27 March 2020
EMA/CHMP/43518/2020 Corr.3[1]
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 27-30 January 2020

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

27 January 2020, 13:00 – 19:30, room 1C

28 January 2020, 08:30 – 19:30, room 1C

29 January 2020, 08:30 – 19:30, room 1C

30 January 2020, 08:30 – 16:00, room 1C

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. Regarding intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available.

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

Note on access to documents

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

[1] Corrections in section 3.1.6, 8.1.1 and B.6.9 (Annex)

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 27-30 January 2020. See January 2020 CHMP minutes (to be published post February 2020 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 27-30 January 2020

1.3. Adoption of the minutes

CHMP minutes for 09-12 December 2019

ORGAM Minutes 20 January 2020

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. selinexor - Orphan - EMEA/H/C/005127

Karyopharm Europe GmbH; treatment of patients with relapsed refractory multiple myeloma (RRMM)

Scope: Possible Oral explanation/List of Outstanding Issues

Action: Oral explanation to be held on Tuesday, 28 January 2020 at time 11:00

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 24.04.2019.

2.1.2. cholera vaccine, oral, live - EMEA/H/C/003876

indicated for active immunisation against disease caused by Vibrio cholerae serogroup O1 in adults and children aged 6 years and older

Scope: Possible Oral explanation/Opinion

Action: Oral explanation to be held on Tuesday, 28 January 2020 at time 14:00

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 29.05.2019.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Emgality - galcanezumab - EMEA/H/C/004648/X/0004

Eli Lilly Nederland B.V.

Rapporteur: Daniela Melchiorri (IT) (MNAT with ES for Quality), Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension application to add a new strength of 100 mg/ml solution for injection in pre-filled syringe for Emgality, associated with a new indication (episodic cluster headache)."

Oral explanation

Draft list of experts for SAG Neurology meeting scheduled on 20 January 2020 adopted via written procedure on 17 January 2020, SAG Report

Action: Oral explanation to be held on Wednesday, 29 January 2020 at time 09:00

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 27.06.2019.

2.3.2. WS1372
OPDIVO - nivolumab - EMEA/H/C/003985/WS1372/0053
Yervoy - ipilimumab - EMEA/H/C/002213/WS1372/0057

Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Jorge Camarero Jiménez, Lead Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include first-line treatment of adult patients with metastatic Non-Small Cell Lung Carcinoma (NSCLC) for OPDIVO and Yervoy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information from the pivotal study CA209227 (an open-label, randomised phase 3 trial of nivolumab, or nivolumab plus ipilimumab, or nivolumab plus platinum doublet chemotherapy versus platinum doublet chemotherapy in subjects with chemotherapy-naïve stage IV or recurrent NSCLC). The Package Leaflet and RMP (version 14.0 for Opdivo and version 21.0 for Yervoy) are updated in accordance. In addition, the MAH has taken the opportunity to introduce minor editorial and formatting revisions in the PI."

Oral explanation

Action: Oral explanation to be held on Tuesday, 28 January 2020 at time 16:00

Request for Supplementary Information adopted on 14.11.2019, 13.12.2018, 26.07.2018.

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. arsenic trioxide - EMEA/H/C/005235

treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

3.1.2. azacitidine - EMEA/H/C/005075

Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute myeloid leukaemia (AML)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019, 17.10.2019. List of Questions adopted on 29.05.2019.

3.1.3. azacitidine - EMEA/H/C/004984

treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

3.1.4. budesonide / formoterol fumarate dihydrate - EMEA/H/C/004882

treatment of asthma and COPD

Scope: Opinion

Action: For adoption

List of Questions adopted on 17.10.2019.

3.1.5. cinacalcet - EMEA/H/C/005236

treatment of secondary hyperparathyroidism and hypercalcaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 29.05.2019.

3.1.6. givosiran - Orphan - EMEA/H/C/004775

Accelerated assessment

Alnylam Netherlands B.V.; Treatment of acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.12.2019. List of Questions adopted on 15.10.2019.

3.1.7. insulin lispro - EMEA/H/C/005037

Treatment of diabetes mellitus in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.11.2019. List of Questions adopted on 25.07.2019.

3.1.8. bempedoic acid - EMEA/H/C/004958

treatment of primary hypercholesterolaemia or mixed dyslipidaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.11.2019. List of Questions adopted on 27.06.2019.

3.1.9. bempedoic acid / ezetimibe - EMEA/H/C/004959

treatment of primary hypercholesterolaemia or mixed dyslipidaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.11.2019. List of Questions adopted on 27.06.2019.

3.1.10. darolutamide - EMEA/H/C/004790

treatment of non-metastatic castration resistant prostate cancer (nmCRPC)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.11.2019. List of Questions adopted on 25.07.2019.

3.1.11. rituximab - EMEA/H/C/004696

treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL) and Rheumatoid arthritis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 13.12.2018.

3.1.12. semaglutide - EMEA/H/C/004953

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 19.09.2019.

3.1.13. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019, 28.02.2019. List of Questions adopted on 20.09.2018.

3.1.14. treprostinil sodium - Orphan - EMEA/H/C/005207

SciPharm Sarl; treatment of thromboembolic pulmonary hypertension (CTEPH)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 27.06.2019.

3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable)

3.2.1. indacaterol / mometasone furoate - EMEA/H/C/005067

treatment of asthma

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

3.2.2. budesonide / glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004983

as a maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.04.2019.

3.2.3. indacaterol / glycopyrronium / mometasone - EMEA/H/C/005061

treatment of asthma and to reduce asthma exacerbations

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

3.2.4. pretomanid - Orphan - EMEA/H/C/005167

FGK Representative Service GmbH; treatment of tuberculosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.07.2019.

3.2.5. indacaterol / glycopyrronium / mometasone - EMEA/H/C/005518

treatment of asthma and to reduce asthma exacerbations

Scope: List of outstanding issues

Action: For adoption

3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable)

3.3.1. abiraterone acetate - EMEA/H/C/005408

treatment of metastatic prostate cancer

Scope: List of questions

Action: For adoption

3.3.2. bevacizumab - EMEA/H/C/005181

treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer;
- first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer;
- first line treatment of patients with advanced and/or metastatic renal cell cancer.

Scope: List of questions

Action: For adoption

3.3.3. bulevirtide - Orphan - EMEA/H/C/004854

Accelerated assessment

MYR GmbH; indicated for the treatment of chronic hepatitis delta virus (HDV) infection in adult patients with compensated liver disease.

Scope: List of questions

Action: For adoption

3.3.4. elexacaftor / tezacaftor / ivacaftor - Orphan - EMEA/H/C/005269

Accelerated assessment

Vertex Pharmaceuticals (Ireland) Limited; treatment of cystic fibrosis

Scope: List of questions

Action: For adoption

3.3.5. lenalidomide - EMEA/H/C/005306

treatment of multiple myeloma

Scope: List of questions

Action: For adoption

3.3.6. pegfilgrastim - EMEA/H/C/005085

treatment of neutropenia

Scope: List of questions

Action: For adoption

3.3.7. somapacitan - Orphan - EMEA/H/C/005030

Novo Nordisk A/S; indicated for the replacement of endogenous GH with growth hormone deficiency (AGHD).

Scope: List of questions

Action: For adoption

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

3.4.1. pexidartinib - Orphan - EMEA/H/C/004832

Daiichi Sankyo Europe GmbH; treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT), also referred to as giant cell tumour of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS)

Scope: Updated list of experts and list of questions for SAG Oncology meeting

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

3.4.2. ozanimod - EMEA/H/C/004835

Treatment of multiple sclerosis

Scope: Letter from the applicant dated 16 January 2020 requesting for an extension of clock-stop to respond to the list of outstanding issues adopted in December 2019.

List of Questions to SAG Neurology

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

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

3.5.1. Hopveus - sodium oxybate - EMEA/H/C/004962

D&A PHARMA; for the treatment of alcohol dependence

Scope: Draft list of experts to the ad-hoc expert group meeting

Action: For adoption

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

Opinion adopted on 17.10.2019. List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 15.11.2018.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Halimatoz - adalimumab - EMEA/H/C/004866/X/0013

Sandoz GmbH

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 20mg (20mg/0.4ml) for Halimatoz solution for injection in pre-filled syringe.
The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1)."

Action: For adoption

List of Questions adopted on 14.11.2019.

4.1.2. Hefiya - adalimumab - EMEA/H/C/004865/X/0013

Sandoz GmbH

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 20mg (20mg/0.4ml) for Hefiya solution for injection in pre-filled syringe.
The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/10) and to align the PI with the latest QRD template (v.10.1)."

Action: For adoption

List of Questions adopted on 14.11.2019.

4.1.3. Hyrimoz - adalimumab - EMEA/H/C/004320/X/0013

Sandoz GmbH

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 20mg (20mg/0.4ml) for Hyrimoz solution for injection in pre-filled syringe.
The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1)."

Action: For adoption

List of Questions adopted on 14.11.2019.

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 questions

4.3.1. IDELVION - albutrepenonacog alfa - Orphan - EMEA/H/C/003955/X/0035

CSL Behring GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add a new strength of 3500 IU (700 IU/ml) for albutrepenonacog alfa powder and solvent for solution for injection. The RMP version 3.1 was updated in accordance.
In addition, the applicant took the opportunity to update sections 3.2.S.4, 3.2.P.1-2-3-5-8 with editorial changes and align the dossier."

Action: For adoption

4.3.2. Pemetrexed Accord - pemetrexed - EMEA/H/C/004072/X/0010

Accord Healthcare S.L.U.

