29 January 2016
EMA/CHMP/71842/2016
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 14-17 December 2015

Chair: Tomas Salmonson – Vice-Chair: Pierre Demolis

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes 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. 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.

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

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of 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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

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 14-17 December 2015. See (current) December 2015 CHMP minutes (to be published post January 2016 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 14-17 December 2015

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 16-19 November 2015.

The CHMP adopted the minutes.

1.4. Membership Announcement

The Committee welcomed new UK alternate member Dr Nithyanandan Nagercoil, replacing Dr Rafe Suvarna.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - selexipag - Orphan - EMEA/H/C/003774

Actelion Registration Ltd.; treatment of pulmonary arterial hypertension (PAH; WHO Group I)

Scope: Oral explanation

Action: Oral explanation was held on Tuesday 15 December 2015 at 14.00.

List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 23.04.2015.

See also 3.2.10 List of Outstanding Issues

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Caspofungin Accord - caspofungin - EMEA/H/C/004134

Accord Healthcare Ltd; treatment of invasive candidiasis and invasive aspergillosis

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Cancidas

List of Outstanding Issues adopted on 22.10.2015. List of Questions adopted on 23.07.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.2. Dropcys - mercaptamine - Orphan - EMEA/H/C/004038

Lucane Pharma; treatment of corneal cystine deposits

Scope: Opinion

Action: For adoption

Well-established use application (Article 10a of Directive No 2001/83/EC)

An oral explanation was held on 18 November 2015. List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 26.03.2015.

The Committee noted that that the studies from the medical literature presented to support the application were insufficient. Although the role of mercaptamine eye drops in the treatment of corneal deposits appears sufficiently supported by the literature, clinical

recommendations and its routine use in hospital preparations, there were few data supporting the effectiveness of the concentration of mercaptamine used in Dropcys (0.1% solution). In addition, the Committee had concerns regarding other ingredients of the medicine, their impact on long-term safety, particularly in children, and how stable and sterile the solution would be once prepared.

The CHMP adopted a negative opinion by majority (27 positive out of 29 votes), together with the Assessment Report.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The divergent position (David Lyons and Nela Vilceanu) was appended to the opinion.

The refusal question and answers document was circulated for information.

3.1.3. Feraccru - ferric maltol - EMEA/H/C/002733

Iron Therapeutics (UK) Ltd; treatment of iron deficiency anaemia

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

Oral explanation held on 19.11.2015. List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 23.04.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that ferric maltol is not a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.4. Iblias - octocog alfa - EMEA/H/C/004147

Bayer Pharma AG; Treatment and prophylaxis of haemophilia A
Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)

Scope: Opinion

Action: For adoption

Known active substance (Article 8(3) of Directive No 2001/83/EC), Duplicate of Kovaltry

List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 23.04.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.5. Kovaltry - octocog alfa - EMEA/H/C/003825

Bayer Pharma AG; Treatment and prophylaxis of haemophilia A
Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)

Scope: Opinion

Action: For adoption

Known active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 23.04.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.6. Neofordex - dexamethasone - Orphan - EMEA/H/C/004071

Laboratoires CTRS; treatment of symptomatic multiple myeloma in combination with other medicinal products.

Scope: Opinion

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 19.11.2015, 24.09.2015. List of Questions adopted on

18.12.2014.

The Committee discussed the benefit of halving 40 mg dose and concluded that 20 mg dose is approvable (in elderly and/or frail patients). The applicant plans to authorise the 20 mg strength oral dosage form, and after that the applicant is requested to remove the scoreline for sub-division of the 40 mg tablet and delete the 20 mg posology.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (22 positive out of 31 votes) together with the CHMP assessment report and translation timetable.

The divergent position (Bruno Sepodes, Daniel Brasseur, Greg Markey, Harald Enzmann, Jan Mueller-Berghaus, Jean-Louis Robert, Karsten Bruins Slot, Kolbeinn Gudmundsson, Outi Maki-Ikola, Pieter de Graeff, Robert Hemmings) was appended to the opinion.

The Icelandic and Norwegian Members were not in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The CHMP adopted an updated similarity assessment report of Neofordex.

3.1.7. Portrazza - necitumumab - EMEA/H/C/003886

Eli Lilly Nederland B.V.; treatment of squamous non-small cell lung cancer

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 19.11.2015, 24.09.2015. List of Questions adopted on 23.04.2015.

The Committee discussed the benefit-risk of the product and concluded that the product is approvable.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (25 positive out of 30 votes) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that necitumumab is a new active substance, as claimed by the applicant.

The divergent position (Daniela Melchiorri, Dimitrios Kouvelas, Jan Mazag, Juris Pokrotnieks, Kolbeinn Gudmundsson, Pieter de Graeff) was appended to the opinion.

The Norwegian Member was in agreement with the CHMP recommendation, the Icelandic Member against.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.8. Tagrisso - osimertinib - EMEA/H/C/004124

Accelerated assessment

AstraZeneca AB; Non-small-cell lung cancer (NSCLC)

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Questions adopted on 22.10.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a **conditional** marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that osimertinib is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.9. Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982

Sanofi Pasteur MSD SNC; vaccination against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and invasive diseases caused by Haemophilus influenzae typeb (Hib)

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 22.10.2015. List of Questions adopted on 21.05.2015.

The members discussed the proposed age range in the indication. As possible options, it was considered to either state an age range from 6 weeks to 24 months or the term infants and toddlers, which would also be in line with other products. After discussion the CHMP agreed to the wording infants and toddlers above 6 weeks of age.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.10. Zurampic - lesinurad - EMEA/H/C/003932

AstraZeneca AB; treatment of hyperuricaemia

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 22.10.2015. List of Questions adopted on 21.05.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that lesinurad is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.11. Solumarv - insulin human - EMEA/H/C/003858

Marvel Lifesciences Ltd; treatment of diabetes

Scope: Revised grounds

Action: For adoption

Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Negative opinion was adopted in November 2015 CHMP.

The CHMP adopted a corrected opinion by consensus together with the CHMP assessment report.

3.1.12. Pemetrexed Actavis - pemetrexed - EMEA/H/C/004109

Actavis Group PTC ehf; Treatment of malignant pleural mesothelioma and non-small cell lung cancer.

Scope: Revised CHMP AR

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

Positive opinion was adopted in November 2015 CHMP.

The CHMP adopted a corrected opinion by consensus together with the CHMP assessment report.

3.2. Initial applications; Day 180 list of outstanding issues

3.2.1. - emtricitabine / tenofovir alafenamide - EMEA/H/C/004094

treatment of HIV

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues, SAG involvement was considered necessary.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to consult the SAG HIV/viral diseases.

3.2.2. - migalastat - Orphan - EMEA/H/C/004059

Amicus Therapeutics UK Ltd; Treatment of patients with Fabry disease

Scope: Day 150 list of outstanding issues

Action: For adoption

List of Questions adopted on 22.10.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.3. - trifluridine / tipiracil - EMEA/H/C/003897

treatment of colorectal cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.4. - sirolimus - Orphan - EMEA/H/C/003978

Santen Oy; treatment of chronic non-infectious uveitis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.06.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to consult an ad-hoc expert group. Nomination of expert with expertise: *Ophthalmologists with experience in eye disease affecting the posterior segment, preferably in the treatment of non-infectious uveitis involving the posterior segment of the eye*) should be sent.

3.2.5. - rasagiline - EMEA/H/C/004064

treatment of idiopathic Parkinson's disease (PD)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.6. - infliximab - EMEA/H/C/004020

treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.7. - glycopyrronium bromide - PUMA - EMEA/H/C/003883

treatment of sialorrhoea

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.06.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.8. - ixekizumab - EMEA/H/C/003943

treatment of moderate to severe plaque psoriasis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.9. - daclizumab - EMEA/H/C/003862

treatment of multiple sclerosis (RMS)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues,

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.10. - selexipag - Orphan - EMEA/H/C/003774

Actelion Registration Ltd.; treatment of pulmonary arterial hypertension (PAH; WHO Group I)

Scope: Oral explanation

Action: Oral explanation was held on Tuesday 15 December 2015 at 14.00.

