09 August 2017
EMA/CHMP/516741/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda of CHMP written procedure* 14-17 August 2017

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

*** Written Procedure - comments on the draft documents should be forwarded to the Product Manager (PM) as identified in the CHMP agenda.**

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.

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).

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1. Introduction

1.1. Adoption of agenda

CHMP agenda for 14-17 August 2017

2. Oral Explanations

No items

3. Initial applications

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

3.1.1. - trastuzumab - EMEA/H/C/002575

treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

Scope: Letter from the applicant dated 28 July 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 23.02.2017

Action: For adoption

List of Questions adopted on 23.02.2017.

3.1.2. - expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue - Orphan - ATMP - EMEA/H/C/004258

TIGENIX, S.A.U.; treatment of complex perianal fistula(s)

Scope: Request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted on 23 February 2017

Action: For adoption

List of outstanding issues adopted on 23.02.2017, List of Questions adopted on 15.07.2016.

3.1.3. - ropeginterferon alfa-2b - Orphan - EMEA/H/C/004128

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: Request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 22.06.2017.

Action: For adoption

List of Questions adopted on 22.06.2017.

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

3.2.1. Fanaptum - iloperidone - EMEA/H/C/004149

Vanda Pharmaceuticals Ltd.; treatment of schizophrenia

Scope: Letter from the applicant dated 27 July 2017 requesting a re-examination of the Opinion adopted on 20 July 2017/re-examination Rapporteurs.

Action: For information

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

Opinion adopted on 20.07.2017, Oral explanation 17.05.2016, List of Outstanding Issues adopted on 18.05.2017, 23.02.2017. List of Questions adopted on 28.04.2016.

3.2.2. Onzeald - etirinotecan pegol - EMEA/H/C/003874

Nektar Therapeutics UK Limited; treatment of breast cancer with brain metastases

Scope: Letter from the applicant dated 26 July 2017 requesting a re-examination of the Opinion adopted on 20 July 2017/re-examination Rapporteurs.

Action: For information

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

Opinion adopted on 20.07.2017, Oral explanation 16.05.2017, List of Outstanding Issues adopted on 18.05.2017, 23.03.2017. List of Questions adopted on 10.11.2016.

3.2.3. Masipro - masitinib - Orphan - EMEA/H/C/004159

AB Science; treatment of mastocytosis

Scope: SAG list of questions adopted via written procedure on 28.07.2017.

Action: For information

Opinion adopted on 18.05.2017.

3.3. Initial applications in the decision-making phase

No items

3.4. Withdrawals of initial marketing authorisation application

3.4.1. - tigecycline - EMEA/H/C/004419

Treatment of:
- complicated skin and soft tissue infections, excluding diabetic foot infections
- complicated intra-abdominal infections.

should be used only in situations where it is known or suspected that other alternatives are not suitable

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 18.05.2017, List of Questions adopted on 13.10.2016.

3.4.2. - pegfilgrastim - EMEA/H/C/004262

treatment of neutropenia

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Questions adopted on 13.10.2016.

treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 18.05.2017. List of Questions adopted on 15.12.2016.

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

No items

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

No items

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

No items

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

No items

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. Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0026

Gilead Sciences International Limited

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of Indication to include paediatric patients from 6 of age to less than 12 years of age, with body weight of at least 25kg, infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir, for Genvoya.
As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the analysis of the paediatric study GS-US-292-0106 (Cohort 2) "A Phase 2/3, Open-Label Study of the Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in HIV-1 Infected Antiretroviral Treatment Naive Adolescents and Virologically Suppressed Children". The Package Leaflet and the Risk Management Plan (v. 3) are updated in accordance."

Scope: Letter from the applicant dated 26 July 2017 requesting an extension to the clock stop to respond to the Request for Supplementary Information adopted on 20.07.2017.

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017, 23.03.2017.

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

No items

10. Referral procedures

10.1.1. Alcover 750 mg, 1250 mg, 1750 mg Granulat im Beutel – Sodium oxybate – EMEA/H/A-29(4)/1451

D&A Pharma

Re-examination Rapporteur: Martina Weise, Re-examination Co-Rapporteur: Luca Pani

Rapporteur: Andrea Laslop, Co-Rapporteur: Fatima Ventura

Scope: re-examination timetable

Action: For adoption

Decentralised Procedure number: AT/H/0552/01-03/DC, notification by the Austrian Agency dated 22 December 2016 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

Opinion adopted on 22 June 2017, List of Outstanding issues adopted on 21.04.2017. List of Questions adopted on 26.01.2017.

Draft re-examination timetable.