Rapporteur: John Joseph Borg, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (25 mg/ml solution for infusion)"

Action: For adoption

4.3.3. Velphoro - iron - EMEA/H/C/002705/X/0020/G

Vifor Fresenius Medical Care Renal Pharma France

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Romaldas Mačiulaitis, PRAC
Rapporteur: Kimmo Jaakkola

Scope: "Extension application to add a new pharmaceutical form with a new strength - powder for oral suspension 125 mg, and extension of indication to add indication to use Velphoro for the control of serum phosphorus levels in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 ml/min/1.73 m^2) or with CKD on dialysis, based on the results from an open-label, randomised, active-controlled, parallel group, multicentre, phase 3 study investigating the safety and efficacy of Velphoro and calcium acetate in paediatric and adolescent CKD patients with hyperphosphataemia (Study PA-CL-PED-01). As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 7.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

Action: For adoption

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

No items

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

No items

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

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

5.1.1. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0070

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC
Rapporteur: Menno van der Elst

Scope: "Treatment of adults with previously untreated CD30+ PTCL"

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

5.1.2. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0039/G

Biofrontera Bioscience GmbH

Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely

Scope: "C.I.6.a - To modify the approved therapeutic indication to include the treatment of mild to severe actinic keratosis on extremities, trunk and neck. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PL are updated accordingly.
C.I.4 - To update section 5.1 of the SmPC based on follow-up data from study ALA-AK-CT009; this is a randomized, observer-blind, intra-individual phase III study to evaluate the safety and efficacy of Ameluz in combination with daylight PDT (photodynamic therapy) in comparison with Metvix for the treatment of mild to moderate actinic keratosis."

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

5.1.3. CRYSVITA - burosumab - Orphan - EMEA/H/C/004275/II/0010/G

Kyowa Kirin Holdings B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of adults with X-linked hypophosphataemia (XLH), and modification of the currently approved indication in children and adolescents, by removing the qualification 'with growing skeletons', in order to include treatment in all children with radiographic evidence of bone disease.
The application provides new week-48 data from Study UX023-CL304; a randomized, double-blind, placebo-controlled, phase 3 study with open-label extension to assess the efficacy and safety of KRN23 in adults with XLH.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10.1.
The updated RMP version 2.0 has also been submitted."

Action: For adoption

5.1.4. ECALTA - anidulafungin - EMEA/H/C/000788/II/0040

Pfizer Europe MA EEIG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of the approved indication "treatment of invasive candidiasis (ICC)" to include paediatric patients aged from 1 month to less than 18 years of age; consequently, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated in order to add paediatric dosing instructions, warnings and precautions, clinical, and non-clinical information. The Package Leaflet is updated accordingly consequent to the revisions to the SmPC. In addition, the Marketing Authorisation Holder (MAH) has taken the opportunity to update the information in the SmPC and Package Leaflet in line with the current excipient's guideline for fructose.
The RMP Version number 13.0 dated 08 March 2019 which includes GVP module V rev 2

changes has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 19.09.2019.

5.1.5. INTELENCE - etravirine - EMEA/H/C/000900/II/0058

Janssen-Cilag International NV

Rapporteur: Jean-Michel Race, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Adrien Inoubli

Scope: "To extend the approved therapeutic indication of Intelence in order to include patient population from 2 to 6 years of age based on the 48 week study results from study TMC125-C234/P1090 (A Phase I/II, Open-label Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Antiviral Activity of Etravirine (ETR) in Antiretroviral (ARV) Treatment-experienced HIV-1 Infected Infants and Children, Aged ≥2 Months to <6 Years). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and sections 1, 2 and 3 of the PL are updated accordingly. The updated RMP version 13.1 has also been submitted. The RMP (version 13.1) of the product has been updated to remove the completed additional pharmacovigilance activities (TMC125-C234/P1090 (Week 48) and TMC125-EPPICC) from the pharmacovigilance plan of the RMP. The RMP has also been updated to meet the requirements and updated definitions in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module V Revision 2 (EMA/838713/2011; Rev 2) and Guidance on the format of the RMP in the European Union (EMA/164014/2018 Rev 2.0.1) including proposed removal of safety concerns.
The MAH took the opportunity to include some typographic changes in Annex II C and D."

Action: For adoption

5.1.6. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0082

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of indication to include new population for Kalydeco 150 mg tables to extend the use to patients with cystic fibrosis (CF) aged 6 years and older and weighing 25 kg or more who have an R117H mutation in the CFTR gene and for Kalydeco granules 75 mg and 50 mg, to add patients with CF aged 12 months and older and weighing 7 kg to less than 25 kg who have an R117H mutation in the CFTR gene. This is based on a clinical trial and literature data, and post-marketing experience with Kalydeco. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 8.5 has also been submitted."

Action: For adoption

5.1.7. Kineret - anakinra - EMEA/H/C/000363/II/0070

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Mark Ainsworth, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to include the treatment of Familial Mediterranean Fever (FMF) for Kineret, to be given in combination with colchicine, if appropriate; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 5.0 has also been submitted."

Action: For adoption

5.1.8. Lynparza - olaparib - EMEA/H/C/003726/II/0033

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to support the use of Lynparza tablets (100mg and 150 mg) for the maintenance treatment of gBRCAm metastatic pancreatic cancer based on the results from the pivotal Phase 3 study, POLO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.8 for Lynparza hard capsules (50 mg) to revise the list of ADR based on the pooled safety data analysis. The RMP version 18 has also been submitted. Furthermore, the PI is brought in line with the latest guideline regarding the sodium content. The MAH also took the occasion to include some minor editorial changes in the PI."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

5.1.9. MabThera - rituximab - EMEA/H/C/000165/II/0162

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to include the treatment of paediatric patients (aged ≥ 2 to <18 years old) with active polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA), for MA numbers EU/1/98/067/001-002 for MabThera; following efficacy and safety data from Clinical study report (CSR) WA25615 (also known as Paediatric Polyangiitis and Rituximab Study [PePRS]) which was conducted to fulfil the measure of the Paediatric Investigational Plan (PIP: EMEA-000308-PIP02-11-M01) agreed upon in the context of rituximab development for treatment of adult patients with GPA and MPA (RAVE study). The CSR for Study 1: WA 25615 was submitted on 30th Oct 2018 as the Post Approval Measure submission according to Article 46 requirement. Linked to this variation the final compliance check procedure to close the PIP has started on 3rd January 2019.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and sections 2, 3 and 4 of the package leaflet are updated accordingly. Furthermore, the PI is brought in line with the latest QRD template (version 10) and the opportunity is taken to combine the SmPC and PIL for 100mg and 500mg IV as they are identical except for strength specifications.
In addition, the applicant took the opportunity to implement minor editorial changes in the SmPC.
The RMP version 20.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019, 17.10.2019, 29.05.2019.

5.1.10. MabThera - rituximab - EMEA/H/C/000165/II/0168

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication in previously untreated, advanced stage paediatric B-cell Non-Hodgkin's Lymphoma (B-NHL)"

Action: For adoption

Request for Supplementary Information adopted on 19.09.2019.

5.1.11. Rezolsta - darunavir / cobicistat - EMEA/H/C/002819/II/0033

Janssen-Cilag International NV

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ilaria Baldelli

Scope: "To extend the approved therapeutic indication of Rezolsta to include the adolescent population (aged 12 years old and older with body weight at least 40 kg). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and sections 1, 2 and 3 of the PL are updated accordingly. The updated RMP version 6.0 has also been submitted. The RMP of the product has been updated to meet the requirements and updated definitions in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module V Revision 2 (EMA/838713/2011; Rev 2) and Guidance on the format of the RMP in the European Union (EMA/164014/2018 Rev 2.0.1) including proposed removal of safety concerns.
In addition, in order to align the PI with recommendations for other HIV products, the MAH has also taken the opportunity to update section 4.2 of the SmPC with regards to administration of Rezolsta in case of vomiting."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

5.1.12. Ruconest - conestat alfa - EMEA/H/C/001223/II/0053/G

Pharming Group N.V

Rapporteur: Andrea Laslop, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Jan Neuhauser

Scope: "Update of indication to include children in the treatment of acute angioedema attacks with hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency. This is based from Study C1 1209 in
children.
In addition, final efficacy and safety data from the OLE phases of Studies C1 1304 and 1205 and the completed Study C1 1310 are submitted together with final study results of Studies C1 1207 and 3201, concerning

prophylactic treatment of HAE patients. Consequently, the product information has been updated.
Furthermore, the company is requesting an extension for the completion of registry Study C1 1412. The current RMP (V 18.0) states that completion of the final study report for Study C1 1412 is anticipated 31 March 2020.
Although patient enrolment has increased, the study will not be completed on time. The MAH would therefore like to request an extension of the study completion date to submit the final report date for Study C1 1412 on 30 June 2022. In addition, as mentioned below, the RMP has also been aligned to RMP template version 2.0.1.
The product information has also been updated to align with the most recent QRD template, version 10.1."

Action: For adoption

5.1.13. Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0011

sanofi-aventis groupe

Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include "treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise in addition to other oral medicinal products for the treatment of diabetes" based on the phase 3 Study EFC13794; a 26-week randomized, open-label, active controlled, parallel-group, study assessing the efficacy and safety of the insulin glargine/lixisenatide fixed ratio combination in adults with Type 2 Diabetes inadequately controlled on GLP-1 receptor agonist and metformin (alone or with pioglitazone and/or SGLT2 inhibitors), followed by a fixed ratio combination single-arm 26-week extension period.
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update the contact details of the local representatives in Denmark, the Netherlands and the UK in the Package Leaflet and to implement minor editorial changes in the annexes. An updated RMP version 4.0 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019, 27.06.2019.

5.1.14. Taltz - ixekizumab - EMEA/H/C/003943/II/0031

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and adolescents who are candidates for systemic therapy for Taltz; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated with new safety and efficacy information. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 7.1 has also been submitted."

Action: For adoption

5.1.15. Tremfya - guselkumab - EMEA/H/C/004271/II/0017

Janssen-Cilag International N.V.

Rapporteur: Melinda Sobor, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Addition of a new indication for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy. Consequently sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package leaflet is updated accordingly. Additionally, minor QRD changes are introduced in annex II."