List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 23.04.2015.

An oral explanation was held on Tuesday 15 December 2015 at 14.00. The presentation by the applicant focused on the mortality risk in patients with PAH.

The Committee adopted a list of outstanding issues with a specific timetable.

See also 2.1.1.Oral Explanation

3.3. Initial applications; Day 120 list of questions

3.3.1. - darunavir - EMEA/H/C/004068

treatment of HIV-1

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.2. - emtricitabine / rilpivirine / tenofovir alafenamide - EMEA/H/C/004156

treatment of HIV-1

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.3. - palbociclib - EMEA/H/C/003853

treatment of breast cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the

list of questions.

3.3.4. - ixazomib - Orphan - EMEA/H/C/003844

Takeda Pharma A/S; multiple myeloma

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.5. - methotrexate - EMEA/H/C/003983

treatment of active rheumatoid arthritis; severe, active juvenile idiopathic arthritis; severe recalcitrant disabling psoriasis

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.6. - tenofovir disoproxil - EMEA/H/C/004049

treatment of HIV-1 infection and hepatitis B infection

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.7. - rociletinib - EMEA/H/C/004053

treatment of patients with mutant epidermal growth factor receptor (EGFR) non-small cell lung cancer (NSCLC).

Scope: Day 120 list of questions

Action: For adoption

The Committee noted the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.8. - fluticasone propionate / salmeterol xinafoate - EMEA/H/C/002752

treatment of asthma and COPD

Scope: Revised Day 120 list of questions

Action: For adoption

List of Questions adopted on 22.10.2015.

The CHMP adopted a revised List of Questions (editorial changes).

3.3.9. - fluticasone propionate / salmeterol xinafoate - EMEA/H/C/004267

treatment of asthma and COPD

Scope: Revised Day 120 list of questions

Action: For adoption

List of Questions adopted on 22.10.2015.

The CHMP adopted a revised List of Questions (editorial changes).

3.3.10. - obeticholic acid - Orphan - EMEA/H/C/004093

Intercept Italia s.r.l; treatment of primary biliary cirrhosis

Scope: Revised Day 120 list of questions

Action: For adoption

List of Questions adopted on 22.10.2015.

The CHMP adopted a revised List of Questions and agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions.

3.4. Update on on-going initial applications for Centralised procedure

3.4.1. - cediranib - Orphan - EMEA/H/C/004003

AstraZeneca AB; treatment of platinum sensitive relapsed (PSR) ovarian cancer relapsed (PSR) ovarian cancer

Scope: Similarity assessment

Action: For adoption

List of Questions adopted on 19.11.2015.

The CHMP adopted the similarity assessment report

3.4.2. - docetaxel - EMEA/H/C/004086

treatment of breast cancer, non-small cell lung cancer, prostate cancer, gastric adenocarcinoma, head and neck cancer

Scope: Letter from the applicant dated 5th December 2015 requesting extension of timeframe to respond to Day 120 List of Questions,

Action: For information

List of Questions adopted on 24.09.2015.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Day 120 list of questions adopted in September 2015.

3.4.3. - parathyroid hormone - Orphan - EMEA/H/C/003861

NPS Pharma Holdings Limited; treatment of hypoparathyroidism

Scope: list of experts for ad hoc expert group meeting

Action: For adoption

Day 180 list of outstanding issues adopted 24.09.2015. List of Questions adopted on 26.03.2015.

The CHMP adopted the list of experts for the ad hoc expert group meeting.

3.4.4. - albutrepenonacog alfa - Orphan - EMEA/H/C/003955

CSL Behring GmbH; prophylaxis and treatment of bleeding in all patients with haemophilia B, treatment of bleeding in all patients with haemophilia B

Scope: Letter from the applicant dated 8th December 2015 requesting extension of timeframe to respond to Day 180 List of Questions,

Action: For adoption

Day 180 list of outstanding issues adopted 19.11.2015. List of Questions adopted on 23.07.2015.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Day 120 list of questions adopted in November 2015.

3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Brilique - ticagrelor - EMEA/H/C/001241/X/0029/G

AstraZeneca AB; prevention of atherothrombotic events, treatment of atherothrombotic events in adult patients

Rapporteur: Pieter de Graeff, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Menno van der Elst

Scope: "Annex I_2.(c) - extension application for a new strength of 60mg with a new indication: History of Myocardial Infarction.
C.I.4. Type II - To update the product information of the existing Brilique 90mg license with important clinical information from the PEGASUS study."

Action: For adoption

List of Outstanding Issues adopted on 19.11.2015. List of Questions adopted on 23.07.2015.

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

4.1.2. Lojuxta - lomitapide - EMEA/H/C/002578/X/0016

Aegerion Pharmaceuticals Limited

Rapporteur: Pieter de Graeff,

Scope: "The applicant has submitted an application for a line extension to include 30 mg, 40 mg and 60 mg hard capsules."

Action: For adoption

List of Questions adopted on 24.09.2015.

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

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

4.2.1. Instanyl - fentanyl / fentanyl citrate - EMEA/H/C/000959/X/0030/G

Takeda Pharma A/S

Rapporteur: Pierre Demolis, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Arnaud Batz

Scope:–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 packsize 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%.

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".

Action: For adoption

List of Outstanding Issues adopted on 23.07.2015. List of Questions adopted on 26.02.2015.

The Committee discussed the issues identified in this application. The members noted the withdrawal of the line extension procedure to introduce a new dose strength (400 µg/dose) to the already available range of Instanyl multi-dose presentations (50, 100 and 200 µg/dose).

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

4.3.1. Fycompa - perampanel - EMEA/H/C/002434/X/0025

Eisai Europe Ltd.

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams

Scope: “Annex 1_2.(d) - To add a new pharmaceutical form, oral solution, to the one currently approved (EU/1/12/776/024).

To add a new strength of 0.5 mg/ml for Fycompa finshed product (EU/1/12/776/024).”

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP discussed the available bioequivalence data for the two formulations in the fed state as well as observed food effects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.2. Keytruda - pembrolizumab - EMEA/H/C/003820/X/0001/G

Merck Sharp & Dohme Limited

Rapporteur: Daniela Melchiorri,

Scope: “To introduce concentrate for solution for infusion (25 mg/mL) as additional pharmaceutical form for Keytruda

In addition, the following changes have been grouped with this extension application:

B.I.a.1.e – To add Boehringer Ingelheim (BIB), Pharma GmbH & Co. KG, Birkendorfer Straße 65, 88397, Biberach an der Riss, Germany as additional site responsible for the manufacturing and quality control of the active substance.

B.I.a.1.j – To add Schering Plough Brinny Co., Ballinacurra Road, Innishannon, County Cork, Ireland as additional site responsible for the quality control of the active substance.

B.I.a.1.z – To add Biotec House, Central Park , Western Avenue, Bridgend , Industrial Estate, Bridgend, CF31 3RT, UK as a site responsible for storage of the active substance.

B.I.a.1.k – To add Biostorage Technologies, 2910 Fortune Circle W, Suite E, Indianapolis, IN 46241, U.S as additional site responsible for the storage of the WCB and MCB.”

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.3. Paliperidone Janssen - paliperidone - EMEA/H/C/004066/X/0007/G

Janssen-Cilag International NV

Rapporteur: Filip Josephson, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue

Scope: "This variation is part of a grouped application consisting of an extension application to introduce four new strengths of a once-every-3-month paliperidone injection formulation (175 mg, 263 mg, 350 mg and 525 mg) together with the variations identified below:

C.I.6.a - extension of indication for to revise the injection frequency to ' once-every-3-months' following prior adequate treatment with XEPLION for at least four months. Consequently, changes to Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are proposed. The PL and RMP are proposed to be revised accordingly.

A.2.a - Change of the Name of the Medicinal Product (Section 1 of the SmPC) "Paliperidone Janssen"

6 x C.I.7.b - deletion of all 6 currently authorised Paliperidone Janssen dosage strengths (i.e. Paliperidone Janssen 25 mg, 50 mg, 75 mg, 100 mg, 150 mg and 150 mg / 100 mg - EU/1/14/971/001-006)."

