28 March 2015
EMA/CHMP/203276/2015
Procedure Management and Business Support Division

Committee for medicinal products for human use (CHMP)

Minutes of meeting held on 23-26 February 2015

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

23 February 2015, 13:00 – 18:45, room 2A

24 February 2015, 08:30 – 20:00, room 2A

25 February 2015, 08:30 – 19:45, room 2A

26 February 2015, 08:30 – 14:45, room 2A

Note on access to documents

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

Health & Safety Information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential and therefore not disclosed. With regards to therapeutic indications listed against products it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. The procedures discussed by the CHMP are on-going and therefore are considered confidential. Additional details on some of these procedures will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available. For orphan medicinal products the applicant details are published as this information is already publicly available.

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

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

For adoption

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

For information

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 23-26 February 2015	The pre-meeting list was noted.
Membership announcement The Committee was asked to note that Ingunn Hagen Westgaard is no longer Norwegian CHMP alternate and Janne Komi is no longer alternate from Finland. The Committee was asked to note that Ivana Pankuchová was nominated as the CHMP Alternate from Slovakia, replacing Jana Klimasová in this role.	The CHMP noted the changes in membership and welcomed Ivana Pankuchová.
Draft Agenda of CHMP meeting to be held on 23-26 March 2015.	The draft agenda was noted.

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1. Oral explanations

1.1. Pre-authorisation procedure oral explanations

(EMEA/H/C/002629), (edoxaban), (prevention of stroke; embolism and treatment of venous thromboembolism)
List of Outstanding Issues adopted on 20.11.2014.
List of Questions adopted on 26.06.2014.
An Oral explanation was held on Tuesday 24 February 2015 at 11.00.
See section 2.2. Initial full applications; Day 180 List of outstanding issues

1.2. Re-examination procedure oral explanation

No items

1.3. Post-authorisation procedure oral explanation

Ferriprox (EMEA/H/C/000236/II/0089/G), (deferiprone), MAH: Apotex Europe BV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Arnaud Batz, "Update of section 4.5 of the SmPC regarding combination of deferiprone with other iron chelators further to request of the PRAC in the assessment of the PSUR (PSUV/083). Update of section 5.1 of the SmPC and the RMP with the results of Study LA37-111 conducted to evaluate the effect of deferiprone on cardiac QT and QTC interval duration. The Package leaflet is updated accordingly. The MAH also takes the opportunity to align the product information with QRD template (version 9) and to make minor editorial corrections. The package leaflet is also updated to add the local representatives in Croatia."
Request for Supplementary Information adopted on 20.11.2014, 24.07.2014.
An Oral explanation was held on Wednesday 25 February 2015 at 14.00.
See section 11 Post Authorisation Issues.

1.4. Referral procedure oral explanation

No items

2. Initial full applications

2.1. Initial full applications; Opinions

Jinarc (EMEA/H/C/002788), Orphan, (tolvaptan), Applicant: Otsuka Pharmaceutical Europe Ltd, (treatment of kidney disease (ADPKD))
Known active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 20.11.2014. List of Questions adopted on 25.04.2014.
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 reviewed the data submitted by the Marketing Authorisation Holder, taking into account the provisions of Article 14(11) of Regulation (EC) No 726/2004 and considers by consensus, that the new therapeutic indication brings significant clinical benefit in comparison with existing therapies, as set out in Annex IV.
The Committee adopted the CHMP assessment report on the novelty of the indication/significant clinical benefit in comparison with existing therapies.
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.

Ristempa (EMEA/H/C/003910), (pegfilgrastim), Applicant: Amgen Europe B.V., (treatment of neutropenia)
Informed consent application (Article 10c of Directive No 2001/83/EC)
Request for Supplementary Information adopted on 20.11.2014.
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.

Zykadia (EMEA/H/C/003819), (ceritinib), Applicant: Novartis Europharm Ltd (treatment of non-small cell lung cancer (NSCLC)
treatment of anaplastic lymphomakinase (ALK)-positive locally advanced or metastatic non-small cell lung cancer (NSCLC))
New active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 18.12.2014.
List of Questions adopted on 24.07.2014.
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 ceritinib 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.
The CHMP noted the EMA press release.
The members noted that the clinical trial data results from the ongoing confirmatory phase II and phase III studies will be submitted by 2018.

Saxenda (EMEA/H/C/003780), (liraglutide), Applicant: Novo Nordisk A/S, (treatment of obesity)
Known active substance (Article 8(3) of Directive No 2001/83/EC)
An Oral explanation was held in December 2014. List of Outstanding Issues adopted on 23.10.2014
List of Questions adopted on 22.05.2014. Opinion was adopted at January 2015 CHMP.
The CHMP noted the revised opinion which was adopted via written procedure on 11 February 2015,

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

(EMEA/H/C/003803), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
List of Questions adopted on 20.11.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003899), (aripiprazole), (treatment of schizophrenia and prevention of manic episodes in bipolar I disorder)
List of Questions adopted on 20.11.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues .
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003870), Orphan, (tasimelteon), Applicant: Vanda Pharmaceuticals Ltd., (treatment of Non-24-Hour Sleep-Wake Disorder (Non-24))
List of Questions adopted on 25.09.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/002629), (edoxaban), (prevention of stroke; embolism and treatment of venous thromboembolism)
List of Outstanding Issues adopted on 20.11.2014. List of Questions adopted on 26.06.2014.
See also section 1.1. Pre-authorisation procedure oral explanations.
An oral explanation was held on Tuesday 24 February 2015 at 11.00.
The presentation focused on the efficacy in patients with normal renal function in Atrial Fibrillation.
The Committee agreed to request further data from the applicant.
The CHMP adopted a 3rd List of Outstanding Issues with a specific timetable.

(EMEA/H/C/002749), (lutetium, isotope of mass 177), (used only for the radiolabelling of carrier molecules)
List of Questions adopted on 26.06.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003962), (pregabalin), (treatment of neuropathic pain, epilepsy and generalised anxiety disorder (GAD))
List of Questions adopted on 18.12.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues, .
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/004078), (pregabalin), (treatment of epilepsy and generalised anxiety disorder (GAD))
List of Questions adopted on 18.12.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003834), Orphan, (idebenone), Applicant: Santhera Pharmaceuticals (Deutschland) GmbH, (treatment of Leber's Hereditary Optic Neuropathy (LHON))
List of Questions adopted on 25.09.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues
The CHMP adopted a list of Outstanding Issues with a specific timetable.

2.3. Initial full applications; Day 120 List of Questions

(EMEA/H/C/003731), Orphan, (blinatumomab), Applicant: Amgen Europe B.V., (treatment of adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia)
The Committee noted the issues identified in this application,
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions
The Committee adopted the BWP Report.

(EMEA/H/C/003788), (pemetrexed), (treatment of malignant pleural mesothelioma and non-small cell lung cancer)
The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003964), Orphan, (efmoroctocog alfa), Applicant: Biogen Idec Ltd, (treatment of Haemophilia A)
The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP report.

(EMEA/H/C/003938), (betulae cortex dry extract (5-10 : 1); extraction solvent: n-heptane 95% (w/w)), (treatment of partial thickness wounds).
The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
Furthermore the CHMP adopted a timetable for the assessment of similarity.

