on held on 11-13 February 2015: **For information**

18.4. Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 19-20 February 2015: **For information**

19. Invented name issues

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

20. Any other business

Vaccines Working Party (VWP)

Vaccines Working Party (VWP) work plan for 2015: **For adoption**
VWP responses to CHMP questions on pertussis resurgence in the EU: **For discussion**

Biostatistics Working Party (BSWP)

Guideline on adjustment for baseline covariates in clinical trials (Doc Ref: EMA/CHMP/295050/2013): **For adoption**
Biostatistics Working Party (BSWP) work plan for 2015 (EMA/CHMP/801811/2014): **For adoption**
BSWP 2014 activity report (EMA/796149/2014): **For information**

Blood Products Working Party (BPWP)

BPWP work plan for 2015: **For adoption**
Final Minutes from 02/10/2014 virtual meeting (EMA/CHMP/BPWP/607670/2014): **For information**
Guideline on core SmPC for human normal immunoglobulin for subcutaneous and intramuscular administration (EMA/CHMP/BPWP/143744/2011 rev. 1): **For final adoption**
Overview of comments received

Agenda of BPWP virtual meeting to be held 5 March 2015 (EMA/CHMP/BPWP/769704/2014): **For information**

Oncology Working Party (ONCWP)

"Concept paper on the need to revise the "Guideline on the evaluation of anticancer medicinal products in man" in order to provide guidance on the reporting of safety data from clinical trials": **For adoption and release for 3-month public consultation**

Rheumatology / Immunology Working Party (RIWP)

Concept paper on clinical investigation of medicinal products for the treatment of Axial Spondyloarthritis (EMA/CHMP/61287/2015): **For adoption and release 3 months consultation**

Guideline on clinical investigation of medicinal products for the treatment systemic lupus erythematosus and lupus nephritis (EMA/CHMP/51230/2013): **For adoption**
Overview of external comments received (EMA/CHMP/51230/2013)

Cardiovascular Working Party (CVSWP)

Final agenda of WP meeting held by teleconference on 28 January 2015 (EMA/6665/2015): **For information**

Final minutes of WP meeting held face-to-face on 26 November 2014 (EMA/732357/2014): **For information**

Draft Guideline on clinical investigation of medicinal products for the treatment of venous thromboembolic disease (EMA/CHMP/41230/2015 Rev. 1, prev. CPMP/EWP/563/98): **For adoption for 6-month public consultation**

Paediatric Addendum to the Note for Guidance on Clinical Investigation of Medicinal Products in the Treatment of Hypertension (EMA/CHMP/206815/2013): **For adoption**
Overview of comments received (EMA/CHMP/68390/2015)

Biosimilar Medicinal Product Working Party (BMWP)

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 and implementation**

SWP chair's report on the EU position on pregnancy labelling in relation to the on the FDA final rule on changes to pregnancy and lactation information for prescription drug and biological products.

Update on activities related to revised RMP Assessment process in 2015

Modelling and Simulation Working Group (MSWG)

Report from EMA EFPIA Dose Finding Workshop
MSWG activity report for 2014: **For information**
MSWG work plan for 2015 : **For adoption**

Biologics Working Party (BWP)

Nomination of Catherine Milne as an additional EDQM representative at BWP: **For endorsement**

Nomination of Louise Bisset as the new BWP Alternate for UK, replacing Adrian Thomas in this role: **For endorsement**

Draft agenda for BWP face-to face meeting to be held 16-18 February 2015 (EMA/CHMP/BWP/804840/2014): **For information**

Draft agenda for BWP face-to face meeting to be held 16-18 March 2015 (EMA/CHMP/BWP/19894/2015): **For information**

Final minutes from face-to-face meeting held 10-12 November 2014 (EMA/CHMP/BWP/701931/2014): **For information**

Final minutes from face-to-face meeting held 8-10 December 2014 (EMA/CHMP/BWP/772128/2014): **For information**

Excipients Labelling Drafting Group (Excp DG)