Action: For adoption

The Committee discussed the issues identified in this application. The discussion mainly focused on the wording of the indication and dosing recommendations.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions .

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

No items

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

No items

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

5.1.1. Cyramza - ramucirumab - Orphan - EMEA/H/C/002829/II/0003

Eli Lilly Nederland B.V.

Rapporteur: Pieter de Graeff, Co-Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur:

Brigitte Keller-Stanislawski

Scope: “Extension of Indication to include a new indication for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with progression after platinum-based chemotherapy for CYRAMZA; as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, one minor typographical error was corrected in section 4.2 of the SmPC. Version 6 of the Risk Management Plan was agreed.”, Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015, 21.05.2015.

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.2. Cyramza - ramucirumab - Orphan - EMEA/H/C/002829/II/0004

Eli Lilly Nederland B.V.

Rapporteur: Pieter de Graeff, Co-Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: “Extension of Indication to include a new indication for Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), for the treatment of adult patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, Annex II has been updated to include an obligation for the MAH to conduct a Post Authorisation Efficacy Study (PAES). In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor editorial mistakes and to align Annex II to the QRD version 9.1.”

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015, 25.06.2015.

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.3. Ferriprox - deferiprone - EMEA/H/C/000236/II/0103

Apotex Europe BV

Rapporteur: Pierre Demolis, Co-Rapporteur: Concepcion Prieto Yerro

Scope: "Extension of Indication to include a new indication for Ferriprox in combination with another chelator for the treatment of iron overload in patients with thalassaemia major when monotherapy with any one iron chelator is inadequate.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the MAH took the opportunity of this procedure to update the Product Information in compliance with the QRD template version 9.1 and combine the SmPC for the 500mg and 1000mg tablets. The contact details of France and Portugal have been updated in the PL."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to indication wording.

The Committee adopted Request for Supplementary Information with a specific timetable.

5.1.4. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0007

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams

Scope: "Extension of indication to add the treatment of patients with follicular lymphoma based on the results of the pivotal study GAO4753g. Consequently, updates to sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC, the Package Leaflet and RMP have been proposed. Furthermore, the MAH took the opportunity to make minor editorial changes to sections 4.4, 4.6, 5.3 and 6.6 of the SmPC."

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted Request for Supplementary Information with a specific timetable.

5.1.5. Humira - adalimumab - EMEA/H/C/000481/II/0146

AbbVie Ltd.

Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include treatment of non-infectious intermediate, posterior and panuveitis in adult patients for Humira.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application. The main discussion focused on the wording of the indication with specific regard to the MAH's proposal for use as first line treatment. The Committee looked at the effects size in the clinical trials and whether a monotherapy and maintenance treatment was supported by clinical data.

The Committee adopted Request for Supplementary Information with a specific timetable.

The CHMP agreed to consult an ad-hoc expert group

Nomination of expert with expertise: *Ophthalmologists with experience in eye disease affecting the posterior segment, preferably in the treatment of non-infectious uveitis involving the posterior segment of the eye*) should be sent.

5.1.6. Nplate - romiplostim - Orphan - EMEA/H/C/000942/II/0051

Amgen Europe B.V.

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of Indication to include second line treatment of all non-splenectomised patients (including those without a contraindication to surgery). As a consequence, section 4.1 of the SmPC has been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in Croatia and Italy in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 25.06.2015.

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.7. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0023

Novartis Europharm Ltd

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Greg Markey, Scope: "Extension of indication to extend the use of Revolade to non-splenectomized patients; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015, 25.06.2015.

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.8. Ruconest - conestat alfa - EMEA/H/C/001223/II/0031

Pharming Group N.V

Rapporteur: Greg Markey

Scope: "Extension of Indication to include adolescents in the treatment of acute angioedema attacks in adults with hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency. As a consequence sections 4.1, 4.2, and 5.1 of the SmPC have been updated. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted Request for Supplementary Information with a specific timetable.

The CHMP adopted the similarity assessment report for Ruconest.

5.1.9. Tarceva - erlotinib - EMEA/H/C/000618/II/0043

Roche Registration Limited

Rapporteur: Sinan B. Sarac

Scope: "Modification of the indication to limit maintenance treatment to NSCLC patients with an EGFR-activating mutation and stable disease after first-line chemotherapy based on the data from study BO25460 (IUNO). Consequently, SmPC sections 4.1, 4.8 and 5.1 have been updated. The Package leaflet is updated accordingly."

Action: For adoption

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

The CHMP agreed to the wording of a DHPC letter and communication plan.

5.1.10. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0012

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus

Scope: "Extension of indication for Translarna to include the treatment of cystic fibrosis resulting from a nonsense mutation in at least one allele of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Consequently, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC were updated. The Package leaflet and RMP are being updated accordingly. The MAH took also the opportunity to implement the QRD template v9.1. and proposed combined SmPC for Translarna 125 mg, 250 mg and 1000 mg granules for oral suspension. Minor editorial changes have been introduced throughout the PI.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

The Committee discussed the issues identified in this application. The main issues were related to the efficacy of ataluren in nmCF patients as a whole and in a subgroup of patients without concomitant treatment with inhaled aminoglycosides. Furthermore, the Committee discussed ataluren's potential for renal and urinary toxicity.

The Committee adopted Request for Supplementary Information with a specific timetable.

The CHMP adopted the similarity assessment report for Translarna.

5.1.11. Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0022

AstraZeneca AB

Rapporteur: Greg Markey

Scope: "Extension of Indication to include new population, children over the age of 2 months and adolescents, for Zinforo. As a consequence, sections 4.1, 4.2, 5.2, 5.3 and 6.6 of the SmPC are updated with new information on dosing, PK and pre-clinical safety. The Package Leaflet is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015.

The Committee discussed the issues identified in this application.

The Committee adopted Request for Supplementary Information with a specific timetable.

5.1.12. Zontivity - vorapaxar - EMEA/H/C/002814/II/0005

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension of Indication to include treatment of patients with Peripheral Arterial

Disease (PAD) and as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of local representative in Luxembourg in the Package Leaflet.
Furthermore, the PI is brought in line with the latest QRD template version 9.1. Moreover, revised RMP version 2.0 was provided as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the lack of robust evidence of efficacy in the PAD stratum alone and whether the benefit can outweigh the safety concerns and uncertainties.

The Committee adopted Request for Supplementary Information with a specific timetable.

5.1.13. Zydelig - idelalisib - EMEA/H/C/003843/II/0011

Gilead Sciences International Ltd

Rapporteur: Kristina Dunder, PRAC Rapporteur: Rafe Suvarna

Scope: "Extension of Indication to include new indication for Zydelig to include the combination of idelalisib with ofatumumab. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for United Kingdom and Ireland in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015.

The Committee discussed the issues identified in this application.

The Committee adopted Request for Supplementary Information with a specific timetable.

The CHMP adopted the similarity assessment report for Zydelig

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

5.2.1. Opdivo - nivolumab - EMEA/H/C/003985/II/0002 and EMEA/H/C/003985/II/0003

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Arantxa Sancho Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: List of experts to SAG Oncology meeting to be held on 14 January 2016

II/ 0002 "Extension of Indication to add treatment as monotherapy of patients with advanced renal cell carcinoma (RCC) after prior therapy in adults, based on Study CA209025; a phase 3 study of nivolumab vs. everolimus in subjects with advanced or metastatic clear-cell RCC who

have received prior anti-angiogenic therapy, and the CA209010 addendum study report; phase 2 dose-ranging study of nivolumab in subjects with progressive advanced/metastatic clear-cell RCC who have received prior anti-angiogenic therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet.
An updated RMP version 4.0 was provided as part of the application. Further, the MAH requested one additional year of market protection for a new indication."

Request for Supplementary Information adopted on 22.10.2015.

II/0003 "Extension of Indication to include treatment in combination with ipilimumab of advanced (unresectable or metastatic) melanoma in adults based on interim data from study CA209067 and the final CSR of study CA209069. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been revised accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II and Package Leaflet. An updated RMP version 3.0 was provided as part of the application as well as a paediatric non-clinical biomarker study provided to fulfil paediatric requirements."