(EMEA/H/C/003970), (pemetrexed), (treatment of malignant pleural mesothelioma and non-small cell lung cancer (excluding predominantly squamous cell histology))
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003905), (pemetrexed), (treatment of malignant pleural mesothelioma and non-small cell lung cancer)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/004011), (pemetrexed), (in combination with cisplatin is indicated for the treatment malignant pleural mesothelioma and non-small cell lung cancer)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003914), (human fibrinogen / human thrombin), (supportive treatment for improvement of haemostasis and as a suture support in vascular surgery)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

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

(EMEA/H/C/002739), (human alpha1-proteinase inhibitor), (treatment of lung tissue)
List of Outstanding Issues adopted on 20.11.2014. List of Questions adopted on 25.04.2014.
The members noted the report from the ad-hoc meeting held on 14 January 2015.

(EMEA/H/C/002800), Orphan, (dinutuximab), Applicant: United Therapeutics Europe Ltd, (treatment of neuroblastoma, treatment of high-risk neuroblastoma)
List of Outstanding Issues adopted on 22.01.2015.
The members agreed to the request by the applicant for an extension of clock stop to submit the responses to the Day 180 List of Outstanding Issues adopted on 22 January 2015.

(EMEA/H/C/002801), Orphan, ATMP, (allogeneic t cells genetically modified to express suicide gene), Applicant: MolMed SpA (treatment in haploidentical haematopoietic stem cell transplantation)
List of Questions adopted on 24 July 2014.
The CHMP was reminded of the timetable.

2.5. Products in the Decision Making Phase

Mysimba (EMEA/H/C/003687), (naltrexone / bupropion), Applicant: Orexigen Therapeutics Ireland Limited, (indicated for the management of obesity)
Fixed combination application (Article 10b of Directive No 2001/83/EC). Opinion adopted on 18.12.2014. The members noted the update.

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

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

Toujeo (previously known as Optisulin) (EMEA/H/C/000309/X/0079/G), (insulin glargine), MAH: Sanofi-aventis Deutschland GmbH, Duplicate of Lantus, Rapporteur: Pieter de Graeff, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "To extend MA of Optisulin to

register additional strength 300 U/ml, grouped with type IA variation to vary the invented name from Optisulin to Toujeo".
List of Questions adopted on 25.09.2014.
The members discussed the educational material to healthcare professionals on possible medication errors when switching between the two formulations and agreed in general that such information was required.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive opinion by consensus, together with the CHMP Assessment report and Translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The Committee noted the letter of recommendation dated 25.02.2015.

Orfadin (EMEA/H/C/000555/X/0042), Orphan, (nitisinone), MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, "To add a new strength 20 mg capsule, hard."
List of Outstanding Issues adopted on 18.12.2014. List of Questions adopted on 24.07.2014.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive opinion by consensus, together with the CHMP Assessment report and Translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The Committee noted the letter of recommendation dated 26.02.2015.

JETREA (EMEA/H/C/002381/X/0013), (ocriplasmin), MAH: ThromboGenics NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "to introduce a ready-to-use (RTU) formulation with adjusted fill volume for Jetrea 0.375 mg/0.3 mL"
List of Questions adopted on 20.11.2014.
The members discussed the DHPC and were updated on the discussions at the PRAC.
The Committee confirmed that all issues previously identified in this application had been addressed. .
The Committee adopted a positive opinion by consensus, together with the CHMP Assessment report and Translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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

Somavert (EMEA/H/C/000409/X/0072), (pegvisomant), MAH: Pfizer Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Arnaud Batz, "Addition of 25 mg and 30 mg powder and solvent for solution for injection."
List of Questions adopted on 25.09.2014
The Committee was reminded of the status of this application and its remaining outstanding issues, which related to the representativeness of the bio-batch size and the analysis of Cmax.
The CHMP adopted a List of Outstanding Issues with a specific timetable.
Furthermore the CHMP adopted a timetable on similarity.

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

Instanyl (EMEA/H/C/000959/X/0030/G), (fentanyl / fentanyl citrate), MAH: Takeda Pharma A/S, Rapporteur: Pierre Demolis, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Arnaud Batz, "Annex I_2.(c) To add the new strength of 400 micrograms/dose in a multi-dose nasal spray in pack size of 10's, 20's, 30's & 40 doses.
Type II cat. B.II.e.4.b) To replace the current multi-dose nasal spray by a new improved child resistant multi-dose nasal spray.
3 X Type IB cat. B.II.e.5.d) To add a new pack size of 30 doses for each current strength (50 micrograms/dose, 100 micrograms/dose & 200 micrograms/dose).
Type IA cat. B.II.d.1.a) – To tighten the assay release limit of the multi-dose finished product to 98.0%-102.0%.
Type IA cat. B.II.f.1.a) 1. – To reduce the shelf life of all strengths of the multi-dose finished product to 24 months.
Additionally, the Applicant took the opportunity to include an editorial change, as to change the wording of the specification footnote regarding the droplet size distribution test from "The test is performed by the vendor on every pumping system batch" to "The test is performed at release of the pumping system"."
The Committee discussed the issues identified in this application relating to the trial design, the safety analysis, the dose-response relation and some drug product aspects related to potential misuse or overdose.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

Kalydeco (EMEA/H/C/002494/X/0034/G), Orphan, (ivacaftor), MAH: Vertex Pharmaceuticals (U.K.) Ltd., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia, "Line extension to the Marketing Authorisation to include a new pharmaceutical form (granules) in two new strengths (50 mg and 75 mg unit doses) to enable administration of Kalydeco to patients aged 2 to less than 6 years of age. Changes to SmPC sections 4.2, 4.4, 4.5, 4.8 and 5.2 to provide clarity and relevant updates in line with the proposed paediatric extension application. Consequential changes are made to the Package Leaflet."
The Committee discussed the issues identified in this application, mainly relating to the administration in very young children and the available data on liver function parameters.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

Pyramax (EMEA/H/W/002319/X/0008/G), (pyronaridine / pyronaridine phosphate / artesunate), MAH: Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Arnaud Batz, "Line Extension to add a new paediatric formulation PYRAMAX 60 mg/20 mg Granules for Oral Suspension.
The PI for Pyramax 180 mg/60 mg Film Coated Tablets has also been updated with data submitted for the line extension."
The Committee discussed the issues identified in this application, mainly related to the safety in the young age group and in children with a body weight less than 20 kg.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions .
The CHMP agreed to consult a SAG and adopted a draft list of experts as well as a list of questions to this group.

Nomination of additional experts (hepatologists) for the SAG meeting .
The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions with a specific timetable.
The CHMP agreed to consult the PDCO Formulation Working Group.

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

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

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

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

Adenuric (EMEA/H/C/000777/II/0037), (febuxostat), MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, , "Update of sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC for the 120 mg strength further to the introduction of a new indication for prevention and treatment of hyperuricaemia in adult patients undergoing chemotherapy for haematologic malignancies at intermediate to high risk of Tumor Lysis Syndrome (TLS). The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 20.11.2014.
The Committee discussed the issues identified in this application, which were related to the wording of SmPC sections 4.1 and 4.4 about cardiac monitoring.
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 by consensus on 1-year extension of market exclusivity.