11. Pharmacovigilance issue

11.1. Early Notification System

August 2017 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

Action: For information

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

None

14.2. Coordination with EMA Scientific Committees and Working Parties/Working Groups/Drafting Groups

14.2.1. Paediatric Committee (PDCO)

PIPs reaching D30 at August 2017 PDCO

Action: For information

Report from the PDCO meeting held on 15-18 August 2017

Action: For information

14.2.2. Committee for Advanced Therapies (CAT)

The Committee for Advanced Therapies is holding an expert meeting on Adeno-associated viral vector (AAV) based GTMPs on 6 September 2017 from 10.00 – 18.00.

Members/Alternates or experts from CHMP are able to join the meeting in person (non-reimbursed) or remotely (Adobe Connect).

Action: For information

Request of attendance should be sent **by 31 August 2017**.

14.2.3. Oncology Working Party

Chair: Pierre Demolis/Paolo Foggi

Call for nomination of experts for the EMA workshop on "Histology-independent (sometimes referred to as "agnostic") indications for anticancer medicines" to take place at EMA 30-31 October 2017

Follow up from presentation by Pierre Demolis at the July CHMP plenary meeting

Action: For information

Nomination of experts should be sent **by 15 September 2017.**

14.3. Cooperation within the EU regulatory network

None

14.4. Cooperation with International Regulators

None

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

None

14.6. CHMP work plan

None

14.7. Planning and reporting

None

14.8. Others

None

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

None

A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications

None

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

Information related to pre-submission of initial applications cannot be released at the present time as these contain commercially confidential information.

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

B.1.1. Annual reassessment for products authorised under exceptional circumstances

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal

B.2.2. Renewals of Marketing Authorisations for unlimited validity

B.2.3. Renewals of Conditional Marketing Authorisations

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

B.4. EPARs / WPARs

Bavencio - avelumab - EMEA/H/C/004338, Orphan
Applicant: Merck Serono Europe Limited, treatment of Merkel cell carcinoma (MCC), New active substance (Article 8(3) of Directive No 2001/83/EC)

Dupixent - dupilumab - EMEA/H/C/004390
Applicant: sanofi-aventis groupe, treatment of moderate-to-severe atopic dermatitis, New active substance (Article 8(3) of Directive No 2001/83/EC)

Entecavir Accord - entecavir - EMEA/H/C/004458
Applicant: Accord Healthcare Ltd, treatment of chronic hepatitis B virus infection, Generic, Generic of Baraclude, Generic application (Article 10(1) of Directive No 2001/83/EC)

Entecavir Mylan - entecavir - EMEA/H/C/004377
Applicant: Mylan S.A.S, treatment of chronic hepatitis B virus infection, Generic, Generic of Baraclude, Generic application (Article 10(1) of Directive No 2001/83/EC)

Lacosamide Accord - lacosamide - EMEA/H/C/004443
Applicant: Accord Healthcare Ltd, treatment of epilepsy, Generic, Generic of Vimpat, Generic application (Article 10(1) of Directive No 2001/83/EC)

Lutathera - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123, Orphan
Applicant: Advanced Accelerator Applications, treatment of gastro-entero-pancreatic neuroendocrine tumours, New active substance (Article 8(3) of Directive No 2001/83/EC)

Rydapt - midostaurin - EMEA/H/C/004095, Orphan
Applicant: Novartis Europharm Ltd, treatment of mastocytosis and treatment of acute myeloid leukaemia, New active substance (Article 8(3) of Directive No 2001/83/EC)

Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391
Applicant: Janssen-Cilag International N.V., treatment of human immunodeficiency virus type 1 (HIV-1), Fixed combination application (Article 10b of Directive No 2001/83/EC)

Tecentriq - atezolizumab - EMEA/H/C/004143
Applicant: Roche Registration Limited, treatment of locally advanced or metastatic urothelial carcinoma (UC),
treatment of non-small cell lung carcinoma (NSCLC), New active substance (Article 8(3) of Directive No 2001/83/EC)

Verkazia - ciclosporin - EMEA/H/C/004411, Orphan

Applicant: Santen Oy, treatment of severe vernal keratoconjunctivitis (VKC), Duplicate, Duplicate of IKERVIS, Known active substance (Article 8(3) of Directive No 2001/83/EC)	
Imraldi - adalimumab - EMEA/H/C/004279 Applicant: Samsung Bioepis UK Limited, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as these contain commercially confidential information.

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0072 MAH: AstraZeneca AB, Rapporteur: Bart Van der Schueren, "To replace the strain of a seasonal vaccine against human influenza in line with the EU recommendations for the seasonal influenza vaccine composition for the season 2017/2018." Opinion adopted on 28.07.2017. Request for Supplementary Information adopted on 22.06.2017.	Positive Opinion adopted by consensus on 28.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Intanza - influenza vaccine (split virion, inactivated) - EMEA/H/C/000957/II/0054 MAH: Sanofi Pasteur Europe, Rapporteur: Jorge Camarero Jiménez, "Seasonal update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2017/2018"	Positive opinion adopted by consensus via written procedure on 08.08.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

B.5.3. CHMP-PRAC assessed procedures

B.5.4. PRAC assessed procedures

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

B.5.8. Unclassified procedures and worksharing procedures of type I variations

B.5.9. Information on withdrawn type II variation / WS procedure

Enbrel - etanercept - EMEA/H/C/000262/II/0211 MAH: Pfizer Limited, Rapporteur: Robert James Hemmings	The MAH withdrew the procedure on 01.08.2017.