Request for Supplementary Information adopted on 22.10.2015.

Action: For adoption

The CHMP adopted a list of experts to the SAG Oncology meeting to be held on 14 January 2016.

5.2.2. Opdivo - nivolumab - EMEA/H/C/003985/II/0008

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Assessment of similarity, BWP report

"Extension of Indication to add treatment as monotherapy of patients with advanced renal cell carcinoma (RCC) after prior therapy in adults, based on Study CA209025; a phase 3 study of nivolumab vs. everolimus in subjects with advanced or metastatic clear-cell RCC who have received prior anti-angiogenic therapy, and the CA209010 addendum study report; phase 2 dose-ranging study of nivolumab in subjects with progressive advanced/metastatic clear-cell RCC who have received prior anti-angiogenic therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet.
An updated RMP version 4.0 was provided as part of the application. Further, the MAH requested one additional year of market protection for a new indication."

Action: For adoption

The CHMP adopted the similarity assessment report for Opdivo

The CHMP adopted the BWP report on structural similarity.

5.2.3. Imbruvica - ibrutinib – Orphan - EMEA/H/C/003791/II/0016

MAH: Janssen-Cilag International NV,

Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams,

Scope: Assessment of similarity

"Extension of Indication to broaden the existing indication for chronic lymphocytic leukaemia (CLL) to include all previously untreated patients including those with 17p deletion or TP53 mutation based on the results from the final CSR of study PCYC-1115-CA (MEA 021) for Imbruvica. As a consequence, sections 4.1, 4.6, 4.8, 5.1 and 5.3 of the SmPC are being updated. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and to bring Annex II in line with the latest QRD template version 9.1. Moreover, the updated RMP version 5.0 has been submitted."

Action: For adoption

The CHMP adopted the similarity assessment report for Imbruvica.

5.2.4. Revestive - teduglutide - Orphan - EMEA/H/C/002345/II/0020

NPS Pharma Holdings Limited

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Torbjorn Callreus

Scope: Letter from the MAH dated November 2015 requesting extension of timeframe to submit responses to the Request for Supplementary Information adopted on 19.11.2015

"Extension of Indication to include paediatric population for Revestive.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to update the safety information. The Package Leaflet is updated in accordance."

Action: For adoption

The CHMP agreed to the request from the applicant for an extension to the clock stop to respond to the RSI adopted in November 2015 with a specific timetable.

5.2.5. Tysabri - natalizumab - EMEA/H/C/000603/II/0077

Biogen Idec Ltd

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Letter from the MAH dated 24 November 2015 requesting extension of timeframe to submit responses to the Request for Supplementary Information adopted on 19.11.2015

"Extension of Indication to include new indication for Tysabri.
As a consequence, sections 4.1 AND 4.4 of the SmPC are updated in order to provide physicians with more options for treating RRMS patients with high disease activity who fail an initial disease modifying therapy (DMT). Consequential changes to sections 4.2, 4.3, 5.1 and Package Leaflet in Sections 2 and 3 are also proposed."

Action: For adoption

Request for Supplementary Information adopted on 25.06.2015.

The CHMP agreed to the request from the applicant for an extension to the clock stop to respond to the RSI adopted in November 2015 with a specific timetable.

5.2.6. Arzerra - ofatumumab - Orphan - EMEA/H/C/001131/II/0041

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Doris Stenver

PM: Hector Boix Perales, EPL: Kyriaki Tzogani

Scope: Assessment of similarity

"Extension of Indication to include maintenance therapy in Chronic Lymphocytic Leukemia (CLL).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In accordance with the new QRD template version 9.1, the MAH is also taking the opportunity of this procedure to update the Annex II and combine the 2 SmPCs for the 100mg an 1,000mg vials."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015.

The CHMP adopted the similarity assessment report for Arzerra.

5.2.7. Caprelsa - vandetanib - EMEA/H/C/002315/II/0016

AstraZeneca AB

Rapporteur: Pierre Demolis

Scope: "Extension of Indication to include paediatric indication population for Caprelsa.
As a consequence, sections 4.1, 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated in update the safety information. The Package Leaflet is updated in accordance."

Letter from the applicant requesting an extension to the clock stop to respond to the request for supplementary information adopted in November 2015

Request for Supplementary Information adopted on 19.11.2015.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the request for supplementary information adopted in November 2015 with a specific timetable.

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

No items

6. Ancillary medicinal substances in medical devices

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No items

8. Pre-submission issues

8.1. Pre-submission issue

No items

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Xarelto - Rivaroxaban - EMEA/H/C/000944 - LEG 37

Bayer Pharma AG, prevention of venous thromboembolism (VTE), prevention of stroke and systemic embolism in adult patients with non valvular atrial fibrillation

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: Update on ROCKET Trial

Action: For discussion

Request for Supplementary Information adopted on 19 November 2015.

The Committee discussed the issues identified in this application.

The Committee adopted Request for Supplementary Information with a specific timetable.

9.1.2. ChondroCelect- Characterised Autologous Cartilage Cells Expressing A Specific Marker Profile - (EMEA/H/C/000878- MEA 16.5 and 18.5)

TiGenix NV, Repair of single symptomatic cartilaginous defects

CHMP Coordinators: Jan Mueller-Berghaus, Outi Maki-Ikola, Rapporteur: Egbert Flory, Co-Rapporteur: Tiina Palomäki

Scope: Opinion

Scope 16.5.: randomised control trial protocol TIG/ACT/04/2009

Scope 18.5.: non-interventional registry of ChondroCelect, study TGX001-2011 & randomised controlled study in small lesions using microfracture as comparator

Revision of post authorisation measures

Action: For adoption

The CHMP endorsed the CAT assessment report on the revision of the post authorisation measures.

9.1.3. Aclasta - zoledronic acid - EMEA/H/C/000595/II/0059

Novartis Europharm Ltd,

Rapporteur: Kristina Dunder

Scope: Opinion

“Update of section 4.4 of the SmPC with information on osteonecrosis of other bones in patients treated with Aclasta. The Package leaflet is proposed to be updated accordingly. Furthermore, the MAH took the opportunity to align the product information with the latest QRD template version 9.1.”

Action: For adoption

The Committee noted that the applicant does not request an oral explanation.

The CHMP adopted a negative opinion by consensus recommending by consensus the refusal of the variation to the terms of the Marketing Authorisation.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

9.1.4. Gilenya - fingolimod - EMEA/H/C/002202/II/0037

Novartis Europharm Ltd,

Rapporteur: Pierre Demolis

Scope: Opinion or Request for Supplementary information

“Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information to include additional warning and guidance on PML. The Package Leaflet is updated accordingly.”

Request for Supplementary Information adopted on 22.10.2015.

Action: For adoption

The CHMP agreed to the wording of the DHPC letter as proposed by the PRAC.

9.1.5. Exviera / Viekirax – dasabuvir / ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003837 EMEA/H/C/003839 / WS0873

AbbVie Ltd.,

Lead Rapporteur: Filip Josephson

Scope: Opinion or Request for Supplementary information

“Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to update the safety information based on post-marketing reports of hepatic decompensation and hepatic failure, including liver transplantation or fatal outcomes, and to add a warning that Viekirax/Exviera is not recommended in patients with moderate hepatic impairment (Child-Pugh B). The Package Leaflet is updated accordingly.”

Action: For adoption

The Committee confirmed that all issues previously identified in this application had been resolved.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The CHMP agreed to wording of a DHPC letter and communication plan.

9.1.6. Proposal of CHMP Request to PRAC for Floseal assessment further to TachoSil risk of intestinal obstruction

CHMP: Greg Markey / Jan Mueller-Berghaus

Action: For discussion

The CHMP adopted a list of question to the PRAC for investigation on potential risk of intestinal obstruction in Floseal VH SD.