Avastin (EMEA/H/C/000582/II/0072), (bevacizumab), MAH: Roche Registration Ltd, Rapporteur: Christian Schneider, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Doris Stenver, "Extension of Indication to include treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix for Bevacizumab in combination with paclitaxel and cisplatin or paclitaxel and topotecan. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC have been updated. The Package

Leaflet is updated in accordance."
Request for Supplementary Information adopted on 22.01.2015, 25.09.2014.
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.

Esmya (EMEA/H/C/002041/II/0028), (ulipristal), MAH: Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.1 of the SmPC with subsequent updates to sections 4.2, 4.4, 4.8 and 5.1 in order to extend the current indication to long term (repeated intermittent) treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 20.11.2014.
The Committee discussed the issues identified in this application, which were related to endometrial safety. The Committee discussed that further safety data are needed pre- and post-authorisation on the long term use. The Committee discussed that further reassurance is needed concerning the importance and long term implications of the 6 cases of hyperplasia documented in the 006 trial. Occurrence of hyperplasia (including atypical hyperplasia), which is claimed to be normal in this age group of the target population and reversible upon menstruation, should be further discussed and supported by relevant guidance documents and/or expert opinions.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Humira (EMEA/H/C/000481/II/0134), (adalimumab), MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of Indication to add treatment of severe chronic plaque psoriasis in children and adolescents from 4 years of age who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapies , based on data from study M04-717 'A multicentre, randomised, double-dummy, double-blind study evaluating two doses of adalimumab versus methotrexate in paediatric subjects with chronic plaque psoriasis.' As a consequence sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH proposed minor editorial changes in the SmPC and Package Leaflet.
A revised RMP version 11.2 was included as part of this application."
Request for Supplementary Information adopted on 23.10.2014.
The Committee discussed the issues identified in this application, mainly relating to the wording of the indication.
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.

Humira (EMEA/H/C/000481/II/0137), (adalimumab), MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga, "This application seeks to add the following indication: "treatment of active moderate to severe Hidradenitis suppurativa (HS) in adult patients, including treatment of inflammatory lesions and prevention of worsening of abscesses and draining fistulas."
The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and the most appropriate patient population.

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

Imbruvica (EMEA/H/C/003791/II/0001), Orphan, (ibrutinib), MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, Co-Rapporteur: Christian Schneider, PRAC Rapporteur: Julie Williams, "Extension of indication for Imbruvica for the treatment of adult patients with Waldenström Macroglobulinaemia (WM). Consequently, changes are proposed to sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and to the Package Leaflet in order to incorporate all information relevant to the WM indication. In addition, some minor editorial corrections have been made in the SmPC."
The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and the design of the pivotal study.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Kalydeco (EMEA/H/C/002494/II/0027), Orphan, (ivacaftor), MAH: Vertex Pharmaceuticals (U.K.) Ltd., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia, "Extension of indication for Kalydeco to include the treatment of cystic fibrosis in patients aged 18 years and older who have a R117H mutation in the CFTR gene. Consequently, changes are proposed to sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and to the Package Leaflet."
Request for Supplementary Information adopted on 23.10.2014.
The Committee discussed the issues identified in this application.
The Committee adopted a 2nd Request for Supplementary Information with a specific timetable.

Kuvan (EMEA/H/C/000943/II/0033), Orphan, (sapropterin), MAH: Merck Serono Europe Limited, Rapporteur: Patrick Salmon, Co-Rapporteur: Daniel Brasseur "Extension of indication for the 'treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of 4 years of age and over with phenylketonuria (PKU) who have shown to be responsive to such treatment' to include the paediatric population under 4 years old. Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated accordingly."
The Committee discussed the issues identified in this application, mainly relating to the measuring device and administration.
The Committee adopted a Request for Supplementary Information with a specific timetable.

REVOLADE (EMEA/H/C/001110/II/0020), (eltrombopag / eltrombopag olamine), MAH: GlaxoSmithKline Trading Services, Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add a new indication on the treatment of adult patients with severe aplastic anaemia (SAA) who have had an insufficient response to immunosuppressive therapy. The package leaflet is updated accordingly. In addition, the MAH has corrected the acronym used for full blood counts (FBC) in the SmPC, Annex II and PL."
The Committee discussed the issues identified in this application, which were related to uncertainties on the clinical relevance of the observed effects (no survival data or event free survival data presented, and the effect on transfusions needs clarification) and on the representativeness of the data presented.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Simponi (EMEA/H/C/000992/II/0061), (golimumab), MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add a new therapeutic indication for non-radiographic axial spondyloarthritis. The Package Leaflet is updated accordingly."

The Committee discussed the issues identified in this application, mainly on withdrawal and restart of TNF-inhibitors and whether additional studies are required.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Soliris (EMEA/H/C/000791/II/0066), Orphan, (eculizumab), MAH: Alexion Europe SAS, Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pierre Demolis, "Update of sections 4.1 and 5.1 of the SmPC with an extension of the indication in patients with Paroxysmal nocturnal haemoglobinuria (PNH) regardless of their history of transfusion. The PL has been updated accordingly. In addition, some minor corrections are proposed in Section 5.1 of the SmPC and in the PL."
Request for Supplementary Information adopted on 20.11.2014, 24.07.2014.
The Committee discussed the issues identified in this application.
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.

Sustiva (EMEA/H/C/000249/II/0126/G), (efavirenz), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Margarida Guimarães"Grouped variation consisting of extension of indication for the treatment of HIV-1 to include children from 3 months to 3 year of age and weighing at least 3.5kg and removal of the oral solution pharmaceutical form for Sustiva (efavirenz)."
Request for Supplementary Information adopted on 23.10.2014, 22.05.2014.
The Committee discussed the issues identified in this application.
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.

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

Revlimid (EMEA/H/C/000717/II/0079), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Arnaud Batz, "Extension of Indication to add treatment of adult patients with relapsed and/ or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 have been updated

and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. A revised version of the RMP (version 25.0) was provided as part of this application."
The CHMP adopted the CHMP Similarity Assessment Report.

Perjeta (EMEA/H/C/002547/II/0010), (pertuzumab), MAH: Roche Registration Ltd, Rapporteur: Christian Schneider, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver, "The Marketing authorisation holder (MAH) applied for an extension of the indication for Perjeta in combination with trastuzumab and docetaxel for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (> 2 cm in diameter) as part of the treatment for early breast cancer. Consequently changes are proposed to sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC." Request for Supplementary Information adopted on 18.12.2014.
The CHMP adopted the list of experts for the SAG Oncology meeting.

5. Ancillary medicinal substances in medical devices

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

(EMEA/H/D/003740), (human serum albumin),(the storage, manipulation, in-vitro culture and transfer of human gametes)
List of Outstanding Issues adopted on 18.12.2014, 25.09.2014.
List of Questions adopted on 23.01.2014.The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted the BWP Report.
Post-meeting note: The CHMP adopted a 3rd List of Outstanding Issues by written procedure on 05.03.2015 with a specific timetable.