Action: For adoption

5.1.16. Tybost - cobicistat - EMEA/H/C/002572/II/0051

Gilead Sciences Ireland UC

Rapporteur: Bruno Sepodes, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "To modify the approved therapeutic indication to include new population (adolescents aged 12 years and older, weighing at least 35 kg) for the treatment of HIV-1. Consequently, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC and sections 1 ,2, 3 of the PL are updated accordingly. The updated RMP version 4.1 has also been submitted"

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

5.1.17. Venclyxto - venetoclax - EMEA/H/C/004106/II/0023/G

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Filip Josephson, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of the indication to include treatment with Venclyxto in combination with an anti-CD20 antibody (obinutuzumab) for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL) based on the results of the pivotal CLL14/BO25323 phase 3 study. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC and corresponding sections of the PL have been revised. The updated RMP version 5.1 has been submitted.
Additionally, the SmPC section 5.3 has been updated based on the 6-month carcinogenicity mouse study report, supported by the 4 week dose ranging study in mice and the embryo-foetal development (EFD) data. Minor editorial changes have been introduced throughout the PI."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

5.1.18. WS1695
Braftovi - encorafenib - EMEA/H/C/004580/WS1695/0008
Mektovi - binimetinib - EMEA/H/C/004579/WS1695/0007

Pierre Fabre Medicament

Lead Rapporteur: Janet Koenig

Scope: "Extension of indication to include encorafenib in combination with binimetinib and cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, who have received prior systemic therapy; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 1.1 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

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. Brilique - ticagrelor - EMEA/H/C/001241/II/0047/G

AstraZeneca AB

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) without a history of myocardial infarction who have undergone percutaneous coronary intervention (PCI) based on the final results of study D513BC00001 (THEMIS), a phase III multinational, randomised, double-blind, placebo controlled study to evaluate the effect of ticagrelor twice daily on the incidence of cardiovascular death, myocardial infarction or stroke in patients with T2DM; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated.
Update of section 4.8 of the SmPC with new safety information on traumatic haemorrhages based on the final results from study D513BC00001 (THEMIS) and data from the ticagrelor clinical development programme and post-marketing data.
The Package Leaflet is updated in accordance. The RMP version 12 has also been submitted."

Letter from the applicant dated 22 January 2020 requesting an extension of clock stop to respond to the Request for Supplementary Information adopted on 14.11.2019

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019

5.2.2. Fycompa - perampanel - EMEA/H/C/002434/II/0047

Eisai GmbH

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include adjunctive treatment in paediatric patients from 2 to 11 years of age in Partial-Onset (focal) Seizures with or without secondary generalisation and Primary Generalised Tonic-Clonic Seizures with idiopathic generalised epilepsy for Fycompa;
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 4.3 has also been submitted." Clockstop extension requested to respond to RSI.

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

5.2.3. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0026

Boehringer Ingelheim International GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD).
As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The MAH takes this opportunity to also introduce minor linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Updated list of experts for the ad-hoc expert group meeting adopted via written procedure on 14 January 2020; Report from the ad-hoc expert group scheduled on 22 January 2020 (see also OFEV II/27)

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019, 27.06.2019.

5.2.4. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0027

Boehringer Ingelheim International GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include new indication for OFEV for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype based on the results of pharmacology studies and the double-blind, randomised, placebo-controlled phase III trial (INBUILD). Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to reflect the use of Ofev in the new indication. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to introduce minor formatting changes in the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The RMP version 9.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Updated list of experts for the ad-hoc expert group meeting adopted via written procedure on 14 January 2020; Report from the ad-hoc expert group scheduled on 22 January 2020 (see also OFEV II/26)

Action: For adoption

Request for supplementary information adopted on 12.12.2019.

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

8.1.1. crisantaspase - H0005424

treatment of patients with acute lymphoblastic leukaemia (ALL) who have developed hypersensitivity to E. coli-derived asparaginase

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

8.1.2. Combination of bifikafusp alfa and onfekafusp alfa - H0005385 and H0005370

intended for the treatment of stage IIIB and IIIC melanoma

Scope: Request for combination pack

Action: For adoption

8.1.3. dostarlimab - H0005204

treatment of patients with recurrent or advanced mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) endometrial cancer (EC)

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

8.2. Priority Medicines (PRIME)

Disclosure of information related to priority medicines cannot be released at present time as these contain commercially confidential information

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. ECALTA - anidulafungin - EMEA/H/C/000788

Pfizer Europe MA EEIG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: DHPC and communication plan on market disruption adopted via written procedure on 10 January 2020

Action: For information

9.1.2. Fexeric (EXP) - ferric citrate coordination complex - EMEA/H/C/003776

Akebia Europe Limited c/o Matheson

Rapporteur: Romaldas Mačiulaitis, Co-Rapporteur: Daniela Melchiorri

Scope: The marketing authorisation of Fexeric expired on 13 January 2020 due to the sunset clause

Action: For discussion

9.1.3. Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0037

Apotex Europe BV; generic of Zyprexa

Rapporteur: John Joseph Borg

Scope: "Update of sections 4.8 and 4.4 in order to add information regarding the risk of metabolic syndrome with the use of olanzapine, based on review of the available data."

Action: For discussion

9.1.4. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0049

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Updated of section 4.8 of the SmPC with the safety data from the Phase 3, open-label, rollover study for Studies 109 and 011 Part B (Study 011B) designed to evaluate the long-term safety and tolerability of Orkambi treatment for 96 weeks in patients with cystic fibrosis, 6 years of age and older, homozygous for F508del."

Action: For discussion

Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.

9.1.5. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0049

Novartis Europharm Limited

Re-examination Rapporteur: Milena Stain and re-examination Co-Rapporteur: Sinan B Sarac

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include first line treatment of adult and paediatric patients aged 2 years and older with severe aplastic anaemia for Revolade in combination with IST; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 50 has also been updated."

Post-authorisation European Public Assessment Report

Action: For information

Opinion adopted on 17.10.2019, 27.06.2019. Oral explanation held on 24.06.2019. Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

9.1.6. Stelara - ustekinumab - EMEA/H/C/000958/II/0073

Janssen-Cilag International NV

Rapporteur: Jayne Crowe, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication to include the treatment of children aged 6 to 12 years with moderate to severe psoriasis for Stelara solution for injection; as a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Section 4.8 for Stelara concentrate for solution for infusion is updated accordingly. Minor editorial changes are made to Section 4.5 for both formulations.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 16.1 has also been submitted."

Revised Opinion adopted via written procedure on 14 January 2020

Action: For information

9.1.7. Varuby - rolapitant - EMEA/H/C/004196

Tesaro UK Limited; prevention of nausea and vomiting

Rapporteur: Alexandre Moreau, Co-Rapporteur: Peter Kiely

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.8. WS1587/G Abasaglar-EMEA/H/C/002835/WS1587/0028/G Humalog-EMEA/H/C/000088/WS1587/0178/G

Applicant: Eli Lilly Nederland B.V.

Lead Rapporteur: Kristina Dunder

Scope: "Type II variation. B.IV.z. to introduce an additional prefilled pen presentation for Abasaglar, solution for injection (EU/1/14/944/007, EU/1/14/944/008, EU/1/14/944/012, EU/1/14/944/013), Humalog, solution for injection (EU/1/96/007/002, EU/1/96/007/004, EU/1/96/007/020, EU/1/96/007/021 EU/1/96/007/023), Humalog Kwikpen solution for injection (EU/1/96/007/031, EU/1/96/007/032, EU/1/96/007/039, EU/1/96/007/040, EU/1/96/007/041, EU/1/96/007/042) and Humalog Junior Kwikpen, solution for injection (EU/1/96/007/043, EU/1/96/007/044, EU/1/96/007/045). The pack contains 5 pre-filled pens.
Type IAIN B. II.e.5.a.1 to request the 2x5 multipack.
As a consequence, the following sections were updated 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6, 8 of the SmPC in order to add new pre-filled pen presentation; the Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make an editorial change (removing comma in SK address in the PL)."

Letter from the applicant dated 07 January 2020 requesting an extension of clock-stop to respond to the request for supplementary information adopted on 14 November 2019 – adopted via written procedure on 17 January 2020.

Action: For information

Request for Supplementary Information adopted on 14.11.2019, 19.09.2019

9.1.9. Yondelis - trabectedin- EMEA/H/C/000773

Pharma Mar, S.A.; treatment of soft tissue sarcoma and ovarian cancer

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez

Scope: Risk assessment

Action: For discussion

9.1.10. Zynteglo - autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - EMEA/H/C/003691/R/0005, Orphan, ATMP

bluebird bio (Netherlands) B.V

CHMP Coordinator Rapporteur: Paula Boudewina van Hennik, CHMP Coordinator Co-Rapporteur: Alexander Moreau

Scope: Renewal

Action: For discussion

10. Referral procedures

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

No items

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

10.2.1. Direct Oral Anticoagulants (DOAC) - EMEA/H/A-5(3)/1478

MAHs: various

Referral Rapporteur: Martina Weise, Referral Co-Rapporteurs: Kristina Dunder

Rapporteurs for involved CAPs:

Eliquis (APIXABAN):
Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart van der Schueren;

Pradaxa (DABIGATRAN ETEXILATE):
Rapporteur: Mark Ainsworth, Co-Rapporteur: Jean-Michel Race;

Xarelto (RIVAROXABAN):
Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: List of outstanding issues/Opinion

To assess the results of a non-interventional study regarding the risks of major bleeding in patients with non-valvular atrial fibrillation.