10. Referral procedures

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

No items

10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004

10.2.1. Desloratadine-containing products

Rapporteur: Daniel Brasseur, Co-Rapporteur: Andrea Laslop,

Scope: Appointment of Rapporteurs, List of Questions and timetable

Prescription status of desloratadine-containing products

Action: For adoption

Letter from BfArM in Germany dated 16 December 2015 requesting a scientific opinion of CHMP under article 5(3) on the prescription status of desloratadine**.**

The CHMP appointed Daniel Brasseur (interest level 1) as Rapporteur and Andrea Laslop as Co-Rapporteur (interest level 1).

The CHMP adopted a list of questions together with a specific timetable.

Notification: 16.12.2015

Start of the procedure (CHMP): 17.12.2015

List of questions: 17.12.2015

Submission of responses: 17.03.016

Re-start of the procedure: 31.03.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 29.04.2016

Comments: 12.05.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 17.05.2016

CHMP list of outstanding issues or CHMP Opinion: May 2016 CHMP

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

No items

10.4. 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

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

10.5.1. Clenil and associated names - Beclometasone dipropionate - EMEA/H/A-30/1418

Chiesi group of companies and associated companiesRapporteur: Daniela Melchiorri, Co-Rapporteur: Martina Weise,Scope: Letter from the MAH dated 27 November 2015 requesting a 1-month extension of timeframe to respond to the List of Outstanding Issues adopted on 19 November 2015.

Harmonisation exercise for Clenil and associated names (beclometasone dipropionate). The review was triggered by Italy due to the need to harmonise the product information across all Member States, including the therapeutic indication, the target populations and the posology recommendations.

Action: For adoption

List of Questions adopted on 25.06.2015. List of outstanding issues adopted 19 November 2015.

The CHMP adopted a revised timetable:

Submission of responses: 19.02.2016

Re-start of the procedure: 04.03.2016

Rapporteur and co-rapporteur assessment reports circulated to CHMP: 15.03.2016

CHMP member comments: 21.03.2016

Updated rapporteur and co-rapporteur assessment reports circulated to CHMP: 23.03.2016

Adoption of second list of outstanding issues / CHMP Opinion: March 2016 CHMP

10.5.2. Saroten and associated names - amitriptyline - EMEA/H/A-30/1430

Lundbeck group of companies and associated companies

Rapporteur: George Aislaitner, Co-Rapporteur: Alar Irs,

Scope: Appointment of Rapporteurs, List of Questions and timetable

Harmonisation exercise for Saroten and associated names (amitriptyline). Review triggered by Greece due to the need to harmonise the product information across all Member States, including the therapeutic indication, the posology, the contra-indications, the adverse effects and the recommendations for use.

Action: For adoption

Letter from Greece dated 11 December 2015 notifying of the official referral under Article 30. Note: A corrected notification dated 17 December was received.

The CHMP appointed George Aislaitner (interest level 1) as Rapporteur and Alar Irs as Co-Rapporteur (interest level 2).

The CHMP adopted a list of questions together with a specific timetable.

Notification: 11.12.2015, corrected version 17.12.2015

Start of procedure (CHMP): December 2015

List of Questions: 17.12.2015

Submission of responses: 19.02.2016

Re-start of the procedure: 04.03.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 15.03.2016

Comments: 21.03.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 23.03.2016

CHMP list of outstanding issues/CHMP opinion: March 2016 CHMP

10.5.3. Lovenox and associated names – enoxaparin - EMEA/H/A-30/1429

Sanofi Aventis group of companies and associated companies

Rapporteur: Joseph Emmerich, Co-Rapporteur: Pieter de Graeff,

Scope: Revised timetable

Harmonisation exercise for Lovenox and associated names. The review was triggered by France, due to the need of harmonisation of the Summary of Product Characteristics across Member States.

Letter from the MAH dated 27 November 2015 requesting 2-month extension of timeframe to submit responses to the List of Questions adopted on 19 November 2015.

List of Questions adopted on 19.11.2015

Action: For adoption

The CHMP adopted a revised timetable.

Adoption of LoQ: 19.11.2015

Submission of responses: 17.03.2016

Re-start of the procedure: 31.03.2016

Rapporteur and co-rapporteur assessment reports circulated to CHMP: 13.04.2016

CHMP member comments: 18.04.2016

Updated rapporteur and co-rapporteur assessment reports circulated to CHMP: 21.04.2016

Adoption of second list of outstanding issues / CHMP Opinion: April 2016 CHMP

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

10.6.1. Fusafungine (NAP), nasal and oral solution - EMEA/H/A-31/1420

Les Laboratoires Servier, various

PRAC Rapporteur: Julia Pallos; PRAC Co-rapporteur: Jana Mladá

Scope: List of questions and draft List of experts for SAG anti-infectives

Action: List of questions for adoption and draft List of experts for SAG anti-infectives for information

The CHMP noted to the draft list of experts for the SAG anti-infectives meeting and adopted a list of questions to this expert group.

Nominations of experts in ENT (Ear Nose Throat), paediatrics as well as General Practitioners to be

The final list of experts will be adopted in January 2016.

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

No items

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

No items

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

No items

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

No items

10.11. 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

11. Pharmacovigilance issue

11.1. Early Notification System

December 2015 Early Notification System on Envisaged CHMP Recommendations for Regulatory Action (based on Identified Safety Concerns) Accompanied by Communication to the General Summary of recommendations and advice of PRAC meeting held on 30-03 December 2015.

Action: For information

12. Inspections

12.1. GMP inspections

Disclosure of information related to GMP inspections will not be published as it undermines the purpose of such inspections

Scope: GMP inspections requested by CHMP during 2015

Final GMP Re-Inspection Programme for 2015

Action: For adoption

The CHMP adopted the GMP inspections.

Scope: Results of sampling and testing programme 2014

Action: For discussion

The CHMP noted the information.

12.2. GCP inspections

Disclosure of information related to GCP inspections will not be published as it undermines the purpose of such inspections

12.3. Pharmacovigilance inspections

Disclosure of information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections

12.4. GLP inspections

Disclosure of information related to GLP inspections will not be published as it undermines the purpose of such inspections

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

13.2. Innovation Task Force briefing meetings

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

13.2.1. ITF Briefing Meeting

Action: For adoption

The CHMP adopted the ITF meeting.

13.2.2. ITF Briefing Meeting

Action: For adoption

The CHMP adopted the ITF meeting.

13.2.3. ITF Briefing Meeting

Action: For adoption

The CHMP adopted the ITF meeting.

13.2.4. Completed ITF Briefing Meetings in 2015

Meeting reports

Action: For information

The CHMP noted the completed ITF meetings.

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

No items

13.4. Nanomedicines activities

2nd TC of the IPRF Nano Working Group on 12 November 2015

Action: For information

The CHMP noted the information.

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of CHMP co-opted member

The election of co-opted member is to take place at the December 2015 CHMP Plenary.

The CHMP elected Dr Koenraad Norga as CHMP co-opted member with expertise in Pharmacology.

14.1.2. Update on the pilot on patient involvement at CHMP

Action: For discussion

The CHMP discussed and noted the update. The CHMP noted the three cases of patients' involvement and positive feedback received. Involvement of patients has been a learning curve and has improved with experience. However, in order to complete the pilot, at least 2-3 more cases are needed before being able to deliver a sufficient analysis.

14.1.3. Workshop on estimands to be held in EMA 25-26 February 2016

Action: For information

The CHMP noted the planned workshop on estimands. Limited places for reimbursed participation are available. Please send your expression of interest in attending this workshop to: biostatistics@ema.europa.eu by **29 January 2016**.

14.1.4. Workshop on the role of pharmacokinetic and pharmacodynamic measurements in the use of direct oral anticoagulants DOACs held on 23 November 2015

Scope: Debriefing from the workshop and actions

Action: For discussion

The CHMP discussed and noted the feedback from the workshop. Further discussions will continue in January CHMP.

14.1.5. Cardiac safety research consortium (CSRC) workshop

Scope: Role for pharmacokinetic/pharmacodynamics guided dosing for novel anticoagulants held on 3 December 2015

Debriefing from the workshop and actions

Action: For discussion

The CHMP discussed and noted the feedback from the workshop.

14.1.6. Initial marketing authorisation - revised accelerated assessment procedural timetables

Action: For discussion

The CHMP noted the information. The guideline was revised and final version will be presented in January 2016 CHMP. Accelerated assessment will be split into 3 evaluation phases: 90/30/30 days.