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

No items

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

No items

8. Withdrawal of full initial application

Ketoconazole AID-SCFM (EMEA/H/C/003800), Orphan (ketoconazole), Applicant: Agenzia Industrie Difesa-Stabilimento Chimico Farmaceutico Militare, (treatment of Cushing's syndrome)
Well-established use application (Article 10a of Directive No 2001/83/EC).
The CHMP noted the letter from the applicant dated 20 February 2015 informing of the decision to withdraw the Marketing Authorisation Application.

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

IV Zanamivir (EMEA/H/K/002288 procedure OTH004)
(zanamivir), MAH: Glaxo Group Ltd., (treatment of pandemic A(H1N1)v infection or infection due to seasonal influenza A or B virus)
This is an application to update the Conditions of Use document for Zanamivir injection (10mg/mL) compassionate use supplies under Article 83(4) of Regulation (EC) 726/2004.
The Committee adopted a positive opinion by consensus together with the CHMP assessment report.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

10. Pre-submission issues

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

(H0003986) (Idarucizumab), (indicated in adults treated with dabigatran etexilate when rapid reversal of the anticoagulant effects of dabigatran is required:
• life-threatening or uncontrolled bleeding
• emergency surgery/procedures),
The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

11. Post-authorisation issues

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

BSWP response to letter received from Dr Fuglsang regarding Kinetica software used in BE studies (EMA/108507/2015)
The CHMP noted the response to the letter regarding Kinetica but requested further numerical examples to clarify the problem before a final position can be agreed.

Brintellix (EMEA/H/C/002717/II/0004), (vortioxetine), MAH: H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC with information on the effect of vortioxetine on cognitive dysfunction in Major Depressive Disorder."
Request for Supplementary Information adopted on 20.11.2014.
The members discussed whether to reflect the clinical data on the claimed effect of vortioxetine on cognitive function in section 5.1 of the SmPC. Furthermore the Committee discussed the relation of treatment of depression on cognitive function.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive opinion by consensus, together with the CHMP Assessment report and Translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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

Update of section 4.5 to include the outcomes of the H4613g/GO01305 study and the updated population pharmacokinetic analysis of PK data from BO22227/HannaH study."
The Committee adopted a Request for Supplementary Information with a specific timetable.

Nplate (EMEA/H/C/000942/II/0049), Orphan, (romiplostim), MAH: Amgen Europe B.V., Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.8 and 5.1 of the SmPC based on the final CSR for Study 20080009: a long-term open-label prospective study to assess changes in bone marrow morphology. The provision of the CSR addresses MEA 005.3. In addition, the MAH took the opportunity to implement a minor change in SmPC section 4.6 for increased clarity. A revised RMP version 16 was provided as part of the application."
The Committee discussed the issues identified in this application. The committee discussed the risk for bone marrow fibrosis and it was agreed that the MAH should be asked to comment, whether there is a possibility to follow up the subjects included in cohort 3 for at least two more years to detect in which way the trend for an increase of bone marrow fibrosis is developing.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Ferriprox (EMEA/H/C/000236/II/0089/G), (deferiprone), MAH: Apotex Europe BV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Arnaud Batz, "Update of section 4.5 of the SmPC regarding combination of deferiprone with other iron chelators further to request of the PRAC in the assessment of the PSUR (PSUV/083). Update of section 5.1 of the SmPC and the RMP with the results of Study LA37-111 conducted to evaluate the effect of deferiprone on cardiac QT and QTC interval duration. The Package leaflet is updated accordingly. The MAH also takes the opportunity to align the product information with QRD template (version 9) and to make minor editorial corrections. The package leaflet is also updated to add the local representatives in Croatia."
Request for Supplementary Information adopted on 20.11.2014, 24.07.2014.
See also section 1.3. Post-authorisation procedure oral explanation
An Oral explanation was held on Wednesday 25 February 2015 at 14.00 and focused on a proposed warning on the use of Ferriprox with other iron chelators in section 4.4 of the SmPC.
The members discussed the available data and agreed that further information was required before concluding on this variation.
The CHMP adopted a 3rd Request for Supplementary Information with a specific timetable.

Revlimid (EMEA/H/C/000717/II/0076), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, "Update of section 4.4 of the SmPC with a new warning regarding an increased risk of mortality with the use of Revlimid in patients with chronic lymphocytic leukemia (CLL). The package leaflet is updated accordingly."
Request for Supplementary Information adopted on 18.12.2014, 20.11.2014, 26.06.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee discussed, whether off-label use should be incorporated into SmPC or is mentioning in DHPC sufficient. It was concluded that off label use should be mentioned in SmPC only if there is clear evidence on off-label use. For Revlimid, it was considered that there is no clear evidence on the off-label use in CLL patients in the EU.
The procedure was withdrawn by the applicant.

WS0689/G
TECFIDERA-EMEA/H/C/002601/WS0689/0011/G
NAPs included in WS: Fumaderm, Fumaderm Intial (fumarate containing products), MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 of the SmPC in order to add a recommendation to consider interruption of treatment in patients with low

lymphocyte counts (<0.5 x 109/L) persisting for more than six months and to monitor lymphocyte counts until recovery. Update of section 4.8 of the SmPC with information on observed low lymphocyte counts in clinical studies with tecfidera and PML (Progressive multifocal leukoencephalopathy) occurrence in the setting of severe and prolonged lymphopenia. Furthermore, the due dates of two commitments as part of the RMP have been revised."
The Committee discussed the issues identified in this application, which were related to the SmPC changes and wording. The Committee discussed, whether SmPC section 4.4 should be harmonised for both Tecfidera and Fumaderm. Also the need to involve ad-hoc expert group was deliberated and it was concluded that ad-hoc expert group is needed. The questions to the ad-hoc expert group should relate to the adequacy of the proposed studies, further risk minimisation measures and advice on CBC-monitoring frequency, definition of cut-off-points and advice on anti-JCV-antibody testing.
The Committee adopted a Request for Supplementary Information with a specific timetable.
The CHMP agreed to consult an ad-hoc expert group.
The list of questions to the ad-hoc expert group was discussed but will be adopted at a later stage.

Xofigo (EMEA/H/C/002653) (Radium-223 Chloride), MAH: Bayer Pharma AG, Rapporteur: Harald Enzmann, Co-Rapporteur: Daniela Melchiorri, (treatment of castration-resistant prostate cancer), New active substance (Article 8(3) of Directive No 2001/83/EC).
Change of NIST standard reference material and impact on qualification of radium-223 radioactivity
CHMP discussed and adopted the DHPC and communication plan about the change in NIST Standard Reference Material.