Action: For adoption

10.2.2. Presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients EMEA/H/A-5(3)/1490

MAHs: various

Referral Rapporteur: Martina Weise, Referral Co-Rapporteurs: Kristina Dunder

Scope: Update on presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients

List of questions to the ad-hoc expert meeting adopted via written procedure on 03 January 2020

List of experts for the ad-hoc expert meeting

List of questions to EU trade associations

Action: For adoption

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

No items

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

10.4.1. Budesonide SUN – budesonide – EMEA/H/A-29(4)/1492

Sun Pharmaceutical Industries Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Giuseppa Pistritto

Scope: List of outstanding issues

Action: For adoption

The applicant has submitted an Art. 10(3) application for Budesonide SUN nebuliser suspension and associated names. Concerns regarding the demonstration of bioequivalence have been raised by IT and UK who were of the view that the data presented (comparative in vitro data of the product before nebulisation, including Particle Size Distribution (PSD) of the active substance) are not sufficient to demonstrate bioequivalence. The procedure was initiated because of disagreements regarding which in-vitro data are considered pivotal.

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

January 2020 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 it is 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

No items

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 13-16 January 2020

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for January 2020

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 22-24 January 2020

Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 13-15 January 2020

Action: For information

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 20-22 January 2020

Action: For information

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP January 2020 meeting to CHMP for adoption:

- 12 reports on products in scientific advice and protocol assistance
- 7 reports on products in pre-authorisation procedures
- 1 report on products in post-authorisation procedures
- 4 reports on products in plasma master file

Action: For adoption

14.3.2. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

CMDh question to CNSWP- Bioequivalence requirements for Cmax for carbamazepine as NTI drug

Action: For adoption

14.3.3. Name Review Group (NRG)

Lipid complex formulations – safety concerns linked to naming

Action: For discussion

14.3.4. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 13-16 January 2020. Table of conclusions

Action: For information

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

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

14.7.1. CHMP 2020 Work Plan

Action: For adoption

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Oncology Training

Action: For information

16. 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)*

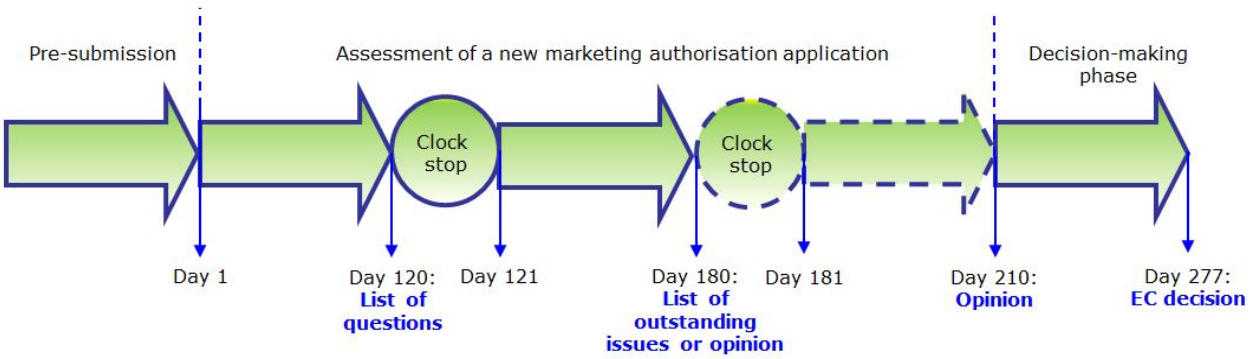
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (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.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

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



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

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

Extensions of marketing authorisations are applications for the change or addition of new strengths,

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

Type II variations - Extension of indication procedures *(section 5)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 6)*

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

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 3.5)*

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

Scientific advice working party (SAWP) *(section 14.3.1)*

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27 March 2020
EMA/CHMP/43575/2020 Corr[1]

Annex to 27-30 January 2020 CHMP Agenda

Pre-submission and post-authorisations issues

[1] Correction in B.6.9

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for January 2020: **For adoption**

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

Final Outcome of Rapporteurship allocation for January 2020: **For adoption**

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

Increlex - mecasermin - EMEA/H/C/000704/S/0061
Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka

Lojuxta - lomitapide - EMEA/H/C/002578/S/0036
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 14.11.2019.

Myalepta - metreleptin - EMEA/H/C/004218/S/0009, Orphan
Aegerion Pharmaceuticals B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Adam Przybylkowski

Raxone - idebenone -

EMEA/H/C/003834/S/0019, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH,
Rapporteur: John Joseph Borg, PRAC
Rapporteur: Amelia Cupelli

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Ivabradine Anpharm - ivabradine -
EMEA/H/C/004187/R/0014
ANPHARM Przedsiebiorstwo Farmaceutyczne S.A., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Menno van der Elst

Repatha - evolocumab -
EMEA/H/C/003766/R/0040
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Aripiprazole Zentiva - aripiprazole -
EMEA/H/C/003899/R/0012
Zentiva, k.s., Generic, Generic of Abilify,
Rapporteur: John Joseph Borg, PRAC
Rapporteur: Ana Sofia Diniz Martins

Bortezomib Accord - bortezomib -
EMEA/H/C/003984/R/0022
Accord Healthcare S.L.U., Generic, Generic of VELCADE, Rapporteur: Milena Stain, PRAC Rapporteur: Amelia Cupelli

Daxas - roflumilast -
EMEA/H/C/001179/R/0039
AstraZeneca AB, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Maria del Pilar Rayon

EVOTAZ - atazanavir / cobicistat -
EMEA/H/C/003904/R/0031
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Adrien Inoubli
Request for Supplementary Information adopted on 12.12.2019.

IKERVIS - ciclosporin - Correction of the warning for cetalkonium

EMEA/H/C/002066/R/0017 Santen Oy, Rapporteur: Peter Kiely, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Jan Neuhauser Opinion adopted on 14.11.2019. Request for Supplementary Information adopted on 19.09.2019.	chloride (CKC).
Jinarc - tolvaptan - EMEA/H/C/002788/R/0027 Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Amelia Cupelli Request for Supplementary Information adopted on 14.11.2019.	
Keytruda - pembrolizumab - EMEA/H/C/003820/R/0081 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 12.12.2019.	
Odomzo - sonidegib - EMEA/H/C/002839/R/0028 Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Željana Margan Koletić	
Pregabalin Mylan - pregabalin - EMEA/H/C/004078/R/0014 Mylan S.A.S, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Mylan Pharma, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan Request for Supplementary Information adopted on 12.12.2019.	
Pregabalin Mylan Pharma - pregabalin - EMEA/H/C/003962/R/0012 Mylan S.A.S, Generic, Generic of Lyrica, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan Request for Supplementary Information adopted on 12.12.2019.	
Pregabalin Sandoz - pregabalin - EMEA/H/C/004010/R/0012 Sandoz GmbH, Generic, Generic of Lyrica, Rapporteur: Tomas Radimersky, PRAC	

Rapporteur: Liana Gross-Martirosyan

Pregabalin Sandoz GmbH - pregabalin - EMEA/H/C/004070/R/0013
Sandoz GmbH, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Sandoz, Rapporteur: Tomas Radimersky, PRAC Rapporteur: Liana Gross-Martirosyan

Pregabalin Zentiva - pregabalin - EMEA/H/C/003900/R/0021
Zentiva k.s., Generic, Generic of Lyrica, Rapporteur: Alar Irs, PRAC Rapporteur: Liana Gross-Martirosyan

Strensiq - asfotase alfa - EMEA/H/C/003794/R/0044, Orphan
Alexion Europe SAS, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald

Synjardy - empagliflozin / metformin - EMEA/H/C/003770/R/0044
Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva A. Segovia
Request for Supplementary Information adopted on 14.11.2019.

Voriconazole Hikma - voriconazole - EMEA/H/C/003737/R/0010
Hikma Farmaceutica (Portugal), S.A., Generic, Generic of Vfend, Rapporteur: Natalja Karpova, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 12.12.2019.

B.2.3. Renewals of Conditional Marketing Authorisations

Deltyba - delamanid - EMEA/H/C/002552/R/0041, Orphan
Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, PRAC Rapporteur: Jean-Michel Dogné

Lorviqua - lorlatinib - EMEA/H/C/004646/R/0004
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Nikica Mirošević Skvrce

Ondexxya - andexanet alfa - EMEA/H/C/004108/R/0004

Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst	
Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/R/0031 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik	
Rubraca - rucaparib - EMEA/H/C/004272/R/0016 Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin	
WAYLIVRA - volanesorsen - EMEA/H/C/004538/R/0003, Orphan Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Martin Huber	
Zynteglo - autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - EMEA/H/C/003691/R/0005, Orphan, ATMP bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, Co-Rapporteur: Violaine Closson Carella, CHMP Coordinators: Paula Boudewina van Hennik and Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski	See agenda item 9.1

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 13-16 January 2020
PRAC:

• **Abiraterone - ZYTIGA** Signal of interaction with sulphonylureas leading to hypoglycaemia – PRAC recommendation on a variation **Action:** For adoption • **Golimumab – SIMPONI** Signal of inflammatory myopathy - PRAC recommendation on a variation **Action:** For adoption	
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its January 2020 meeting:	

B.4. EPARs / WPARs

AMSPARITY - adalimumab - EMEA/H/C/004879 Pfizer Europe MA EEIG, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis, treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, adolescent hidradenitis suppurativa, paediatric uveitis, treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, paediatric uveitis, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Azacitidine Accord - azacitidine - EMEA/H/C/005147 Accord Healthcare S.L.U., Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) and AML with >30% marrow blasts according to the WHO classification., Generic, Generic of Vidaza, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Beovu - brolucizumab - EMEA/H/C/004913 Novartis Europharm Limited, treatment of neovascular (wet) age-related macular degeneration (AMD), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

Dexmedetomidine Accord - dexmedetomidine - EMEA/H/C/005152 Accord Healthcare S.L.U., light to moderate sedation, Generic, Generic of Dexdor, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Recarbrio - imipenem / cilastatin / relebactam - EMEA/H/C/004808 Merck Sharp & Dohme B.V., indicated for the treatment of bacterial infections due to gram-negative microorganisms, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

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

Apidra - insulin glulisine - EMEA/H/C/000557/II/0082/G Sanofi-Aventis Deutschland GmbH, Rapporteur: Mark Ainsworth Request for Supplementary Information adopted on 21.11.2019.
Bemfola - follitropin alfa - EMEA/H/C/002615/II/0022 Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik
Bydureon - exenatide - EMEA/H/C/002020/II/0067 AstraZeneca AB, Rapporteur: Kristina Dunder
CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0149/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 14.11.2019.
Coagadex - human coagulation factor X - EMEA/H/C/003855/II/0023, Orphan BPL Bioproducts Laboratory GmbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 24.10.2019.
CooperSurgical Inc ART Media - human albumin solution -

EMEA/H/D/002307/II/0006/G
BSI Group, Rapporteur: Kristina Dunder

Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0012/G
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0013/G
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Dupixent - dupilumab - EMEA/H/C/004390/II/0024/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0002, Orphan
Novo Nordisk A/S, Rapporteur: Andrea Laslop
Request for Supplementary Information adopted on 21.11.2019.