14.1.7. Presentation on classification of post-authorisation studies

Action: For discussion

The CHMP noted the information. The main scope of Classification of post-authorisation studies (CPAS) is to help defining best practices around classification of Post-Authorisation studies. Criteria will be refined and adjusted as CPAS and Committees will gain experience. CPAS will build on agreed simple principles as a starting point and for orientation. Regular feedback will be provided to allow proper monitoring of the advices given and in case corrections to the principles is needed. Potential start is expected in February 2016.

14.1.8. Implementation of RMP summaries - update and way forward

Action: For discussion

The CHMP noted the information on analysis of the experience of the 1-year pilot phase on Publication of Risk Management Plan (RMP) summaries. During the pilot, RMPs have been prepared and published for all medicines (84 altogether) authorised since March 2014. Interest from different audience groups have been observed - each with different needs and expectations. In 2016, pilot phase will finish, a new template will be published and a transition from its current format for the RMP summaries to the new one will take place.

14.1.9. Seating plan during Dutch presidency 1 January – 30 June 2016

Action: For information

The CHMP noted the new seating plan.

14.1.10. EMA-CDDF Workshop on anticancer immunotherapy

EMA-CDDF Workshop on anticancer immunotherapy will be held 4-5th February 2016 at EMA.

The members noted the planned workshop. A limited number of participants will be reimbursed by EMA.

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 30 November-03

December 2015

Action: For information

The CHMP noted the Summary of recommendations and advice of PRAC.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for December 2015

Action: For adoption

The CHMP adopted the list of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for December 2015.

Scope: Review of governance for pharmacovigilance implementation

Action: For information

The CHMP noted the Review of governance for pharmacovigilance implementation.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 10-11 December 2015
Action: For information

The Committee noted the CAT draft minutes.

Final CAT Summary of Outcomes of the November 2015 meeting

Action: For information

The Committee noted the Summary of Outcomes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 23- 26 November 2015

Action: For information

The Committee noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2015 PDCO

Action: For information

The Committee noted the report.

Report from the PDCO meeting held on 10-12 December 2015

Action: For information

The Committee noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 8-10 December 2015
Action: For information

The Committee noted the report.

14.2.6. CMDh

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 14-16 December 2015

Action: For information

The Committee noted the report.

14.3. Coordination with EMA Working Parties / Working Groups / Drafting Groups

Following the adoption of the 2016 work plans in December 2015, the CHMP Chair has requested to revisit the composition of the working parties and drafting groups to make sure the groups will be able to achieve the 2016 objectives as stated in the work plans. Further reviews of composition will take place in January and February CHMP.

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 30 November 3 December 2015. Table of conclusions

Action: For information

The Committee noted the report.

Scientific advice letters: Disclosure of information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

14.3.2. Safety Working Party (SWP)

Scope: **Work plan for the CHMP Safety Working Party for 2016**
(EMA/CHMP/SWP/735015/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Final minutes of WP meeting held by teleconference on 27 October 2015**
(EMA/CHMP/SWP/713314/2015)

Action: For information

The CHMP noted the final minutes.

Scope: **Final agenda of WP meeting held by teleconference on 24 November 2015** (EMA/CHMP/SWP/734639/2015)

Action: For information

The CHMP noted the final agenda.

14.3.3. Blood Products Working Party (BPWP)

Chair: Anneliese Hilger

Scope: **Final minutes of WP meeting held by teleconference on 1 October 2015** (EMA/CHMP/BPWP/651517/2015)

Final agenda of WP meeting held face-to-face on 26-27 November 2015 (EMA/CHMP/BPWP/731509/2015)

Nomination of Dr. Anders Lindblom as the new Swedish member of BPWP, following the step down of Dr. Bengt Ljungberg (vice-chair)

Action: For information

The CHMP noted the documents and adopted new nomination.

14.3.4. Cardiovascular Working Party (CVSWP)

Election of the CVS WP Vice-Chair

The CHMP elected Kristina Dunder as Vice-chair of the CVS WP.

Scope: **Work plan for the CHMP Cardiovascular Working Party for 2016** (EMA/CHMP/728678/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Final minutes of WP meeting held by teleconference on 30 September 2015** (EMA/665335/2015)

Action: for information

The CHMP noted the final minutes.

Scope: **Final agenda of WP meeting held by face-to-face on 24 November 2015** (EMA/727463/2015): for information

Action: For information

The CHMP noted the final agenda.

Scope: **Draft Table of Decisions of WP meeting held face-to-face on 24 November 2015** (EMA/779429/2015)

Action: For information

The CHMP noted the draft table of decisions.

Scope: **Reflection paper on assessment of cardiovascular safety profile of medicinal products for the treatment of cardiovascular and metabolic diseases** (EMA/CHMP/50549/2015)

Action: For discussion

The CHMP discussed the reflection paper. Further discussions will be held in January CHMP.

14.3.5. Central Nervous System Working Party (CNSWP)

Scope: **Guideline on the clinical investigation of medicinal products for the treatment of Duchenne and Becker muscular dystrophy** (EMA/CHMP/732154/2013)

Action: For adoption

The CHMP adopted the guideline. The scope of the guideline is limited to the X-linked recessive dystrophinopathy Duchenne muscular dystrophy (DMD), the most common and severe form of muscular dystrophy, and its milder version, Becker muscular dystrophy (BMD). Other neuromuscular diseases are not presently within the scope of this guideline. The guideline is prepared to provide guidance on general principles in the development of any medicinal product for the treatment in DMD and BMD (symptomatic, disease modifying, among others).

Scope: **Guideline on the clinical development of medicinal products intended for the treatment of pain** (EMA/CHMP/970057/2011) 2nd draft

Action: For adoption for 3-months public consultation

The CHMP adopted the guideline for a 3-months public consultation. The scope of the document is to provide guidance on the clinical development of new medicinal products intended for the treatment of nociceptive, neuropathic or mixed pain. Recent experience with approval or scientific advice procedures as well as new results in basic science and clinical guidelines reflecting current medical practice has been taken into consideration with the revision of the guidance document. Requirements with regard to study design, duration, target patient population and outcome measures are described.

Scope: **Work plan for the CHMP Central Nervous System Working Party for 2016** (EMA/CHMP/735080/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Final minutes of WP meeting held face-to-face on 7 October 2015** (EMA/665335/2015)

Action: For information

The CHMP noted the final minutes.

Scope: **Final agenda of WP meeting held by teleconference on 8 December 2015** (EMA/737981/2015)

Action: For information

The CHMP noted the final agenda.

14.3.6. Modelling and Simulation Working Group (MSWG)

Scope: Work plan for the Modelling and Simulation Working Group 2016
Action: For adoption
The CHMP adopted the work plan.

14.3.7. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink

Scope: **Guideline on the evaluation of the pharmacokinetics of medicinal products in patients with decreased renal function** (EMA/CHMP/83874/2014)

- Overview of comments received (EMA/CHMP/725881/2015)

Action: For adoption

The CHMP adopted the guideline and noted the overview of comments. The current revision includes clarifications in most sections of the guideline, e.g. on the advice to study the effect of reduced renal function on drugs that are primarily hepatically eliminated and the recommendation to use an accurate method for determination of glomerular filtration rate in the subjects included in the pharmacokinetic study. In addition, the recommendation to use an absolute measure of renal function (in ml/min) in the dosing recommendations for patients with impaired renal function has been emphasised.

Scope: **Work plan for the CHMP Pharmacokinetics Working Party for 2016** (EMA/CHMP/PKWP/671542/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Draft agenda of PKWP meeting to be held by adobe on 07 December 2015** (EMA/737635/2015)

Action: For information

The CHMP noted the draft agenda.

Scope: **Minutes of the PKWP F2F meeting held on 21-22 October 2015** (EMA/720447/2015)

Action: For information

The CHMP noted the minutes.

14.3.8. Biostatistics Working Party (BSWP)

Scope: **Work plan for the CHMP Biostatistics Working Party for 2016**

Action: For adoption

The CHMP adopted the work plan.