List of products to be tested in the sampling and testing programme 2016.
The CHMP adopted the list of products to be tested in the sampling and testing programme 2016

Pradaxa (EMEA/H/C/000829/ LEG 043 and LEG2 043.1
dabigatran etexilate), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jens Heisterberg, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Torbjorn Callreus,Scope of LEGs: The need and feasibility of therapeutic drug monitoring (TDM).The Committee discussed the PRAC advice. It was concluded that there is currently no basis for a general recommendation of regular TDM in all patients treated with Pradaxa in the licensed indications but further questions should be posed to the company. The Committee agreed that, the company should be requested to discuss the design and the feasibility of prospective clinical trials which could potentially further support recommendations on TDM in case further data may be helpful and that similar questions should be posed to the MAHs/applicants of other new oral anticoagulants. The CHMP discussed the need to request further analysis of post-marketing cases of overexposure and decided not to request such an analysis, because it will be associated with many biases/confounders and that it is unlikely that meaningful recommendations can be derived. The Committee discussed the management of patients undergoing acute surgery, thrombolysis or other interventions associated with significant bleeding risk and agreed that the lack of recommendations for the lower safety exposure threshold that would allow to initiate urgent surgery/invasive procedure is limiting factor in the management of these. The committee discussed the concomitant use of proton pump inhibitors and bleeding risk associated to it and whether it is relevant to mention it in SmPC, and concluded that the current SmPC is adequate on this issue.
The Committee adopted the recommendation from the CHMP Rapporteur Assessment Report.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Tybost (EMEA/H/C/002572/II/0009), (cobicistat), MAH: Gilead Sciences International Ltd, Rapporteur: Robert James Hemmings, "Submission of a final study report of the physiologically based/pharmacokinetic (PBPK) simulations of the effect of potent cytochrome P450 3A4 (CYP3A4)

inhibitors on cobicistat (COBI) exposure to fulfil a Tybost post authorisation measure MEA 14 and in order to provide further information on drug-drug interactions with COBI."
Request for Supplementary Information adopted on 25.09.2014.
The Committee adopted a Request for Supplementary information.
The CHMP agreed to the request by the applicant for a clock stop to respond to the RSI with a specific timetable.

12. Referral procedures

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

No items

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

Polymyxin-based products (EMEA/H/A-5(3)/1384)
(colistin, colistimethate), Rapporteur: Robert James Hemmings, Co-Rapporteur: Martina Weise, Review of the module 3 (quality) and European Pharmacopeia monograph. Triggered by the EMA Executive Director.
The CHMP adopted an opinion by consensus, recommending changes to the Ph. Eur. monographs of both colistin sulfate and colistimethate sodium as well as changes to the drug product dossier and the SmPC of polymyxin-based products.
The CHMP agreed to the letter to EDQM.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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

No items

12.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC

No items

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

Amoxil (EMEA/H/A-30/1372) (amoxicillin), MAH: GlaxoSmithKline, Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro, List of Questions adopted on 25.07.2013. List of Outstanding Issues adopted 23.10.2014, 25.04.2014.
The CHMP noted the recommendations by the IDWP and further discussed the SmPC wording, especially the posology and method of administration.
The CHMP adopted a 3rd List of Outstanding Issues with a specific timetable.

3rd LoOI: February 2015 CHMP; Responses to list of outstanding issues: 25.03.2015; Restart of the procedure: 21.04.2015; Assessment report: 06.05.2015; Comments from CHMP: 11.05.2015; 4th LoOI or CHMP opinion: May 2015 CHMP

Cymevene IV and associated names (EMEA/H/A-30/1406) (ganciclovir), F. Hoffmann-La Roche
Rapporteur: Rugile Pivliene, Co-Rapporteur: Alar Irs, , List of Questions adopted on 25.09.2014.
The CHMP further discussed the SmPC wording, especially with regard to the wording of the indication, the posology as well as the contraindications.
The CHMP adopted the List of Outstanding Issues with a specific timetable after the meeting via written procedure
List of outstanding issues: February 2015 CHMP; Submission of responses: 27.04.2015; Re-start of the procedure: 26.05.2015; Rapporteurs assessment report(s) circulated to CHMP: 08.07.2015; Comments: 13.07.2015; CHMP opinion: July 2015 CHMP

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

Adrenaline auto injectors (EMEA/H/A-31/1398) Rapporteur: Alar Irs, Co-Rapporteur: Robert James Hemmings,
Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients. List of Outstanding Issues adopted on 25.09.2014.
The members noted the report from the ad-hoc expert group meeting held on 23 January 2015. The experts considered that multiple factors could influence the site of delivery (subcutaneous or intramuscular). The group emphasized the need for appropriate training and education of both the patients and healthcare professionals on the usage of the devices. Furthermore the experts discussed possible further studies to be conducted and suggested that a PK/PD study including an imaging techniques could be feasible.
The CHMP adopted a 2nd List of Outstanding Issues with a specific timetable.
2nd LoOI: 26.02.2015; Submission of responses: 27.04.2015; Re-start of the procedure: 26.05.2015; Joint assessment report circulated to CHMP: 10.06.2015; Comments: 15.06.2015; LoOI or CHMP opinion: June 2015 CHMP
Furthermore, the Committee agreed to consult the PRAC.

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

GVK Biosciences (EMEA/H/A-31/1408)
Rapporteur: Harald Enzmann, Co-Rapporteur: Christian Schneider, ,
Article 31 procedure triggered by the European Commission concerning GVK Biosciences Private Limited (GVK Bio), Swarna Jayanthi commercial complex, Ameerpet, Hyderabad 500 038, India following critical GCP deficiencies reported during an inspection performed by the ANSM (Agency for Medicines and Health Products Safety, France) on 19-23 May 2014. Opinion adopted on 22.01.2015.
The members noted the draft timetable.

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

No items

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

No items

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

No items

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

No items

13. Pharmacovigilance issues

Summary of recommendations and advice of PRAC meeting held on 9-12 February 2015: **For information**	The Committee noted the report. The members noted the Summary of recommendations and advices of the PRAC meeting.
List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for February 2015: **For adoption**	The EURD list was adopted.
Early Notification System: February 2015 Early Notification System on Envisaged CHMP Recommendations for Regulatory Action (based on Identified Safety Concerns) Accompanied by Communication to the General Public: **for information**	See individual items

14. Inspections

14.1. GMP inspections

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

14.2. GCP inspections

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

14.3. Pharmacovigilance inspections

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

14.4. GLP inspections

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

15. Innovation Task Force

15.1. Minutes of Innovation Task Force: For information

15.2. Briefing meetings (Innovation Task Force)

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

ITF Briefing Meeting	
For information	The CHMP noted the report from the briefing meeting.
ITF Briefing Meeting	
For discussion	The CHMP noted the report from the briefing meeting.
ITF Briefing Meeting	
For discussion	The CHMP agreed to the ITF meeting.

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

Request from EC for EMA scientific Opinion under Art. 57 (1)P of Regulation (EC) No 726/2004 • Final report: **For adoption**	The CHMP adopted the opinion by consensus. . The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

15.4. Nanomedicines activities

No items.

16. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on January 2015. Table of conclusions: **For information**	The CHMP 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.*

17. Satellite Groups

17.1. Coordination Group for Mutual Recognition and Decentralised Procedures

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 23-25 February 2015: **For information**	The CHMP noted the report.

18. Other Committees

18.1. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 10-12 February 2015: **For information**	To be sent in the Post-mail.

18.2. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 27-30 January 2015: **For information**	To be sent in the Post-mail.

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2015 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on 11-13 February 2015: **For information**	The CHMP noted the report.

18.4. Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 19-20 February 2015: **For information**	The CHMP noted the Table of Decision.