Fasenra - benralizumab - EMEA/H/C/004433/II/0025/G
AstraZeneca AB, Rapporteur: Fátima Ventura

Fiasp - insulin aspart - EMEA/H/C/004046/II/0018/G
Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Amelia Cupelli

Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0037, Orphan
Roche Registration GmbH, Rapporteur: Sinan B. Sarac
Request for Supplementary Information adopted on 12.12.2019.

GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0148
Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege

Humalog - insulin lispro - EMEA/H/C/000088/II/0181
Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder

IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0037, Orphan
CSL Behring GmbH, Rapporteur: Jan Mueller-

Berghaus	
IKERVIS - ciclosporin - EMEA/H/C/002066/II/0018 Santen Oy, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 16.01.2020.	
Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0023, Orphan Alexion Europe SAS, Rapporteur: Bart Van der Schueren	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0084 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri	
Kineret - anakinra - EMEA/H/C/000363/II/0072 Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth	
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0029/G Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth	
NeuroBloc - botulinum toxin type B - EMEA/H/C/000301/II/0104/G Sloan Pharma S.a.r.l, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 05.12.2019, 31.10.2019, 26.09.2019.	
Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0094/G Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad Opinion adopted on 16.01.2020.	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0095/G Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad Opinion adopted on 16.01.2020.	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nivestim - filgrastim - EMEA/H/C/001142/II/0059 Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola	
NovoEight - turoctocog alfa -	

EMEA/H/C/002719/II/0033/G
Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 05.12.2019.

Nplate - romiplostim - EMEA/H/C/000942/II/0074
Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro

OPDIVO - nivolumab - EMEA/H/C/003985/II/0076/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez
Request for Supplementary Information adopted on 28.11.2019.
Letter from the applicant dated 13.12.2019 requesting a clock stop extension. **For information.**

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0053/G
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri
Request for Supplementary Information adopted on 28.11.2019.

Palynziq - pegvaliase - EMEA/H/C/004744/II/0002, Orphan
BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege
Request for Supplementary Information adopted on 14.11.2019.

Pemetrexed Hospira - pemetrexed - EMEA/H/C/003970/II/0020/G
Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs
Request for Supplementary Information adopted on 24.10.2019, 12.09.2019.

Pifeltro - doravirine - EMEA/H/C/004747/II/0010/G
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0154/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 26.09.2019.

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0155 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	
Rizmoic - naldemedine - EMEA/H/C/004256/II/0005/G Shionogi B.V., Rapporteur: Mark Ainsworth	
Ruconest - conestat alfa - EMEA/H/C/001223/II/0052 Pharming Group N.V, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 21.11.2019.	
Simulect - basiliximab - EMEA/H/C/000207/II/0101/G Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 16.01.2020. Request for Supplementary Information adopted on 10.10.2019.	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0039/G Bracco International B.V., Rapporteur: Alexandre Moreau	
Spectrila - asparaginase - EMEA/H/C/002661/II/0015/G medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop	
Starlix - nateglinide - EMEA/H/C/000335/II/0036/G Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola	
Stelara - ustekinumab - EMEA/H/C/000958/II/0075 Janssen-Cilag International NV, Rapporteur: Jayne Crowe Opinion adopted on 16.01.2020.	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trazimera - trastuzumab - EMEA/H/C/004463/II/0011 Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus	
Ultomiris - ravulizumab - EMEA/H/C/004954/II/0003/G Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez	

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0052/G MCM Vaccine B.V., Rapporteur: Bart Van der Schueren	
Xadago - safinamide - EMEA/H/C/002396/II/0034 Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 16.01.2020.	Request for supplementary information adopted with a specific timetable.
Ziextenzo - pegfilgrastim - EMEA/H/C/004802/II/0004 Sandoz GmbH, Rapporteur: Andrea Laslop	
WS1630 **Bretaris Genuair-EMEA/H/C/002706/ WS1630/0041** **Eklira Genuair-EMEA/H/C/002211/ WS1630/0041** AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra Request for Supplementary Information adopted on 12.09.2019.	
WS1632/G **Brimica Genuair-EMEA/H/C/003969/ WS1632/0027/G** **Duaklir Genuair-EMEA/H/C/003745/ WS1632/0027/G** AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra Request for Supplementary Information adopted on 12.09.2019.	
WS1691/G **Infanrix hexa-EMEA/H/C/000296/ WS1691/0266/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren	
WS1720/G **Ambirix-EMEA/H/C/000426/WS1720/ 0104/G** **Twinrix Adult-EMEA/H/C/000112/ WS1720/0139/G** **Twinrix Paediatric-EMEA/H/C/000129/ WS1720/0140/G** GlaxoSmithkline Biologicals SA, Lead	

Rapporteur: Bart Van der Schueren	
WS1740 **ProQuad-EMEA/H/C/000622/WS1740/0136** **Zostavax-EMEA/H/C/000674/WS1740/0126** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus	
WS1728/G **Hexacima-EMEA/H/C/002702/WS1728/0094/G** **Hexaxim-EMEA/H/W/002495/WS1728/0099/G** **Hexyon-EMEA/H/C/002796/WS1728/0098/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	

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

Abraxane - paclitaxel - EMEA/H/C/000778/II/0097 Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC based on the results of study ABI-007-PST-001. This was a phase 1/2, multicenter, open-label, dose-finding study to assess the safety, tolerability and efficacy of weekly abraxane in paediatric patients with recurrent or refractory solid tumours, listed in the PIP, submitted in order to fulfil Article 46." Request for Supplementary Information adopted on 14.11.2019.	
Ambirix - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000426/II/0105 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Ambirix SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 15 years after primary immunisation of adolescents, based on data from the Phase IV study HAB-084 EXT Y11-15 (An open, long-term follow-up study to evaluate long-term antibody persistence and immune memory between 11 and 15 years after the primary study HAB-084). The Package Leaflet is updated accordingly. In	

addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and make some minor editorial changes. Furthermore, the MAH took the opportunity to update Annex II with regards to PSUR requirements."

Baraclude - entecavir - EMEA/H/C/000623/II/0063

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Submission of responses to the final clinical study report (CSR) from a Paediatric Safety and Efficacy Study (AI463189), a comparative study of the antiviral efficacy and safety of Entecavir (ETV) versus placebo in paediatric subjects with chronic Hepatitis B Virus (HBV) infection who are HBeAg positive, in order to provide additional clarification regarding the on-treatment and long-term follow-up haematology findings. The final CSR for AI463189 was already submitted and assessed within the context of procedure EMEA/H/C/000623/P46/010."
Request for Supplementary Information adopted on 05.12.2019, 10.10.2019.

BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0030

Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: John Joseph Borg, "Update of sections 4.2, 4.4 and 6.6 of the SmPC to add the use as reliever for allergen- and exercise-induced bronchoconstriction following assessment of the same change for the reference product Symbicort Turbohaler 160 mcg/4.5 mcg; the Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to introduce some minor editorial amendments in the PI for the following languages: FR, NO and PT."

Brintellix - vortioxetine - EMEA/H/C/002717/II/0022/G

H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC to describe the effects of vortioxetine on treatment-emergent sexual dysfunction based on the outcome of the clinical studies 318 and

4001.
Update of sections 4.4 and 5.2 to reflect the outcome of pharmacokinetic study 401 in subjects with severe hepatic impairment. Section 4.2 is also updated to add a cross reference to section 4.4 and 5.2 for hepatic impairment and section 4.4 wording for renal impairment is aligned to the one regarding hepatic impairment."
Request for Supplementary Information adopted on 14.11.2019, 27.06.2019.

Bydureon - exenatide - EMEA/H/C/002020/II/0066
AstraZeneca AB, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to include information about the new ADR drug-induced thrombocytopenia (DITP) based on spontaneous reports post-marketing. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in line with the latest QRD template."
Request for Supplementary Information adopted on 21.11.2019.

BYETTA - exenatide - EMEA/H/C/000698/II/0071
AstraZeneca AB, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to include information about the new ADR drug-induced thrombocytopenia (DITP) based on spontaneous reports post-marketing. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in line with the latest QRD template."
Request for Supplementary Information adopted on 21.11.2019.