B.5.10. Information on type II variation / WS procedure with revised timetable

Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0017 MAH: Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and long term use information in the posology following final results from study CAMMS03409 - An Extension Protocol For Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab (ongoing at the time of the initial MAA) to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received alemtuzumab during prior company-sponsored studies. The RMP version 3.0 has also been submitted. The PL has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to introduce editorial corrections in the PI."	Request for an extension to the clock stop to respond to the RSI adopted on 20.07.2017

Request for Supplementary Information adopted on 20.07.2017, 21.04.2017.	
RotaTeq - rotavirus vaccine (live, oral) - EMEA/H/C/000669/II/0069/G MAH: MSD Vaccins, Rapporteur: Greg Markey Request for Supplementary Information adopted on 21.04.2017.	Request for an extension to the clock stop to respond to the RSI adopted on 21.04.2017

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

B.6.1. Start of procedure for New Applications: timetables for information

B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information

B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information

- hydrocortisone - EMEA/H/C/004416, PUMA
treatment of adrenal insufficiency
List of Questions adopted on 21.04.2017.

- betrixaban - EMEA/H/C/004309
treatment of prophylaxis of venous thromboembolism (VTE)
List of Questions adopted on 21.04.2017.

B.6.4. Annual Re-assessments: timetables for adoption

Atriance - nelarabine - EMEA/H/C/000752/S/0038, Orphan
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Torbjorn Callreus

Evoltra - clofarabine - EMEA/H/C/000613/S/0055
MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

IMVANEX - modified vaccinia Ankara virus - EMEA/H/C/002596/S/0029
MAH: Bavarian Nordic A/S, Rapporteur: Greg Markey, Co-Rapporteur: Jan Mueller-Berghaus,

PRAC Rapporteur: Julie Williams

Naglazyme - galsulfase - EMEA/H/C/000640/S/0067
MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed

Alecensa - alectinib - EMEA/H/C/004164/R/0007
MAH: Roche Registration Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Patrick Batty

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0015, Orphan, ATMP
MAH: Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, CHMP Coordinators: Jan Mueller-Berghaus, Daniela Melchiorri, PRAC Rapporteur: Julie Williams

HyQvia - human normal immunoglobulin - EMEA/H/C/002491/R/0037
MAH: Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski

Memantine LEK - memantine hydrochloride - EMEA/H/C/002630/R/0009
MAH: Pharmathen S.A., Generic, Generic of Ebixa, Rapporteur: Martina Weise, PRAC Rapporteur: Dolores Montero Corominas

Memantine Mylan - memantine - EMEA/H/C/002660/R/0010
MAH: Generics UK Limited, Generic, Generic of Ebixa, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Nemdatine - memantine - EMEA/H/C/002680/R/0008
MAH: Actavis Group PTC ehf, Generic, Generic of Ebixa, Rapporteur: Milena Stain, PRAC Rapporteur: Dolores Montero Corominas

Stayveer - bosentan -

EMEA/H/C/002644/R/0021
MAH: Marklas Nederlands BV, Rapporteur: Alexandre Moreau, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Caroline Laborde

Votrient - pazopanib - EMEA/H/C/001141/R/0042
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Doris Stenver

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.7. Type II Variations scope of the Variations: Extension of indication

Bosulif - bosutinib - EMEA/H/C/002373/II/0025/G, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "Extension of Indication to include treatment of adult patients with newly diagnosed Philadelphia Chromosome positive (Ph+) Chronic Phase (CP) Chronic Myelogenous Leukaemia (CML) for Bosulif based on study AV001. In addition, the MAH updated SmPC with safety and efficacy date from studies B1871006 and B1871008. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 4.0 has been submitted, as part of this application. Furthermore, the Annex IIIA is brought in line with the latest QRD template version 10."