19. Invented name issues

Table of Decisions of the NRG meeting held on 28 January 2015: **For adoption**	The CHMP adopted the Table of Decision of the NRG meeting

20. Any other business

Vaccines Working Party (VWP)	
Vaccines Working Party (VWP) work plan for 2015: **For adoption**	The CHMP adopted the VWP work plan 2015
VWP responses to CHMP questions on pertussis resurgence in the EU: **For discussion**	The CHMP discussed the VWP responses to CHMP questions on pertussis resurgence in the EU.
Biostatistics Working Party (BSWP)	
Guideline on adjustment for baseline covariates in clinical trials (Doc Ref: EMA/CHMP/295050/2013): **For adoption**	The CHMP adopted the guideline.
Biostatistics Working Party (BSWP) work plan for 2015 (EMA/CHMP/801811/2014): **For adoption**	The CHMP adopted the work plan.
BSWP 2014 activity report (EMA/796149/2014): **For information**	The CHMP noted the report.

Blood Products Working Party (BPWP)	
BPWP work plan for 2015: **For adoption** Final Minutes from 02 October 2014 virtual meeting (EMA/CHMP/BPWP/607670/2014): **For information**	The CHMP adopted the BPWP work plan 2015. The VHMP noted the Final Minutes from 02 October 2014 virtual meeting.
Guideline on core SmPC for human normal immunoglobulin for subcutaneous and intramuscular administration (EMA/CHMP/BPWP/143744/2011 rev. 1): **For final adoption** Overview of comments received	The Guideline on core SmPC for human normal immunoglobulin for subcutaneous and intramuscular administration was adopted and the comments received noted.
Agenda of BPWP virtual meeting to be held 5 March 2015 (EMA/CHMP/BPWP/769704/2014): **For information**	The members noted the agenda of BPWP virtual meeting to be held 5 March 2015 and the minutes of 2 October 2014 virtual meeting.
Oncology Working Party (ONCWP)	
"Concept paper on the need to revise the “Guideline on the evaluation of anticancer medicinal products in man” in order to provide guidance on the reporting of safety data from clinical trials": **For adoption and release for 3-month public consultation**	The aim of the revision was to find ways on how to report adverse effects in order to improve the understanding of the toxicity and tolerability profiles of medicinal products. The CHMP adopted the concept paper for release 3-months public consultation.

Rheumatology / Immunology Working Party (RIWP)	
Concept paper on clinical investigation of medicinal products for the treatment of Axial Spondyloarthritis (EMA/CHMP/61287/2015): **For adoption and release 3 months public consultation**	The CHMP adopted the concept paper for release 3-months public consultation.
Guideline on clinical investigation of medicinal products for the treatment systemic lupus erythematosus and lupus nephritis (EMA/CHMP/51230/2013): **For adoption** Overview of external comments received (EMA/CHMP/51230/2013)	The guideline provides guidance on the clinical investigation of medicinal products for the chronic treatment of systemic lupus erythematosus. The guideline describes patient characteristics, inclusion and exclusion criteria and concomitant use of other medicines that should be considered in the recruitment phase. Acceptable endpoints include reduction of disease activity/induction of remission parameters; prevention of flares/increased time intervals between flares (maintenance of remission) and prevention of long term damage. Criteria that should be considered for inclusion and exclusion and the required efficacy readouts for lupus nephritis and juvenile lupus are also discussed separately within this guideline. The CHMP adopted the guideline. The CHMP noted the overview of external comments received.
Cardiovascular Working Party (CVSWP)	
Final agenda of WP meeting held by teleconference on 28 January 2015 (EMA/6665/2015): **For information**	The CHMP noted the final agenda of WP meeting held by teleconference on 28 January 2015.
Final minutes of WP meeting held face-to-face on 26 November 2014 (EMA/732357/2014): **For information**	The CHMP noted the final minutes of WP meeting held face-to-face on 26 November 2014
Draft Guideline on clinical investigation of medicinal products for the treatment of venous thromboembolic disease (EMA/CHMP/41230/2015 Rev. 1, prev. CPMP/EWP/563/98): **For adoption for 6-month public consultation**	The CHMP adopted the draft guideline for 6-months public consultation.
Paediatric Addendum to the Note for Guidance on Clinical Investigation of Medicinal Products in the Treatment of Hypertension (EMA/CHMP/206815/2013): **For adoption** Overview of comments received (EMA/CHMP/68390/2015)	The CHMP adopted the paediatric addendum.

Biosimilar Medicinal Product Working Party (BMWP)	
Guideline on non-clinical and clinical development of similar biological medicinal products containing recombinant human insulin and insulin analogues (EMEA/CHMP/BMWP/32775/2005 Rev. 1): **For adoption and implementation**	The guideline lays down the non-clinical and clinical requirements for recombinant insulin-containing products, including human insulin and insulin analogues (both referred to as insulin), claiming to be similar to another one already authorised (the reference medicinal product). The CHMP adopted the guideline. The guideline will come into effect 1 September 2015.
BMWP response to Huub Schellekens and Ellen Moors correspondence in Nature Biotechnology, "Biosimilars or semi-similars" Correspondence from Huub Schellekens & Ellen Moors "Biosimilars or semi-similars?" (Nature Biotechnology): **For information** BMWP Correspondence - in response to Huub Schellekens and Ellen Moors: **For discussion and agreement**	The CHMP agreed with the response to the above mentioned correspondence in the same journal.
WHO Informal Consultation meetings on 27-28 and 29-30 April 2015 on: 1) the amendment for similar biotherapeutic products of monoclonal antibodies; 2) regulatory risk assessment for biotherapeutic products	The nomination of Pekka Kurki to attend the WHO Informal Consultation meetings on behalf of BMWP was agreed.
SWP chair's report on the EU position on pregnancy labelling in relation to the FDA final rule on changes to pregnancy and lactation information for prescription drug and biological products.	The report presents similarities and differences between EMA and FDA pregnancy labelling. The CHMP noted the report.
Update on activities related to revised RMP Assessment process in 2015	The CHMP noted the update on activities related to revised RMP Assessment process in 2015.
Modelling and Simulation Working Group (MSWG)	
Report from EMA EFPIA Dose Finding Workshop	The CHMP noted the report.
MSWG activity report for 2014: **For information**	The CHMP noted the activity report. The CHMP agreed with the next steps following the dose finding workshop.
MSWG work plan for 2015 : **For adoption**	The CHMP adopted the 2015 MSWG Work plan.