CABOMETYX - cabozantinib - EMEA/H/C/004163/II/0012
Ipsen Pharma, Rapporteur: Bjorg Bolstad, "Update of section 4.4 of the SmPC to include the risk of Osteonecrosis as a warning. Update of Section 4.8 of the SmPC based on the Company Core Safety Information:
- to remove Anaemia, Oral pain and Dry mouth from the list of adverse reactions (ADRs), - to add Dysphagia and Hyperkeratosis to the existing ADR, - to replace Peripheral sensory neuropathy by Peripheral neuropathy in order to

reflect the broader medical concept and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the product information with the QRDv10.1 and update the local representative information of Hungary."	
Cometriq - cabozantinib - EMEA/H/C/002640/II/0035, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.2 to introduce a clarification in alignment with Cabometyx; update of section 4.4 of the SmPC to include the addition of the risk of diarrhoea and additional test to the existing risks of thromboembolic events, haemorrhage, wound complications and RPLS (Reversible posterior leukoencephalopathy syndrome). Update of section 4.8 of the SmPC, based on the Company Core Safety Information, to remove oropharyngeal pain from the list of adverse reactions (ADRs) and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the product information with the QRDv10.1 and update the local representative information of Hungary."	
Cufence - trientine dihydrochloride - EMEA/H/C/004111/II/0002/G Univar Solutions BV, Rapporteur: Milena Stain"B.II.a.3.b.2) (type II) B.II.b.4.b) (type IA) B.II.b.3.a) (type IB) B.II.a.1.a) (type IB) B.II.d.1.a) (type IA) B.II.f.1.d) (type IB) C.1.4. Update of sections 4.5 and 5.2 of the SmPC in order to add information on food interaction and pk based on results from study TR-003 PK are proposed. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in	

line with the latest QRD template."
Request for Supplementary Information adopted on 14.11.2019.

DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0030
Teva Pharma B.V., Rapporteur: John Joseph Borg, "Update of sections 4.2, 4.4 and 6.6 of the SmPC to add the use as reliever for allergen- and exercise-induced bronchoconstriction following assessment of the same change for the reference product Symbicort Turbohaler 160 mcg/4.5 mcg; the Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to introduce some minor editorial amendments in the PI for the following languages: FR, NO and PT."

Eliquis - apixaban - EMEA/H/C/002148/II/0064
Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study CV185316 (AUGUSTUS), an open-label, randomised, controlled clinical trial to evaluate the safety of apixaban in patients with atrial fibrillation and acute coronary syndrome and/or percutaneous coronary intervention."
Request for Supplementary Information adopted on 19.09.2019.

Emgality - galcanezumab - EMEA/H/C/004648/II/0009
Eli Lilly Nederland B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC following final results from a CONQUER study (A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Adults with Treatment-Resistant Migraine; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity correct Slovakian contact information in the Package Leaflet."

Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0078
Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8

and 5.1 of the SmPC in order to update the safety information following the final results from study 400-12-006 listed as in the paediatric investigation plan; this is a prospective, randomized, controlled study evaluating Evicel (fibrin sealant) as an adjunct to hemostasis during abdominal, retroperitoneal, pelvic or thoracic (non-Cardiac) surgery in pediatric patients. The Package Leaflet is updated accordingly."

Glivec - imatinib - EMEA/H/C/000406/II/0117

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.6 of the SmPC to include that women of childbearing potential must be advised to use effective contraception for at least 15 days after stopping treatment with imatinib, based on a company review of the company Core Data Sheet. The PL has been updated accordingly."
Request for Supplementary Information adopted on 10.10.2019.

ILARIS - canakinumab - EMEA/H/C/001109/II/0067

Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC and relevant sections of the PL with the results of study CACZ885GDE01T (a Multi-centre, phase II, randomized, placebo-controlled trial of Ilaris for the Treatment of adult-onset Still's Disease) and an updated pooled analyses of Systemic Juvenile Idiopathic Arthritis (SJIA) studies CACZ885A2203 (safety only), CACZ885G2305, CACZ885G2301, CACZ885G2301E1, CACZ885G2306 and CACZ885G1301."

Imnovid - pomalidomide - EMEA/H/C/002682/II/0036/G, Orphan

Celgene Europe BV, Rapporteur: Jorge Camarero Jiménez, "Group of two type II variations to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with information on anaphylaxis and section 4.8 of SmPC with hypothyroidism ADR following a safety review. This group also includes a Type IB Variation to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH

has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment."
Request for Supplementary Information adopted on 12.09.2019.

Kuvan - sapropterin - EMEA/H/C/000943/II/0068, Orphan
BioMarin International Limited, Rapporteur: Peter Kiely, "Update of section 5.1 of the Summary Product Characteristics (SmPC) in order to reflect new paediatric information based on study PKU-015 evaluating the effect of Kuvan on neurocognitive function, maintenance of blood phenylalanine concentrations, safety, and population Pharmacokinetics in young Children with Phenylketonuria.
The study is listed as MEA-C-Clinical, category 3 in the RMP for Kuvan and submitted in accordance to article 46 of the paediatric regulation."
Request for Supplementary Information adopted on 12.09.2019.

Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0019
Norgine B.V., Rapporteur: Peter Kiely, "To update SmPC sections 4.2, 4.4, 4.8 in order to correct the radiation dose for patients with hepatic and renal impairment, and section 12 in order to change the labelling-activity that can be added to the vial. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0027
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Submission of the final clinical study report from study M16-133, this is a phase 3b, single Arm, open label, multicenter study aimed to evaluate the efficacy and safety of glecaprevir (GLE)/pibrentasvir (PIB) in treatment of naïve adults with chronic Hepatitis C Virus (HCV) Genotypes 1 – 6 infection and aspartate aminotransferase to platelet ratio index (APRI) ≤ 1."
Request for Supplementary Information adopted

on 24.10.2019.	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0029 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Update of sections 4.2 and 5.1 of the Maviret SmPC to shorten the treatment duration in treatment-naïve subjects with compensated cirrhosis and HCV GT3 infection, from 12 to 8 weeks, based on second interim results from study M16-135: A Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment Naïve Adults with Chronic Hepatitis C Virus (HCV) Genotype 1 - 6 Infection and Compensated Cirrhosis (EXPEDITION-8)."	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0030 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Update of section 4.2 of the Maviret SmPC to improve the clarity of the dosing instruction, based on post-marketing data and pharmacokinetic simulations."	
Menveo - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0093 GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to include lymphadenopathy as a new expected adverse reaction after vaccination in Post-marketing experience based on final results from study V59_77 and substantiated by supportive clinical data only to establish frequency, following CHMP assessment of procedure P46/039. Section 4 of the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."	
Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0009, Orphan Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8, 5.1 and 5.2 of the SmPC following final results from paediatric study UX003-CL203, an open –label study of vestrodinase alfa enzyme replacement therapy in MPS 7 patients less than	

5 years old." Request for Supplementary Information adopted on 12.12.2019.	
Mimpara - cinacalcet - EMEA/H/C/000570/II/0065 Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to the new ADR 'chondrocalcinosis pyrophosphate' with a frequency of unknown. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to implement a minor correction to the List of Excipients in section 6.1 of the SmPC." Request for Supplementary Information adopted on 14.11.2019.	
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0010/G, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "A group of two type II variations, to submit the non-clinical in vitro study reports PFZ-07 and 6000572 relating to the effects of gemtuzumab ozogamicin on platelet development as well as on human platelet function." Request for Supplementary Information adopted on 21.11.2019, 10.10.2019.	
Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0096 Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, "Update of section 5.1 of the SmPC based on final results from 3 extended follow-up paediatric studies (MenACWY-TT-099, MenACWY-TT-100 and MenACWY-TT-101) as well as paediatric study MenACWY-TT-102. Studies MenACWY-TT-099, MenACWY-TT-100 and MenACWY-TT-102 were previously submitted (P46 054, P46 053 and P46 052, respectively). The Package Leaflet is updated accordingly. In addition, the opportunity is taken to bring the PI in line with the latest QRD template version 10.1."	
Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0037 Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg, "Update of sections 4.8 and 4.4 in order to add information	See agenda 9.1

regarding the risk of metabolic syndrome with the use of olanzapine, based on review of the available data."

Portrazza - necitumumab - EMEA/H/C/003886/II/0017

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Rugile Pilviniene, "Submission of the exploratory biomarker analysis from 4 clinical studies (I4X-MC-JFCU, I4X-MC-JFCQ, I4X-MC-JFCP, I6A-MC-CBBE) listed as a category 3 measure in the RMP. The RMP version 8.1 has also been submitted." Request for Supplementary Information adopted on 28.11.2019.

Praluent - alirocumab - EMEA/H/C/003882/II/0053

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study DFI14223, listed as a category 3 study in the RMP in order to fulfil MEA 029. The submission serves also to comply with article 46 of the regulation (EC) N° 1901/2206 (as amended) on medicinal products for paediatric use as study DFI14223 is also part of the PIP (MEA-001169-PIP01-11). This is an 8-week open label, sequential, repeated dose-finding study to evaluate the efficacy, safety and PK profile of alirocumab in children and adolescents with heterozygous familial hypercholesterolemia followed by an extension phase."

Qtern - saxagliptin / dapagliflozin - EMEA/H/C/004057/II/0024

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.2, 4.4 and 5.1 of the SmPC with information on the glycaemic efficacy and renal safety of dapagliflozin in patients with Type 2 Diabetes Mellitus and moderate renal impairment (CKD 3A) based on final results from study D1690C00024 (DERIVE) (dapagliflozin), and to reflect a change in renal cut-off value for saxagliptin. The package leaflet is updated accordingly.
The RMP version 4.1 has also been submitted. In addition, the MAH took the opportunity to update SmPC sections 2, 4.8, 5.2 and Annex II to include the required excipient information in relation to sodium levels and lactose following the update to the Annex to the European

Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use", as well as to bring the PI in line with EMA guidance ("Compilation of QRD decisions on stylistic matters in product information", EMA/25090/2002 Rev.18, published 08 December 2017)."
Request for Supplementary Information adopted on 14.11.2019, 27.06.2019.

Repatha - evolocumab - EMEA/H/C/003766/II/0038
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information based on final results from study 20140213. This is a phase 1 open-label interventional study to evaluate the safety, pharmacokinetics, and pharmacodynamics of evolocumab after a single 140 mg subcutaneous dose in subjects with normal renal function or severe renal insufficiency or end stage renal disease receiving haemodialysis. The Package Leaflet are updated accordingly."
Request for Supplementary Information adopted on 14.11.2019.