Isentress - raltegravir - EMEA/H/C/000860/II/0064/G
MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Extension of indication (for Isentress 100 mg granules for oral suspension) to include treatment of HIV-1 exposed full-term neonates (under the age of 4 weeks) based on safety and PK data from one pivotal Phase 1 study, IMPAACT P1110 (Protocol 080), in a total of 42 HIV-1 exposed full-term infants (defined as ≥37 weeks gestational age and ≥2000 g), who received either 2 single doses of oral suspension, within 48 hours of birth and Day 7-10 of age (Cohort I), or a multiple-dose regimen of

raltegravir over the first 6 weeks of age (Cohort II). 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.
The provision of the study (IMPAACT P1110) addresses the final PIP measure, i.e. Study 4, conducted to generate PK, safety, and tolerability data in HIV exposed neonates and infants <6 weeks of age born to HIV infected mothers.
Further, the Applicant proposed to update the suspension volume to facilitate accurate measurement of the smaller doses required for neonates. As a consequence, there was a need to replace the 5 mL syringe supplied in the current commercial kit with 3 new oral dosing syringes and sizes. As a consequence, sections 6.5 and 6.6 of the SmPC have been updated and the labelling and instructions for use in the Package Leaflet have been updated accordingly.
An updated RMP version 12.0 was submitted as part of the application."

WS1208
Relvar
Ellipta-EMEA/H/C/002673/WS1208/0033
Revinty
Ellipta-EMEA/H/C/002745/WS1208/0029
MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, "Extension of indication to include asthma adequately controlled on both inhaled corticosteroid and long-acting beta2-agonist for Relvar Ellipta and Revinty Ellipta. As a consequence, sections 4.1 and 5.1 of the SmPC are updated."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Bortezomib Hospira - bortezomib - EMEA/H/C/004207/II/0006/G
MAH: Hospira UK Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Brineura - cerliponase alfa - EMEA/H/C/004065/II/0001/G, Orphan
MAH: BioMarin International Limited, Rapporteur: Martina Weise

Cetrotide - cetrorelix - EMEA/H/C/000233/II/0061
MAH: Merck Serono Europe Limited, Rapporteur:

Martina Weise

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0089
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Lartruvo - olaratumab - EMEA/H/C/004216/II/0006/G, Orphan
MAH: Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0062/G
MAH: Roche Registration Limited, Rapporteur: Concepcion Prieto Yerro

Praluent - alirocumab - EMEA/H/C/003882/II/0028/G
MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0123/G
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Ratiograstim - filgrastim - EMEA/H/C/000825/II/0054
MAH: ratiopharm GmbH, Rapporteur: Outi Mäki-Ikola

TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0081
MAH: Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus

Tevagrastim - filgrastim - EMEA/H/C/000827/II/0064
MAH: TEVA GmbH, Duplicate, Duplicate of Biograstim, Rapporteur: Outi Mäki-Ikola

Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0021/G, Orphan
MAH: BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege

Xadago - safinamide - EMEA/H/C/002396/II/0019
MAH: Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege

Zaltrap - aflibercept - EMEA/H/C/002532/II/0038
MAH: sanofi-aventis groupe, Rapporteur: Filip

Josephson

WS1176/G
Nuwiq-EMEA/H/C/002813/WS1176/0019/G
Vihuma-EMEA/H/C/004459/WS1176/0002/G
MAH: Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1243
Rixathon-EMEA/H/C/003903/WS1243/0002
Riximyo-EMEA/H/C/004729/WS1243/0002
MAH: Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus

B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

Adempas - riociguat - EMEA/H/C/002737/II/0023, Orphan
MAH: Bayer AG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.2 of the SmPC in order to add new information regarding posology for transitioning to and from riociguat based on results from study 16719: An open-label, international, multicentre, single-arm, uncontrolled, phase IIIb study of riociguat in patients with pulmonary arterial hypertension (PAH) who demonstrate an insufficient response to treatment with phosphodiesterase-5 inhibitors (PDE-5i). Section 5.1 of the SmPC was updated in parallel to reflect on the main study results. The Package Leaflet is updated accordingly."

Adempas - riociguat - EMEA/H/C/002737/II/0024/G, Orphan
MAH: Bayer AG, Rapporteur: Johann Lodewijk Hillege, "II, C.I.4: Update of section 5.1 of the SmPC in order to reflect on results from study 12935 (PATENT-2): Long-term extension, multi-centre, multi-national study to evaluate the safety and tolerability of oral riociguat (1 mg, 1.5 mg, 2 mg, or 2.5 mg
tid) in patients with symptomatic pulmonary arterial hypertension
II, C.I.4: Update of section 5.1 of the SmPC in order to reflect on results from study 11349 (CHEST-2): Long-term extension, multi-centre,

multi-national study to evaluate the safety and tolerability of oral riociguat (1 mg, 1.5 mg, 2 mg, or 2.5 mg tid) in patients with chronic thromboembolic pulmonary hypertension
II, C.I.4: Update of section 5.1 of the SmPC in order to reflect on results from study 13605 (RISE-IIP): A randomized, double-blind, placebo-controlled phase II study to investigate the efficacy and safety of riociguat (0.5 mg, 1.0 mg, 1.5 mg, 2.0 mg and
2.5 mg tid) in patients with symptomatic pulmonary hypertension associated with idiopathic interstitial pneumonias"

Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/II/0059

MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, "Update of section 4.2 of the SmPC to update the dosing schedule for infants (2 months to 5 months of age) to allow for 2 primary doses plus 1 booster dose in the second year of life based on the results from study V72_28 and its extension V72_28E1 and to update the intervals between primary doses for children (2 years to 10 years of age) to not less than 1 month based on the results from the extension study V72_28E1.
Update of section 4.8 of the SmPC to include the number of subjects exposed to at least 1 dose based on the results from the studies V72_28 and V72_28E1.
Update of section 5.1 of the SmPC to update the information about immunogenicity in infants and children based on the results from the studies V72_28 and V72_28E1.
The Package leaflet is updated accordingly.
In addition, the MAH took the opportunity to make some editorial changes in the SmPC and labelling."

Hycamtin - topotecan - EMEA/H/C/000123/II/0074

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, "To update the section 4.8 (Undesirable effects) of the SmPC in order to add two new identified ADRs: GI perforation and Mucosal inflammation, which have been identified for Hycamtin in the post-marketing experience. The package leaflet will be updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line

with the latest QRD template version 10.0, to update section 6.6 of the SmPC to remove the sentence "Liquid waste may be flushed with large amounts of water" as per EMA request on 25-May-2015 and to correct the renewal date in the section 9 of the SmPC."

Izba - travoprost - EMEA/H/C/002738/II/0008

MAH: Novartis Europharm Ltd, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information in line with Travoprost 40 µg/mL Eye Drops PI, based on the review of clinical trial and post-marketing data along with literature references.
The package leaflet section 4 is updated accordingly."

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0018, Orphan

MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.4 of the SmPC to add a warning about increased incidence of fatal and serious adverse events of carfilzomib in combination with melphalan and prednisone in newly diagnosed transplant-ineligible multiple myeloma patients, with the aim to prevent use in this population. The update is based on CLARION study; a Randomized, Open-label Phase 3 Study of Carfilzomib, Melphalan, and Prednisone Versus Bortezomib, Melphalan, and Prednisone in Transplant-ineligible Patients With Newly Diagnosed Multiple Myeloma."

Savene - dexrazoxane - EMEA/H/C/000682/II/0034/G

MAH: Clinigen Healthcare Ltd, Rapporteur: Alexandre Moreau, "C.I.4 – Update of sections 4.2, 4.4, 5.2 of the SmPC in order to update the information on dose modification in patients with renal impairment based on PK modelling results from a study reported in the literature, the Package Leaflet is updated accordingly.
C.I.4 – Update of section 4.5 of SmPC in order to update the information on PK interaction between dexrazoxane and doxorubicin and epirubicin, based on the literature review.
C.I.4.z – Update of section 5.2 of SmPC in order to update the information on PK data in patients with extravasations based on study TT04.
In addition, the MAH took the opportunity to

update section 6.5 of the Savene SmPC, carton label and package insert to include reference to the bottle hangers and to bring the PI in line with the latest QRD template version 10."

Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0021

MAH: Merck Sharp & Dohme Limited, Rapporteur: Bruno Sepodes, "Submission of the final report for the CANWARD 2016 study, a national population based surveillance system, assessing the prevalence of anti-microbial resistance in pathogens associated with respiratory, skin and soft tissue, urinary and bacteraemic infections in hospitalized patients in Canada, listed as a category 3 study in the RMP. This variation does not propose any changes to the product information."

Spinraza - nusinersen - EMEA/H/C/004312/II/0001, Orphan

MAH: Biogen Idec Ltd, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC to include complications associated with lumbar puncture including serious infection. The package leaflet is updated accrdingly."

Tafinlar - dabrafenib - EMEA/H/C/002604/II/0025

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to include the results of a drug-drug interaction between dabrafenib and rosuvastatin (an OATP1B1/1B3 substrate) and between dabrafenib and midazolam (a CYP3A4 substrate) based on the final results of study 200919, a phase I open-label fixed sequence study to evaluate the effects of an OATP1B1/1B3 substrate (rosuvastatin) and of a CYP3A4 substrate (midazolam) on the repeat dose pharmacokinetics of dabrafenib in subjects with BRAFV60 mutation positive tumours, to fulfil MEA 001."

Trobalt - retigabine - EMEA/H/C/001245/II/0047

MAH: Glaxo Group Ltd, Rapporteur: Hanne Lomholt Larsen, "Submission of amended clinical study report (CSR) for terminated post-authorisation efficacy study (PAES) RTG114855 "A randomised, double-blind, placebo-controlled, parallel-group, multicentre study to determine the efficacy and safety of 2

doses of retigabine immediate release (900 mg/day and 600 mg/day) used as adjunctive therapy in adult Asian subjects with drug-resistant partial-onset seizures”.”