Biologics Working Party (BWP) Nomination of Catherine Milne as an additional EDQM representative at BWP: **For endorsement**	The CHMP endorsed Catherine Milne as an additional EDQM representative at BWP
Nomination of Louise Bisset as the new BWP Alternate for UK, replacing Adrian Thomas in this role: **For endorsement**	The CHMP endorsed Louise Bisset as the new BWP Alternate for UK.
Draft agenda for BWP face-to face meeting to be held 16-18 February 2015 (EMA/CHMP/BWP/804840/2014): **For information**	The CHMP noted the draft agenda for BWP face-to face meeting to be held 16-18 February 2015.
Draft agenda for BWP face-to face meeting to be held 16-18 March 2015 (EMA/CHMP/BWP/19894/2015): **For information**	The CHMP noted the draft agenda for BWP face-to face meeting to be held 16-18 March 2015.
Final minutes from face-to-face meeting held 10-12 November 2014 (EMA/CHMP/BWP/701931/2014): **For information**	The CHMP noted the final minutes from face-to-face meeting held 10-12 November 2014.
Final minutes from face-to-face meeting held 8-10 December 2014 (EMA/CHMP/BWP/772128/2014): **For information**	The CHMP noted the final minutes from face-to-face meeting held 8-10 December 2014.
Excipients Labelling Drafting Group (Excp DG) Questions and answers on benzalkonium chloride in the context of the revision of the guideline on 'Excipients in the label and package leaflet of medicinal products for human use' (EMA/CHMP/495737/2013): **For adoption** Draft overview of comments (EMA/CHMP/601508/2014): **For information**	The CHMP adopted the Question-and-answer document and noted the draft overview of comments.
Final minutes of Excp DG TC held on 27 November 2014 (EMA/755429/2014): **For information**	The CHMP noted the Final minutes of Excp DG TC held on 27 November 2014.
Final minutes of Excp DG teleconference held on 17 December 2014 (EMA/799232/2014): **For information**	The CHMP noted the final minutes of Excp DG teleconference held on 17 December 2014.
European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations **(PCWP)** European Medicines Agency Human Scientific Committees' Working Party with Healthcare	The CHMP noted the documents

Professionals' Organisations **(HCPWP)** Draft Agenda PCWP and HCPWP joint meeting 4 March 2015: **For information** Draft Agenda PCWP and HCPWP joint meeting: Information session on Biosimilars 5 March 2015 **For information** Minutes of the EMA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) meeting with all eligible organisations held on 26 November 2014: **For information**	
Feedback for the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium (PROTECT) symposium held on 18-20 February 2015: **For discussion**	The CHMP discussed the PROTECT Symposium held 18-20 February 2015.
Quality Working Party (QWP)	
Guideline on the Chemistry of Active Substances: **For adoption for public consultation**	The purpose of the guideline is to set out the type of information required for the manufacture and control of active substances (existing or new chemical entities) used in a medicinal product. The differences in requirements for new or existing active substances are clarified in the relevant paragraphs of the guideline where applicable. The guideline is not applicable to herbal, biological, biotechnological products, radiopharmaceuticals and radiolabelled products. The CHMP adopted the guideline on the Chemistry of Active Substances for public consultation.The Question-and-answer document answers to the question - what information on the functional qualities of plastic containers for eye drops should be included in the MAA dossier (human and veterinary).
Question-and-answer on plastic containers for eye drops: **For adoption**	The CHMP adopted the Question-and-answer document.
Question-and-answer on the calculation of thresholds to set limits for impurities in the finished product specification: **For adoption**	The Question-and-answer document gives an answer to the question, what is the basis for the calculation of thresholds to set limits for impurities in the finished product specification. In the answer, mono-component and fixed dose combination products are distinguished. The CHMP adopted the Question-and-answer

	document.
Concept paper on the development of a guideline on quality and equivalence of topical products: **For adoption for public consultation**	The new guideline complements and extends existing guidance and addresses the requirements for topical products containing either new or known active substances with respect to quality, equivalence to existing authorised products or during original product development, and variations to marketing authorisations after approval. The CHMP adopted the concept paper for public consultation.
BWP and QWP letter to EDQM on pharmaceutical containers and closures: **For adoption**	The CHMP adopted the BWP and QWP letter to EDQM.
Letter to EGA - GMP/GDP IWG and QWP request for concrete examples and further information on possible amount of variation triggered by the revised 'Guideline on ASMF procedure' and CMDh 'Q/A on level of details to be provided for AS manufacturers on application forms for new MAs, variations and renewals': **For adoption**	The CHMP adopted the letter.
Rotation speed for dissolution testing - QWP response to CMDh: **For adoption**	The CHMP adopted the QWP response to CMDh.
Elemental impurities in Marketed Products - Recommendations for implementation: **For adoption**	The CHMP adopted the recommendations.
Concept paper on the need for Revision of the Guideline on the Requirements to the Chemical and Pharmaceutical Quality Documentation concerning Investigational Medicinal Products in Clinical Trials: **For adoption for public consultation**	The CHMP adopted the concept paper for public consultation.
Reflection paper on the chemical structure and properties criteria to be considered for the evaluation of New Active Substance (NAS) status of chemical substances**: For adoption for public consultation**	The CHMP discussed the reflection paper. The paper describes the chemical structure and properties criteria to be taken into account by the CHMP to qualify a chemical active substance as NAS, as well as the required elements to be submitted by applicants to substantiate their claims. Comments should be sent by 6 March 2015. If no comments received the reflection paper is

	considered adopted. Post-meeting note: As no comments were received by 6 March 2015, the reflection paper was adopted.
Debriefing on Regulatory Workshop on Clinical Trials Designs in Neuro Myelitis Optica Spectrum Disorders (NMOSD) workshop held 10 October 2014, Draft report: **For discussion**	The CHMP discussed the workshop and draft report.
GLP inspections new requirements for applicants and check list for non-clinical assessors: **For adoption**	The CHMP adopted the GLP inspections new requirements for applicants and checklist for non-clinical assessors. Documents will be published.
Draft CHMP ORGAM meeting dates 2016-2018 (EMA/CHMP/89789/2015): **For adoption**	Postponed to the next ORGAM meeting.
Progress with changes to the MAA process	The CHMP noted the changes to the MAA process.
Rolling assessment timetables as of 1 March 2015: **For information**	The members noted the new rolling timetables to start on 1st March 2015.
Information to CHMP on start of first procedure for the cooperation EMA/WHO on facilitation of registration in developing countries: **For information**	The CHMP noted the information.
Ebola - regulatory pathways & requirements for the vaccines: **For information**	The CHMP noted the update on Ebola.
Information from EFSA about the launch of "Draft Guidance on the scientific requirements for health claims related to the gastro-intestinal tract, the immune system, and defence against pathogenic microorganisms": **For information**	The CHMP noted the information from EFSA. European Food Safety Authority (EFSA) has launched a public consultation on a draft Guidance on the scientific requirements for health claims related to the gastro-intestinal tract, the immune system, and defence against pathogenic microorganisms, with a deadline for comments of March 23rd 2015. EFSA has forwarded the document to EMA for commenting on the draft guidance document.
M8 step 2 DRAFT ICH Implementation Guide v2.0: **For information and comments by 22 May 2015**	The CHMP noted the information.
Information about proposed topics for CHMP/CAT meeting under Latvian Presidency.	The CHMP was informed about the proposed topics and members were invited to submit extra topics until 11th March 2015.
Information about Benefit/Risk workshop	The CHMP noted the information.