Questions and answers on benzalkonium chloride in the context of the revision of the guideline on 'Excipients in the label and package leaflet of medicinal products for human use' (EMA/CHMP/495737/2013): **For adoption**
Draft overview of comments (EMA/CHMP/601508/2014): **For information**

Final minutes of Excp DG TC held on 27 November 2014 (EMA/755429/2014): **For information**

Final minutes of Excp DG teleconference held on 17 December 2014 (EMA/799232/2014): **For information**

European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations **(PCWP)**

European Medicines Agency Human Scientific Committees' Working Party with Healthcare

Professionals' Organisations **(HCPWP)**	
Draft Agenda PCWP and HCPWP joint meeting 4 March 2015: **For information**	
Draft Agenda PCWP and HCPWP joint meeting: Information session on Biosimilars 5 March 2015 **For information**	
Minutes of the EMA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) meeting with all eligible organisations held on 26 November 2014: **For information**	
Feedback for the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium (PROTECT) symposium held on 18-20 February 2015: **For discussion**	

Quality Working Party (QWP)

Guideline on the Chemistry of Active Substances: **For adoption for public consultation**
Question-and-answer on plastic containers for eye drops: **For adoption**

Question-and-answer on the calculation of thresholds to set limits for impurities in the finished product specification: **For adoption**

Concept paper on the development of a guideline on quality and equivalence of topical products: **For adoption for public consultation**

BWP and QWP letter to EDQM on pharmaceutical containers and closures: **For adoption**

Letter to EGA - GMP/GDP IWG and QWP request for concrete examples and further information on possible amount of variation triggered by the revised 'Guideline on ASMF procedure' and CMDh 'Q/A on level of details to be provided for AS manufacturers on application forms for new MAs, variations and renewals': **For adoption**

Rotation speed for dissolution testing - QWP response to CMDh: **For adoption**

Elemental impurities in Marketed Products - Recommendations for implementation: **For adoption**

Concept paper on the need for Revision of the Guideline on the Requirements to the Chemical and Pharmaceutical Quality Documentation concerning Investigational Medicinal Products in Clinical Trials: **For adoption for public consultation**

Reflection paper on the chemical structure and properties criteria to be considered for the evaluation of New Active Substance (NAS) status of chemical substances**: For adoption for public consultation**

Debriefing on Regulatory Workshop on Clinical Trials Designs in Neuro Myelitis Optica Spectrum Disorders (NMOSD) workshop held 10 October

2014, Draft report: **For discussion**
GLP inspections new requirements for applicants and check list for non-clinical assessors
Draft CHMP ORGAM meeting dates 2016-2018 (EMA/CHMP/89789/2015): **For adoption**

List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 23-26 February 2015 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)*

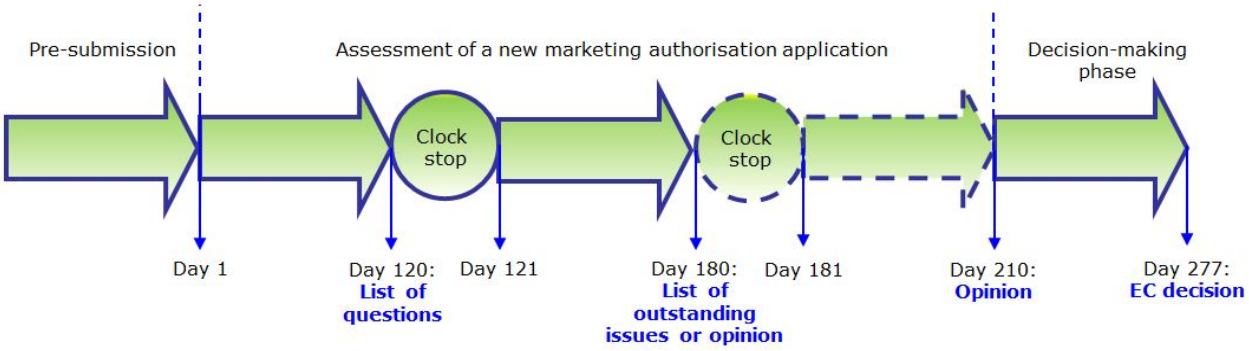
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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