Zydelig - idelalisib -
EMEA/H/C/003843/II/0035/G
MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, “Update of section 5.3 of the SmPC in order to revise the carcinogenicity information for idelalisib based on final results from two long term carcinogenicity studies (TX-312-2017, TX-312-2019). The RMP version 2.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0.”

WS1193
EVOTAZ-EMEA/H/C/003904/WS1193/0018
Reyataz-EMEA/H/C/000494/WS1193/0113
MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Caroline Laborde, “To update sections 4.3 and 4.5 of the SmPC to include information on the contraindicated co-administration with grazoprevir-containing products, including elbasvir/grazoprevir fixed dose combination (used to treat chronic hepatitis C infection) reflecting the results of interaction studies. The Package Leaflets are updated accordingly. The RMP versions 13.0 and 5.0, for Reyataz and Evotaz respectively have been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes and typographical corrections in the REYATAZ and EVOTAZ Product Information.”

WS1210/G
Mekinist-EMEA/H/C/002643/WS1210/0021/G
Tafinlar-EMEA/H/C/002604/WS1210/0026/G
MAH: Novartis Europharm Ltd, Lead Rapporteur: Paula Boudewina van Hennik, “Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 3-years overall survival (OS) results from study MEK115306

(COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma. Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 3-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma."

WS1222
Ryzodeg-EMEA/H/C/002499/WS1222/0025
Tresiba-EMEA/H/C/002498/WS1222/0029
Xultophy-EMEA/H/C/002647/WS1222/0022
MAH: Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.4 and 6.6 of the SmPC and relevant sections of the labelling and PL to minimise the potential risk of medication error as requested by PRAC (EPITT ref. No. 18893)."

B.6.10. CHMP-PRAC assessed procedures

Defitelio - defibrotide - EMEA/H/C/002393/II/0026, Orphan
MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 listed as category 3 in the RMP. This is a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-occlusive disease. The final study report is being submitted together with the revised risk management plan (version 3.0). The package leaflet is also being updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD

template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian languages."

Galafold - migalastat - EMEA/H/C/004059/II/0011, Orphan

MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.2 of the SmPC to provide further information on missing doses and to improve wording on the administration with food. No new data is submitted to support these changes. In addition, the MAH took this opportunity to include the ATC code and to update the local representatives in the Package Leaflet. Consequently changes are proposed in Annex I, IIIA and IIIB. The RMP version 2.0 has also been submitted"

Iclusig - ponatinib - EMEA/H/C/002695/II/0039/G, Orphan

MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "Grouping of two variations to submit the final reports from two nonclinical studies (study RPT-03346 and study RPT-03342), performed to investigate the potential mechanism of action of ponatinib leading to vascular occlusion.
Study RPT-03346 (Evaluation of the effects of ponatinib on arterial remodeling and wall thickening in a murine model of stenosis) is listed in the agreed pharmacovigilance plan.
The second study, RPT-03342 (Investigation of the Effects of Ponatinib on Photochemical-Induced Thrombosis in Mice and Rats) was conducted to further explore the potential relationship between ponatinib and thrombosis in a photochemical induced thrombosis model in mice and rats.
An updated RMP (version 18) has been submitted, with the relevant amendments to reflect the submitted data.
No update to the product information is triggered by these reports."

INOmax - nitric oxide - EMEA/H/C/000337/II/0051

MAH: Linde Healthcare AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "type II-B.IV.1.c-To introduce the INOmeter as additional container closure system

replacing the hand-wheel valve.
Additionally, the MAH took the opportunity to update the RMP v.6 with the information related to the post-authorisation experience with the new cylinder closure system."

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0017/G, Orphan
MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, "C.I.4
Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the second interim analysis of the overall survival data from study ENDEAVOR (study 20130398); this is a randomised, multicentre, open-label, phase 3 study of carfilzomib and dexamethasone compared to bortezomib with dexamethasone in patients with relapse multiple myeloma. The Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted.
C.I.4
Update of section 4.8 of the SmPC in order to revise the frequencies of certain adverse drug reactions based on the pooled data set including ENDEAVOR and 7 recently completed studies.
In addition, the Marketing authorisation holder (MAH) took the opportunity to add editorial changes in sections 4.2, 4.4, 6.3 and 6.6 of the SmPC. Editorial changes have also been included in the package leaflet and labelling."

Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0100
MAH: GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from study ROTA-085-PMS (115927) listed as a category 3 study in the RMP. This is an observational prospective cohort study investigating the incidence of intussusception after vaccination for rotavirus gastroenteritis, conducted to determine the incidence of intussusception after vaccination with Rotarix in Japan."