Scope: **Draft Agenda of the BSWP meeting on 08 December 2015**

Action: For information

The CHMP noted the draft agenda.

Scope: Call for nomination of 2 new core members

Action: For information

Required expertise: Experience of commenting on methodological issues associated with clinical trials submitted to support EU marketing authorisation applications.

Nominations should be sent

The CHMP noted the call for nomination.

14.3.9. Biosimilar Medicinal Products Working Party (BMWP)

Scope: **Work plan for the CHMP Biosimilar Medicinal Products Working Party for 2016**

Action: For adoption

The CHMP adopted the work plan.

Scope **Draft Agenda of the BMWP meeting on 02 December 2015**

Action: For information

The CHMP noted the draft agenda.

Scope: **Concept paper on the revision of the Reflection paper on non-clinical and clinical development of similar biological medicinal products containing recombinant interferon alpha or pegylated recombinant interferon alpha**

Action: For adoption for 3-months public consultation

The CHMP adopted the concept paper for 3-months public consultation. The reflection paper provides recommendations for the non-clinical and clinical development of recombinant interferon alpha claimed to be similar to a reference product already authorised in the EU. This reflection paper was published in April 2009. Since then, no products containing biosimilar interferon alpha have been licensed in the EU. It is proposed to update the guidance based on the experience gained with marketing authorisation applications of reference products and scientific advice on biosimilar interferon alpha.

14.3.10. Gastroenterology Drafting Group (GDG)

Scope: Work plan for the Gastroenterology Drafting Group for 2016
Action: For adoption
The CHMP adopted the work plan.

14.3.11. Infectious Diseases Working Party (IDWP)

Scope: Work plan for the CHMP Infectious Diseases Working Party for 2016
Action: For adoption
The CHMP adopted the work plan.

14.3.12. Vaccines Working Party (VWP)

Scope: **Work plan for the CHMP Vaccines Working Party for 2016**
Action: For adoption
The CHMP adopted the work plan.

Scope: **Joint VWP/BWP position paper: Pentavac/Tetravac (Sanofi Pasteur MSD) - pentavalent combined vaccine (DTaP-IPV-Hib)/tetravalent combined vaccine (DTaP-IPV).** Request from CMDh to CHMP Response letter from CHMP
CHMP coordinators: Filip Josephson and Sol Ruiz
Action: For adoption
The CHMP adopted the joint position paper from VWP and BWP.

14.3.13. Extrapolation Working Group

Scope: **Status report on the Extrapolation Working Group activities in 2015**

CHMP coordinator: Daniel Brasseur

Action: For information

The CHMP noted the status report.

Scope: **Work Plan for Extrapolation Working Group for 2016**

Action: For adoption

The CHMP adopted the work plan.

14.3.14. Quality Working Party (QWP)

Chair: Jean-Louis Robert,

Scope: **QWP response to EDQM request for opinion on revision of tablet monograph (0478)**

Action: For adoption

The CHMP adopted the QWP response.

Scope: **Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials – Revision**

Action: For adoption for 6-months public consultation

The CHMP adopted the guideline for 6-months public consultation. The guideline addresses the documentation on the chemical and pharmaceutical quality of investigational medicinal products and Auxiliary Medicinal Products containing chemically defined drug substances, synthetic peptides, synthetic oligonucleotides, herbal substances, herbal preparations and chemically defined radio- active/radio-labelled substances to be submitted to the competent authority for approval prior to beginning a clinical trial in humans.

Scope: **QWP comments on EDQM enquiry on specification for sub-visible particles in eye drops and eye lotions**

Action: For adoption

The CHMP adopted the QWP comments.

Scope: **Question and answer on the use of powders and granules in medicinal products composed of 100% active substance**

Action: For adoption

The CHMP adopted the document.

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

Action: For adoption

The CHMP adopted the reflection paper. This reflection paper describes the chemical structure and properties criteria to be taken into account to qualify a chemical active substance as NAS,

as well as the required elements to be submitted by applicants. It applies to marketing authorisation applications including solely chemical active substance(s) eligible to the CP, and MPR/DCP and purely national procedures. Biological and biotechnological active substances and active substances to be included in radiopharmaceutical medicinal products are excluded from the scope of this reflection paper.

Scope: **Minutes of the QWP Core Team Adobe meetings held on 11 November 2015**

Action: For information

The CHMP noted the minutes.

Scope: **QWP response to CMDh on radiopharmaceuticals**

Action: for adoption

The CHMP adopted the QWP response.

14.3.15. Geriatric Expert Group (GEG)

Chair: Niccolo Marchionni

Points to consider on Frailty: Evaluation Instruments for Baseline Characterisation of Clinical trial populations (EMA/778709/2015)

Action: For adoption for 6-months public consultation

The CHMP adopted the points to consider on Frailty for 6-months public consultation. Points to consider are intended to provide guidance only for the evaluation of the baseline frailty status of patients (typically, but not exclusively aged > 65 yrs.) enrolled in a clinical trial or other clinical investigation (e.g. registry), and to supplement the requirements of ICH E7 Questions and Answers.

14.3.16. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

Scope: **Work plan for the CHMP Pharmacogenomics Working Party for 2016** (EMA/CHMP/PGWP/707191/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Draft agenda of PGWP meeting to be held by adobe on 15 December 2015** (EMA/774558/2015)

Action: For information

The CHMP noted the draft agenda.

14.3.17. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus / Nils Feltelius

Scope: **Work plan for the CHMP Rheumatology-Immunology Working Party for 2016** (EMA/CHMP/RIWP/649551/2015):

Action: For adoption

The CHMP adopted the work plan.

Election of the RIWP WP Vice-Chair

The CHMP noted the extension of deadline of the call for nomination. Nominations should be sent by **15 January 2016.**

14.3.18. Biologics Working Party (BWP)

Chair: Sol Ruiz,

Scope: **Guideline on Epidemiological Data on Blood Transmissible Infections and Overview stakeholder comments** (EMA/CHMP/548524/2008. Rev)

Action: For adoption

The CHMP discussed the guideline. The adoption is scheduled for January 2016 CHMP.

Scope: **BWP work plan for 2016** (EMA/CHMP/BWP/454652/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Draft agenda for BWP face-to-face meeting to be held 18-20 January 2016**

(EMA/CHMP/BWP/798829/2015)

Action: For information

The CHMP noted the draft agenda.

Scope: **Final minutes from face-to-face meeting held 12-14 October 2015** (EMA/CHMP/BWP/680074/2015)

Action: For information

The CHMP noted the final minutes.

Scope: **Cover letter and BWP position on CMDh question to CHMP regarding Classification of Chondroitin Sulphate Sodium as biological or chemical substance** (EMA/CHMP/BWP/804182/2015)

Action: For adoption

The CHMP adopted the cover letter and BWP position on CMDh question.

14.3.19. Respiratory Drafting Group

Election of the Chair of the Respiratory drafting group

The CHMP elected Karolina Törneke as Chair of the Respiratory drafting group.

Call for nomination of core members of the Respiratory Drafting Group, convened to provide assistance to the CHMP with revision of the guidelines on clinical development of medicinal products for the treatment of cystic fibrosis and orally inhaled medicinal products.

Expertise required: respiratory disease, cystic fibrosis, orally inhaled medicinal products, asthma, COPD

All CHMP members are invited to submit nominations of experts for core members by 20 January 2016, EOB.

The CHMP noted the call for nomination.

14.3.20. Radiopharmaceuticals Drafting Group

Scope: Work Plan or the Radiopharmaceuticals Drafting Group 2016

Action: For adoption

The adoption was postponed to January 2016 CHMP Plenary.

Scope: Guideline on core SmPC and Package Leaflet for nanocolloidal technetium (99mTc) albumin (EMA/CHMP/831653/2015)

Action: For adoption

Postponed to January 2016.

Scope: Guideline on core SmPC and Package Leaflet for gadopentetate dimeglumine (EMA/CHMP/831877/2015)

Action: For adoption

Postponed to January 2016.

14.3.21. Excipients Drafting Group (ExcpDG)

Scope: Mandate of the ExcpDG (EMA/CHMP/74184/2015)

Action: For adoption

The CHMP adopted the mandate.