Revatio - sildenafil - EMEA/H/C/000638/II/0086
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC based on the final results from study A1481316; this is a multi-centre, randomised, placebo-controlled, double-blind, two-armed, parallel group study to evluate efficacy and safety of iv sildenafil in the treatment of neonates with persistent pulmonary hypertension of the newborn (PPHN) or hypoxic respiratory failure and at risk for PPHN, with a long-term follow-up investigation of developmental progress 12 and 24 months after completion of study treatment. In addition some minor editorial updates to the Product Information are being proposed."
Request for Supplementary Information adopted on 05.12.2019.

Revlimid - lenalidomide - EMEA/H/C/000717/II/0112/G
Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the

SmPC and section 4 of the PL with anaphylaxis following a safety review and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment. Finally the MAH took the opportunity to make editorial changes throughout the product information." Request for Supplementary Information adopted on 12.09.2019.	
Rizmoic - naldemedine - EMEA/H/C/004256/II/0004 Shionogi B.V., Rapporteur: Mark Ainsworth, "Submission of the final report from non-clinical study S-297995-PF-360-N as agreed in letter of recommendation to CHMP: In-vitro data determining whether naldemedine inhibits in a time dependent manner the OATP1B1, OATP1B3, OAT1 and OAT3 transporters." Request for Supplementary Information adopted on 14.11.2019.	
Tafinlar - dabrafenib - EMEA/H/C/002604/II/0042 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on pulmonary embolism/deep vein thrombosis (PE/DVT) to be renamed to a broader term venous thromboembolism (VTE) based on cumulative analysis of data received from clinical trials and the post-marketing setting. The Package Leaflet is updated accordingly."	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0032 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to update the safety information and include blood alkaline phosphatase increased, blood creatinine increased and alopecia as adverse drug reactions for atezolizumab given in combination with other medicinal products. The safety update is based on the review of	

safety data from a pooled population. In addition, instruction for treatment interruption for neutropenia and peripheral neuropathies when atezolizumab is used in combination with nab-paclitaxel in metastatic triple negative breast cancer are being revised in section 4.4 of the SmPC. The MAH also took the opportunity of this variation to introduce minor editorial comments. The Package Leaflet is updated accordingly."	
Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0061/G Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity." Request for Supplementary Information adopted on 12.09.2019.	
Twinrix Adult - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000112/II/0140 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Twinrix Adult SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 20 years after primary immunisation of adults, based on data from two phase IV long-term follow-up extension studies, HAB-028 EXT Y16-20 (An open, single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-028) and HAB-032 EXT Y16-20 (An open single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-032). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to make minor	

editorial changes.”	
Twinrix Paediatric - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000129/II/0141 GlaxoSmithkline Biologicals SA, Duplicate, Duplicate of Twinrix Adult, Rapporteur: Bart Van der Schueren, “Update of sections 4.2 and 5.1 of the Twinrix Paediatric SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 15 years after primary immunisation of adolescents, based on data from Phase IV study HAB-084 EXT Y11-15 (An open, long-term follow-up study to evaluate long-term antibody persistence and immune memory between 11 and 15 years after the primary study HAB-084). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to implement some minor editorial changes.”	
Verzenios - abemaciclib - EMEA/H/C/004302/II/0008 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC to include the results of the interim OS analysis from study MONARCH 2, a randomised, double-blind, placebo-controlled, phase 3 study of fulvestrant with or without abemaciclib, for women with hormone receptor positive, HER2 negative locally advanced or metastatic breast cancer.” Opinion adopted on 16.01.2020. Request for Supplementary Information adopted on 05.12.2019.	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0010 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, “Variation to add hypersensitivity reactions (including anaphylaxis) in sections 4.4 and 4.8 of the SmPC.”	
Xagrid - anagrelide - EMEA/H/C/000480/II/0086 Shire Pharmaceuticals Ireland Limited, Rapporteur: Alexandre Moreau, “Update of section 4.8 of the SmPC to include the adverse drug reaction Prinzmetal angina with a	

frequency not known. The PIL is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes throughout the product information."
Request for Supplementary Information adopted on 21.11.2019.

Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0014, Orphan
Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.2 and 5.2 of the SmPC following final results from study LX1606-111; this is a Phase 1, open-label, parallel-group study to evaluate the single-dose pharmacokinetics of Telotristat Ethyl in Male and Female Subjects with Severe Hepatic Impairment and Matched Subjects with Normal Function; the Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 14.11.2019, 19.09.2019, 11.07.2019.

Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0020/G, Orphan
Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.5 and 5.2 of the SmPC to update the information on the interaction with Carboxylesterases 2 inhibitors based on final results from the non-clinical study IPS000610; the Package Leaflet is updated accordingly. Additionally, the final study reports are submitted from studies XT173065, XT175092 and XT174037, with no subsequent changes to the PI. The MAH took the opportunity to update the PI to the latest QRD template v10.1."

Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0049
Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "To add a warning pertaining to severe cutaneous adverse reactions (SCARs) and beta-lactam antibiotics in section 4.4 of the ceftaroline fosamil/Zinforo SmPC, as a result of a summary safety review being published by Health Canada regarding beta-lactam antibiotics and the potential risk of severe skin side effects. The PL is proposed to be updated accordingly."

WS1689
Leganto-EMEA/H/C/002380/WS1689/0031
Neupro-EMEA/H/C/000626/WS1689/0085
UCB Pharma S.A., Lead Rapporteur: Bruno

Sepodes, "Update of section 4.8 of the SmPC in order to include "Rhabdomyolysis" as undesirable effect with frequency "not known" and widen the scope of an existing undesirable effect "increased CPK" based on new pharmacovigilance data. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant took the opportunity to correct some minor editorial discrepancies found within the package leaflets of Germany, Italy, France and Sweden." Request for Supplementary Information adopted on 28.11.2019.	
WS1701 **Epclusa-EMEA/H/C/004210/WS1701/0040** **Vosevi-EMEA/H/C/004350/WS1701/0032** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add new safety information on rash and angioedema following a cumulative review of hypersensitivity with Epclusa and Vosevi, prompted by routine pharmacovigilance and signal detection activities. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes throughout the Product Information." Request for Supplementary Information adopted on 14.11.2019.	
WS1727 **Januvia-EMEA/H/C/000722/WS1727/0068** **Ristaben-EMEA/H/C/001234/WS1727/0060** **TESAVEL-EMEA/H/C/000910/WS1727/0068** **Xelevia-EMEA/H/C/000762/WS1727/0072** Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, "Update of the SmPC sections 4.2, 4.8, 5.1 and 5.2, to include the data from paediatric study P083 (EMEA-000470-PIP01-08-M11)."	
WS1743 **Komboglyze-EMEA/H/C/002059/WS1743/0047** **Onglyza-EMEA/H/C/001039/WS1743/0049** **Qtern-EMEA/H/C/004057/WS1743/0026**	

AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a new warning about Bullous pemphigoid and section 4.8 of the SmPC to include Bullous pemphigoid as a new ADR with a frequency of 'Not known'. The Package Leaflet has been updated accordingly."	
WS1750 **Levitra-EMEA/H/C/000475/WS1750/0066** **Vivanza-EMEA/H/C/000488/WS1750/0062** Bayer AG, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.3 (contraindications) and section 4.5 (Interaction with other medicinal products and other forms of interaction) of the vardenafil SmPCs and relevant sections of the PILs to expand the information regarding vardenafil interactions with P-glycoprotein (P-gp) and cytochrome P450 (CYP) as a result of a general review of vardenafil pharmacokinetic properties." Request for Supplementary Information adopted on 16.01.2020.	Request for supplementary information adopted with a specific timetable.

B.5.3. CHMP-PRAC assessed procedures

Avastin - bevacizumab - EMEA/H/C/000582/II/0110 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study NEJ026 listed as an obligation in the Annex II of the Product Information. This is an open-label, randomized, Phase III study conducted in Japan to compare erlotinib + bevacizumab combination therapy versus erlotinib monotherapy as first-line therapies for patients with NSCLC with EGFR gene mutations (exon 19 deletion or exon 21 L858R substitution). The RMP version 30.0 has also been submitted. In addition, the Package leaflet is updated to reflect information on sodium content in compliance with the revised Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use". Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.	

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0084/G UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information following the final results from studies PS0002 (CIMPASI-2), PS0003 (CIMPACT) and PS0005 (CIMPASI-1) listed as category 3 studies in the RMP; these are results from the open label treatment periods assessing the safety and efficacy of long term use of certolizumab pergola in psoriasis. The RMP version 16.0 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 10.1." Request for Supplementary Information adopted on 16.01.2020.	Request for supplementary information adopted with a specific timetable.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0113 Genzyme Europe BV, PRAC Rapporteur: Liana Gross-Martirosyan, "Submission of the final report from study listed as a category 3 study in the RMP. This is a postauthorisation study (AGALSC08994) on Fabrazyme (agalsidase beta) home infusion educational materials effectiveness evaluation: a survey of healthcare providers and patients / caregivers. The RMP version 2 has also been submitted accordingly and to comply with the Good Pharmacovigilance Practice (GVP) Module V Rev. 2 template and information on study (AGAL02603) and the Fabry Registry/Pregnancy Sub-registry (AGAL 19211)."	
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0043 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Update of section 4.5 of the SmPC in order to add immunogenicity data following the interim results from study Malaria-073 listed as a category 3 study in the RMP; this is a phase 3 randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix when administered as a primary vaccination schedule at 6, 7.5 and 9 months-of-age, with or without co-administration of	

measles and rubella and yellow fever vaccines, to children living in sub-Saharan Africa. The RMP version 5.1 has also been submitted. In addition, the Scientific opinion Holder (SOH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."	
Odomzo - sonidegib - EMEA/H/C/002839/II/0024 Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Željana Margan Koletić, "To submit the final report of study CLDE225X2116, listed as a category 3 study in the RMP. This is an interventional Phase Ib/II, open-label, multi-center, dose-finding study to assess the safety and efficacy of the oral combination of LDE225 and INC424 (Ruxolitinib) in subjects with myelofibrosis. The RMP version 7.1 has also been submitted." Request for Supplementary Information adopted on 31.10.2019.	
Ogivri - trastuzumab - EMEA/H/C/004916/II/0009 Mylan S.A.S, Rapporteur: Koenraad Norga, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final clinical study report (MYL-Her-3001) (a Multicenter, Double-blind, Randomized, Parallel-group, Phase III Study of the Efficacy and Safety of Hercules Plus Taxane Versus Herceptin Plus Taxane as First Line Therapy in Patients With HER2-Positive Metastatic Breast Cancer) with the final overall survival (OS). The RMP version 3 has also been submitted."	
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0049 Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald, "Updated of section 4.8 of the SmPC with the safety data from the Phase 3, open-label, rollover study for Studies 109 and 011 Part B (Study 011B) designed to evaluate the long-term safety and tolerability of Orkambi treatment for 96 weeks in patients with cystic fibrosis, 6 years of age and older, homozygous for F508del." Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.	See agenda item 9.1
Protopic - tacrolimus -	