XGEVA - denosumab - EMEA/H/C/002173/II/0056
MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4, 4.8 and 5.1 of the SmPC

in order to modify the special warnings and precautions for use and undesirable effects sections following the performance of a cumulative safety review of Multiple Vertebral Fractures (MVF) following treatment discontinuation from Xgeva clinical study database from 2 clinical trials 20060359 (ongoing randomized, placebo-controlled, blinded study of denosumab as adjuvant treatment for women with early-stage breast cancer at high risk of recurrence) and 20040113 (a completed phase 2 study comparing denosumab and intravenous (IV) bisphosphonate treatment, collected data on bone turnover markers during the 32-week post-treatment follow-up period) and post-marketing experience. The results of this analysis conclude that MVF may occur following discontinuation of XGEVA treatment; the Package Leaflet is updated accordingly. The RMP version 26.0 has also been submitted accordingly.
A Direct Healthcare Professional Communication is also submitted in Module 1.8.2, to inform prescribers about the new identified risk of MVF following discontinuation of XGEVA.
The proposed minor change to Section 5.1 (Pharmacodynamic Effects) to provide some further information to prescribers regarding the reversibility of the inhibition of bone turnover following cessation of treatment."

Zelboraf - vemurafenib - EMEA/H/C/002409/II/0042/G

MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from studies MO25515 (MEA006) [An Open-Label, Multicenter Study to Assess the Safety of RO5185426 (Vemurafenib) in Patients with Metastatic Melanoma] and GP28492 (MEA010) [ZeSS: A Prospective Observational Safety Study of Patients with BRAFV600 Mutationpositive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf®)]"

WS1190/G
Enbrel-EMEA/H/C/000262/WS1190/0210/G
LIFMIOR-EMEA/H/C/004167/WS1190/0009/G

MAH: Pfizer Limited, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur:

Patrick Batty

B.6.11. PRAC assessed procedures

PRAC Led

Herceptin - trastuzumab - EMEA/H/C/000278/II/0135

MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study BO20652 (OHERA), a non-interventional study aimed to determine the incidence of symptomatic congestive heart failure and cardiac death in patients with HER2-positive early breast cancer treated with Herceptin as per routine clinical practice. This study is listed as a category 3 study in the RMP.
The RMP version 18.0 has also been submitted."

PRAC Led

Inflectra - infliximab - EMEA/H/C/002778/II/0054

MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final study report of the Post-Marketing Surveillance of Inflectra 100 mg (Infliximab) to Evaluate Its Safety and Efficacy in Korea. The study intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general clinical practice and determine any factor that may affect the safety and efficacy."

PRAC Led

Remsima - infliximab - EMEA/H/C/002576/II/0045

MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final study report of the Post-Marketing Surveillance of REMSIMA 100 mg (Infliximab) to Evaluate Its Safety and Efficacy in Korea. The study intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general

clinical practice and determine any factor that may affect the safety and efficacy."

PRAC Led

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0045

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study 109MS419 listed as a category 3 study in the RMP. This is a retrospective, multicentre, observational study aimed to assess the effect of tecfidera delayed-release capsules on lymphocyte subsets in patients with relapsing forms of multiple sclerosis."

PRAC Led

Xarelto - rivaroxaban - EMEA/H/C/000944/II/0055

MAH: Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report of a non-interventional PASS listed as a category 3 study in the RMP (MEA 019): An Observational Post-Authorization Safety Specialist Cohort Event Monitoring Study (SCEM) to Monitor the Safety and Utilization of Rivaroxaban (Xarelto) for the Prevention of Stroke in Patients with AF, Treatment of DVT and PE, and the Prevention of Recurrent DVT and PE in the Secondary Care Setting in England and Wales (The ROSE Study), study number 16171."

PRAC Led

Zavesca - miglustat - EMEA/H/C/000435/II/0057, Orphan

MAH: Actelion Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 12.2 in order to remove important identified risks such as diarrhoea and other gastrointestinal (GI) events and tremor and important potential risks such as seizure in NP-C patients."

PRAC Led

WS1164

Glyxambi-EMEA/H/C/003833/WS1164/0008

Jardiance-EMEA/H/C/002677/WS1164/0033

Synjardy-EMEA/H/C/003770/WS1164/00

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MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "C.I.11: Submission of an updated RMP for Jardiance (v12.1), for Synjardy (9.2) and for Glyxambi (v3.0) in order to address the PRAC recommendation concluded in the Article 20 referral for SGLT2 inhibitors on the important potential risk for lower limb amputation. Additionally, the PRAC request to include pancreatitis as important potential risk for empagliflozin-containing medicines following the conclusion adopted by the PRAC after the review of PSUSA/00010077/201603 (canagliflozin) is discussed."