Scope: Proposed new core members (EMA/CHMP/658081/2015)

Action: For adoption

The CHMP adopted the list of core members.

Call for expression of interest to be Chair or vice-Chair of the ExcpDG

Action: For information

The CHMP noted the call.

Scope: **Work plan for the CHMP Excipients Drafting Group for 2016** (EMA/CHMP/833588/2015)

Action: For adoption

The CHMP adopted the work plan.

Scope: **Final minutes of DG meeting held by teleconference on 4 November 2015** (EMA/779764/2015)

Action: For information

The CHMP noted the final minutes.

Scope: **Final agenda of DG meeting held by teleconference on 3 December 2015** (EMA/797739/2015)

Action: For information

The CHMP noted the final agenda.

14.3.22. Oncology Working Party

Scope: **Guideline on the use of minimal residual disease as an endpoint in chronic lymphocytic leukaemia studies**

Action: For adoption

The CHMP adopted the guideline. The scope of the guideline is to describe the basis and regulatory requirements for the use of minimal residual disease (MRD) as an intermediate endpoint to predict clinical benefit in trials in CLL. At present, this guidance is not applicable to other clinical settings, such as other B-cell lymphomas. Of note, this document is not intended to discuss MRD-guided treatment of CLL.

Election of the Oncology Working Party Vice-Chair

The CHMP elected Dr Pierre Demolis as Oncology Working Party Vice-Chair.

14.3.23. Table of Decisions of NRG plenary meeting held on 25 November 2015

Action: For adoption

The CHMP adopted the table of decisions.

14.3.24. Guideline Consistency Group (GCG)

The Committee appointed Arantxa Sancho Lopez and Kristina Dunder as new members of the GCG and thanked the departing members, Andrea Laslop and Jan Mueller-Berghaus, for their work and contributions.

Expressions of interest for one additional member should be sent.

14.4. Cooperation within the EU regulatory network

Scope: Letter from the European Commission, requesting that a definition for 'principal molecular structural features' as referred to in Art 3(3)c of Reg (EC) No 847/2000 on similar active substance is developed by end of Jan 2016.

Action: For adoption

The CHMP discussed the letter and agreed to involve the BWP and QWP. The CHMP asked whether the deadline could be extended to allow more time for finalisation of a response.

14.5. Cooperation with International Regulators

14.5.1. Cooperation with WHO Cooperation with WHO on Facilitation of Registration of Centrally Authorised Products in Developing Countries

Scope: Update on Facilitation of Registration of Centrally Authorised Products in Developing Countries – Pilot Scheme

Action: For discussion

The members were updated on the progress of the pilot scheme. Further information on the pilot scheme will be published on the EMA website in future.

14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee

No items

14.7. CHMP work plan

CHMP 2016 Work Plan

Action: For discussion

The CHMP discussed the draft CHMP 2016 work plan. The adoption of the final work plan is scheduled for the January 2016 CHMP Plenary.

14.8. Planning and reporting

14.8.1. New Marketing authorisation applications for 2016 with appointed rapporteurs

Action: For information

The CHMP noted the information.

14.9. Others

No items

15. Any other business

15.1. <AOB topic>

16. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 14-17 December 2015 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Daniel Brasseur	Member	Belgium	No interests declared	
Bart Van der Schueren	Alternate	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Viola Macolić Šarinić	Member	Croatia	No interests declared	
Panayiotis Triantafyllis	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Radka Montoniová	Alternate	Czech Republic	No interests declared	
Jens Heisterberg	Member	Denmark	No restrictions applicable to this meeting	
Sinan B. Sarac	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Pierre Demolis	Member (Vice-Chair)	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No interests declared	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			meeting	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Aldona Paluchowska	Alternate	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Patricia Silva	Alternate	Portugal	No interests declared	
Nela Vilceanu	Member	Romania	No interests declared	
Jan Mazag	Member	Slovakia	No interests declared	
Stanislav Primožič	Member	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Arantxa Sancho-Lopez	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Christophe Focke	Expert - in person*	Belgium	No interests declatred	
Mette Madsen	Expert - in person*	Denmark	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Patricia Diaz Ramos	Expert - in person*	Spain	No interests declared	
Jorge Camarero Jiménez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Isabel Sobral	Expert - in person*	Portugal	No interests declared	
Macarena Rodriguez Mendizabal	Expert - via telephone*	Spain	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Elena Martinez Alonso	Expert - via telephone*	Spain	No interests declared	
Eva Nadal Elduayen	Expert - via telephone*	Spain	No interests declared	
Monica Beteta Robles	Expert - via telephone*	Spain	No interests declared	
Jana Schweigertova	Expert - in person*	Slovakia	No restrictions applicable to this meeting	
Antonio Gomez-Outes	Expert - via telephone*	Spain	No interests declared	
Jan Welink	Expert - via telephone*	Netherlands	No interests declared	
Mats Welin	Expert - via telephone*	Netherlands	No interests declared	
Helena Fridborg	Expert - via telephone*	Sweden	No interests declared	
Barbara van Zwieten-Boot	Expert - via telephone*	Netherlands	No interests declared	
Gabriele Schlosser-Weber	Expert - via telephone*	Germany	No interests declared	
Clemens Mittmann	Expert - via telephone*	Germany	No interests declared	
Jörg Zinserling	Expert - via telephone*	Germany	No interests declared	
Cecilia Chisholm	Expert - via telephone*	United Kingdom	No interests declared	
Karl Broich	Expert - in person*	Germany	No interests declared	
Bertil Jonsson	Expert - via telephone*	Sweden	No interests declared	
Marco Coassin	Expert - via telephone*	Italy	No interests declared	
Mair Powell	Expert - via telephone*	United Kingdom	No interests declared	
Mario Miguel Rosa	Expert - via telephone*	Portugal	No interests declared	
Helena Fridborg	Expert - via telephone*	Sweden	No interests declared	
Vincent Gazin	Expert - in person*	France	No interests declared	
Céline Chu	Expert - in person*	France	No interests declared	
Fanny Filley	Expert - in person*	France	No restrictions applicable to this meeting	
Dagmar Stará	EC Representative	European Commission		
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the product(s) they have been invited to talk about.

17. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

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 2)*

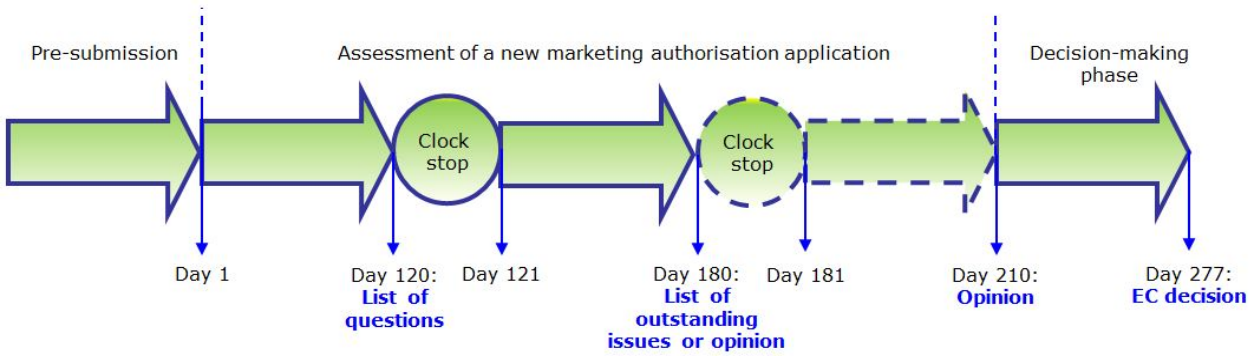
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

Initial applications *(section 3)*

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

Section 3.1 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 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **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 3.6, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 4)*

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 5)*

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 4. 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 6)*

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 3.5)*

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 *(section5.3)*

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 3.7)*

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 7)*

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 8)*

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 9)*

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 10)*

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 11)*

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 12)*

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 13)*

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 14.3.1)*

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 14.2)*

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 14.3)*

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.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/