21. List of participants

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

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	Full involvement	
Milena Stain	Alternate	Austria	Full involvement	
Daniel Brasseur	Member	Belgium	Full involvement	
Bart Van der Schueren	Alternate	Belgium	Full involvement	
Mila Vlaskovska	Member	Bulgaria	Full involvement	
Ivana Mikačić	Member	Croatia	Full involvement	
Panayiotis Triantafyllis	Member	Cyprus	Full involvement	
Ondřej Slanař	Member	Czech Republic	No participation in discussions, final deliberations and voting on:	(EMEA/H/C/003899), (aripiprazole) (EMEA/H/C/003803), (aripiprazole) - Toujeo (EMEA/H/C/000309/X/0079/G), (insulin glargine)
Jens Heisterberg	Member	Denmark	Full involvement	
Christian Schneider	Alternate	Denmark	Full involvement	
Alar Irs	Member	Estonia	Full involvement	
Outi Mäki-Ikola	Member	Finland	Full involvement	
Pierre Demolis	Member (Vice-Chair)	France	Full involvement	
Joseph Emmerich	Alternate	France	Full involvement	
Harald Enzmann	Member	Germany	Full involvement	
Martina Weise	Alternate	Germany	Full involvement	
Dimitrios Kouvelas	Member	Greece	Full involvement	
George Aislaitner	Alternate	Greece	Full involvement	
Agnes Gyurasics	Member	Hungary	Full involvement	
Melinda Sobor	Alternate	Hungary	Full involvement	
Hrefna Gudmundsdottir	Alternate	Iceland	Full involvement	
David Lyons	Member	Ireland	Full involvement	
Patrick Salmon	Alternate	Ireland	Full involvement	
Daniela Melchiorri	Member	Italy	Full involvement	
Juris Pokrotnieks	Member	Latvia	Full involvement	
Natalja Karpova	Alternate	Latvia	Full involvement	
Romaldas Mačiulaitis	Member	Lithuania	Full involvement	
Rugile Pilviniene	Alternate	Lithuania	Full involvement	
Jacqueline	Member	Luxembourg	Full involvement	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Genoux-Hames				
John Joseph Borg	Member	Malta	Full involvement	
Pieter de Graeff	Member	Netherlands	Full involvement	
Johann Lodewijk Hillege	Alternate	Netherlands	Full involvement	
Karsten Bruins Slot	Member	Norway	Full involvement	
Piotr Fiedor	Member	Poland	Full involvement	
Aldona Paluchowska	Alternate	Poland	Full involvement	
Bruno Sepodes	Member	Portugal	Full involvement	
Dinah Duarte	Alternate	Portugal	Full involvement	
Nela Vilceanu	Member	Romania	Full involvement	
Jan Mazag	Member	Slovakia	Full involvement	
Ivana Pankuchova	Alternate	Slovakia	Full involvement	
Stanislav Primožič	Member	Slovenia	Full involvement	
Concepcion Prieto Yerro	Member	Spain	Full involvement	
Arantxa Sancho-Lopez	Alternate	Spain	Full involvement	
Kristina Dunder	Member	Sweden	Full involvement	
Filip Josephson	Alternate	Sweden	Full involvement	
Greg Markey	Member	United Kingdom	Full involvement	
Rafe Suvarna	Alternate	United Kingdom	Full involvement	
Robert James Hemmings	Co-opted member	United Kingdom	Full involvement	
Hubert Leufkens	Co-opted member	Netherlands	Full involvement	
Jan Mueller-Berghaus	Co-opted member	Germany	Full involvement	
Jean-Louis Robert	Co-opted member	Luxembourg	Full involvement	
Sol Ruiz	Co-opted member	Spain	Full involvement	
Christophe Focke	Expert - in person*	Belgium	Full involvement	
Trine Jensen	Expert - in person*	Denmark	Full involvement	
Sabine Mayrhofer	Expert - in person*	Germany	Full involvement	
Adrien Inoubli	Expert - in person*	France	Full involvement	
Tuomo Lapveteläinen	Expert - in person*	Finland	Full involvement	
Karin Franck-Larsson	Expert - in person*	Sweden	Full involvement	
Claire-Li Ding	Expert - in person*	France	Full involvement	
Alexandre Moreau	Expert - in person*	France	Full involvement	
Bronwyn Grimshaw	Expert - in person*	United Kingdom	Full involvement	
Sean Jones	Expert - in	United Kingdom	Full involvement	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	person*			
Ana Alonso Gutierrez	Expert - in person*	Spain	Full involvement	
Jan Willem Van der Laan	Expert - via telephone*	Netherlands	Full involvement	
Brigitte Müller	Expert - via telephone*	Austria	Full involvement	
Nuria Prieto	Expert - via telephone*	Spain	Full involvement	
Antonio Gomez-Outes	Expert - via telephone*	Spain	Full involvement	
Maria Jesus Fernandez Cortizo	Expert - via telephone*	Spain	Full involvement	
Marcel S.G. Kwa	Expert - via telephone*	Netherlands	Full involvement	
Andreas Brandt	Expert - via telephone*	Germany	Full involvement	
Frederike Lentz	Expert - via telephone*	Germany	Full involvement	
Clemens Mittmann	Expert - via telephone*	Germany	Full involvement	
Bernhardt Sachs	Expert - via telephone*	Germany	Full involvement	
Wilma Fischer-Barth	Expert - via telephone*	Germany	Full involvement	
Lies van Vlijmen's	Expert - via telephone*	Netherlands	Full involvement	
Andrew Gray	Expert - via telephone*	United Kingdom	Full involvement	
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.

Explanatory notes

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

Oral explanations *(section 1)*

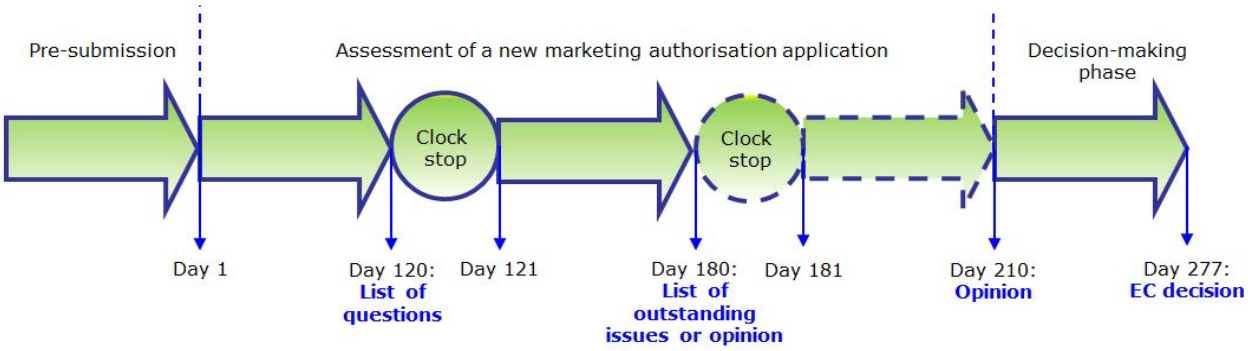
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section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

New applications *(section 2)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section 7)*

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

Withdrawal of application *(section 8)*

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

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

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

Pre-submission issues *(section 10)*

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

Post-authorisation issues *(section 11)*

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

Referral procedures *(section 12)*

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

Pharmacovigilance issues *(section 13)*

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

Inspections Issues *(section 14)*

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

Innovation task force *(section 15)*

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

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

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

Satellite groups / other committees *(section 17)*

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

Invented name issues *(section 18)*

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