PRAC Led

WS1207

Bretaris Genuair-EMEA/H/C/002706/WS1207/0034

Eklira Genuair-EMEA/H/C/002211/WS1207/0034

MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report from study D6560R00005, (Aclidinium Bromide Drug Utilisation Post-Authorisation Safety Studies (DUS 1) in the United Kingdom, Denmark, and Germany) listed as a category 3 study in the RMP (MEA002). The updated RMP version 6.0 has also been submitted."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

B.6.15. Unclassified procedures and worksharing procedures of type I variations

WS1183

Ambirix-EMEA/H/C/000426/WS1183/0085

Cervarix-EMEA/H/C/000721/WS1183/0090
Infanrix hexa-EMEA/H/C/000296/WS1183/0223
Synflorix-EMEA/H/C/000973/WS1183/0122
Twinrix Adult-EMEA/H/C/000112/WS1183/0119
Twinrix Paediatric-EMEA/H/C/000129/WS1183/0120
MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Kristina Dunder

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WS1217
Entresto-EMEA/H/C/004062/WS1217/0015
Neparvis-EMEA/H/C/004343/WS1217/0013
MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege

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WS1228/G
Silodyx-EMEA/H/C/001209/WS1228/0028/G
Urorec-EMEA/H/C/001092/WS1228/0031/G
MAH: Recordati Ireland Ltd, Lead Rapporteur: Nithyanandan Nagercoil

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WS1238/G
Leganto-EMEA/H/C/002380/WS1238/0025/G
Neupro-EMEA/H/C/000626/WS1238/0079/G
MAH: UCB Manufacturing Ireland Limited, Lead Rapporteur: Bruno Sepodes, "B.II.e.z – To replace the secondary packaging of the finished product: a folding cardboard carton is being replaced with a solid plastic box for for Neupro EU/1/05/331/001-012 and EU/1/05/331/014-61 and Leganto EU/1/11/695/001-054.
C.I.z- To change the time that time transdermal patch requires to be pressed against the skin from 20 s to 30 s; point 4.2 of SmPC and the Patient Information have been updated accordingly.
In addition the MAH combined the PI of different strengths and introduced several changes following the user testing."

WS1247/G
Enurev

Breezhaler-EMEA/H/C/002691/WS1247/0022/G
Seebri Breezhaler-EMEA/H/C/002430/WS1247/0022/G
Tovanor Breezhaler-EMEA/H/C/002690/WS1247/0024/G
Ultibro Breezhaler-EMEA/H/C/002679/WS1247/0016/G
Ulunar Breezhaler-EMEA/H/C/003875/WS1247/0016/G
Xoterna Breezhaler-EMEA/H/C/003755/WS1247/0019/G
MAH: Novartis Europharm Ltd, Lead Rapporteur: Hanne Lomholt Larsen

B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

B.7.1. Yearly Line listing for Type I and II variations

B.7.2. Monthly Line listing for Type I variations

B.7.3. Opinion on Marketing Authorisation transfer (MMD only)

B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)

B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)

B.7.6. Notifications of Type I Variations (MMD only)

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

E.2. Time Tables – starting & ongoing procedures: For information

PMF timetables starting and ongoing procedures	Tabled in MMD and sent by post mail (folder E).

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver

F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended

F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health

G. ANNEX G

G.1. Final Scientific Advice (Reports and Scientific Advice letters):

G.2. Ongoing procedures

H. ANNEX H - Product Shared Mailboxes – e-mail address

Explanatory notes

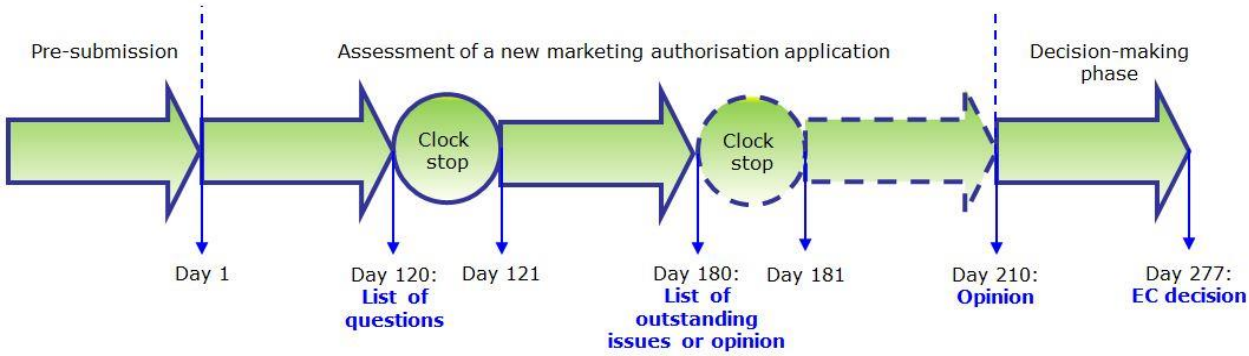
The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 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.



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.

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.1, **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 3.3, **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 3.2)*

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 3.4)*

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.

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).

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