EMEA/H/C/000374/II/0083/G LEO Pharma A/S, Rapporteur: Peter Kiely, PRAC Rapporteur: Rhea Fitzgerald, "Update of sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC following results from two non-interventional post-authorisation safety studies: JOELLE study (Joint European Longitudinal Lymphoma and skin cancer Evaluation, category 3) and APPLES study (a prospective pediatric longitudinal evaluation to assess the long-term safety of tacrolimus ointment for the treatment of atopic dermatitis, category 3). The Package Leaflet is updated accordingly. The RMP version 15.1. 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 10.1."	CHMP Request for PRAC Advice was adopted via written procedure on 7 January 2020. PRAC Advice for adoption via written procedure .
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0058 Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Submission of CSR of study 109MS310, an open-label study to assess the effects of Tecfidera on lymphocyte subsets in subjects with relapsing remitting multiple sclerosis, listed as category 3 study in the RMP. The RMP (version 10.1) has been updated as a consequence of the completion of this study. The revised RMP also includes updates to reflect safety information available through to the data lock point of 24 January 2019 and to align with the EU RMP Module V (revision 2.01)." Request for Supplementary Information adopted on 31.10.2019, 11.07.2019.	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0063 Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC to reflect PML in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly. Additionally, the Product Information has been updated in line with QRD template (version 10.1)." Request for Supplementary Information adopted on 19.09.2019.	
VIZAMYL - flutemetamol (18F) -	

EMEA/H/C/002557/II/0021

GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 5.1 of the SmPC in order to include information on the possibility of quantitative assessment. The evidence based submitted consists of published studies.
Submission of an updated RMP version 2.1 to introduce a new educational programme as a consequence of the changes above and to align with the new RMP template."

Zometa - zoledronic acid - EMEA/H/C/000336/II/0091

Novartis Europharm Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information on ONJ based on final results from study CZOL446EUS122 listed as a category 3 study in the RMP; this is a non-interventional, prospective, observational, multicenter cohort study to assess the incidence of ONJ in cancer patients with bone metastases starting zoledronic acid treatment.
The RMP version 12 has also been submitted."

WS1724
Blitzima-EMEA/H/C/004723/WS1724/0029
Ritemvia-EMEA/H/C/004725/WS1724/0029
Truxima-EMEA/H/C/004112/WS1724/0032

Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study CT-P10 3.3. This is a category 3 study, a Phase 1/3, randomised, parallel-group, active-controlled, double-blind study to demonstrate equivalence of pharmacokinetics and non-inferiority of efficacy for CT-P10 in comparison with Rituxan. Each Administered in Combination With Cyclophosphamide, Vincristine, and Prednisone (CVP) in Patients With Advanced Follicular Lymphoma. The RMP version 9.1 has also been submitted in order to align the safety concerns with those of MabThera and to incorporate the final results of Study CT-P10 3.3."

WS1756
Lixiana-EMEA/H/C/002629/WS1756/0025
Roteas-EMEA/H/C/004339/WS1756/0012
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Adrien Inoubli, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information based on final results from the post-authorisation efficacy study DU176b-C-E314 (Evaluation of Edoxaban in Anticoagulant Naïve Patients with Non-Valvular Atrial Fibrillation [NVAF] and High Creatinine Clearance [protocol MEA004]). This is a study to compare the exposure of edoxaban 75 mg once daily dose to edoxaban 60 mg once daily dose in NVAF anticoagulant-naïve patients with CHADS2 score of ≥2 and CrCL >100 mL/min treated for up to 12 months. The RMP version 9.0 has also been submitted. In addition, the worksharing applicant took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1 and to provide updates due to corrections of typos in several language versions of the Product Information."

B.5.4. PRAC assessed procedures

PRAC Led
AUBAGIO - teriflunomide -
EMEA/H/C/002514/II/0025
sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the patients and HCPs final survey reports to assess the effectiveness of the education materials; the survey reports are part of the additional pharmacovigilance activities in the RMP (category 3 studies).
The RMP (version 5.1) is updated including the alignment to the new template in line with GVP module V Rev.2, to postpone the final report submission of studies OBS12753, EFC11759 and OBS13499, and to update the risk minimisation measures by refining the messages of the educational materials (patient card and HCP Guide) in order to improve clarity and revise the list of safety concerns, updates in the HCP Guide, addition of renal failure as safety concern addressed in the LTS OBS12753 PASS. Relevant

modules (Parts II SVII, Part II SVIII, Part III, Part V, Part VI and Part VII) have been updated accordingly.
Annex IID of the product information is updated to add key elements for HCP educational material."
Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.

PRAC Led

BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0034/G, Orphan

Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, PRAC-CHMP liaison: Ondřej Slanař, "Submission of the final reports from studies 20150163 and 20150228 assessed the effectiveness of Blincyto additional risk minimization measures for healthcare professionals (study 20150163) and patients/caregivers (study 20150228) listed as a category 3 post-authorization safety studies (PASS) in the Risk Management Plan (RMP)."

PRAC Led

Daxas - roflumilast - EMEA/H/C/001179/II/0038

AstraZeneca AB, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Amendment of safety concerns and removal of additional risk minimisation measures. Minor changes are implemented in section 4.4 of SmPC and PL according to QRD template."
Request for Supplementary Information adopted on 28.11.2019.

PRAC Led

Docetaxel Zentiva - docetaxel - EMEA/H/C/000808/II/0061

Zentiva, k.s., Informed Consent of Taxotere, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 1.1 in order to revise the list of safety concerns in line with the GVP Module V Rev.2 and to complete Part II modules."

PRAC Led

Edurant - rilpivirine - EMEA/H/C/002264/II/0037

Janssen-Cilag International NV, PRAC

Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from a Drug Utilization Study (DUS), with register number EUPAS5766, in the EuroSIDA cohort listed as a category 3 study in the RMP. This is an Observational Cohort Study to assess rilpivirine (RPV) utilization according to the European SmPC. The RMP version 9.0 has also been submitted. With the submission of this study report, MEA 011.1 is considered fulfilled. The requested variation proposed amendments to the Risk Management Plan (RMP)." Request for Supplementary Information adopted on 03.10.2019.	
PRAC Led **EXJADE - deferasirox - EMEA/H/C/000670/II/0068** Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report related to the Physician Survey (NO6987) conducted for Exjade to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate used of both formulations (Dispersible Tablets and Film-Coated tablets). The updated RMP version 17.1 is submitted as well." Request for Supplementary Information adopted on 16.01.2020, 03.10.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Glivec - imatinib - EMEA/H/C/000406/II/0115** Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 12 in order to revise the lists of safety concerns in EU RMP and align with the current GVP Rev 2 based on the PRAC advice received on the latest PSUR (11-May-2015 to 10-May-2018)." Request for Supplementary Information adopted on 03.10.2019.	
PRAC Led	

GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0147 Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of RMP version 2.1 in order to: - update as per GVP module V, rev 2.0.1 template; - remove important identified risks of "Ovarian hyperstimulation syndrome (OHSS)", "Thromboembolic events usually with OHSS", "Hypersensitivity reactions, including anaphylactic reactions", "Asthma aggravated/exacerbation", "Multiple pregnancies" and "Gynecomastia in males"; - remove the important potential risks of "Breast cancer", "Other reproductive system cancers", "Ectopic pregnancy" and "Congenital abnormalities"; - increase the age from 40 to 42 years for the missing information of "Women older than 40 years"."	
PRAC Led **Kisplyx - lenvatinib - EMEA/H/C/004224/II/0030** Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.3 to reflect changes related to the category 3 study E7080-G000-307. The protocol for study E7080-G000-307 has been updated to version 06, dated 10 September 2019, to include an interim analysis for profession-free survival and overall survival and the due dates for the interim and final analysis have been adjusted." Request for Supplementary Information adopted on 28.11.2019.	
PRAC Led **Nulojix - belatacept - EMEA/H/C/002098/II/0063/G** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from studies IM103075 and IM103076 listed as category 3 studies in the RMP. Study IM103075 is a prospective cohort study to assess the association between belatacept use and risk of	Request for supplementary information adopted with a specific timetable.

post-transplant lymphoproliferative disorder (PTLD) in renal transplant recipients in the United States (US). IM103076 is a prospective patient registry study to estimate the incidence rates of confirmed PTLD, CNS PTLD and progressive multifocal leukoencephalopathy (PML) in adult renal transplant recipients treated with belatacept in the US. The RMP version 17.0 has also been submitted to reflect the completion of both studies and to make some administrative updates."
Request for Supplementary Information adopted on 16.01.2020.

PRAC Led
Ozurdex - dexamethasone - EMEA/H/C/001140/II/0037
Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 9.0 in order to reflect increased knowledge of the product and align to the new RMP template."

PRAC Led
Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0066
Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Mark Ainsworth, "Submission of an updated RMP version 5.3 in order to:

- adapt to the RMP template as per Good Pharmacovigilance Practice (GVP) Module V, rev 2
- remove the important identified risks of "Ovarian Hyperstimulation Syndrome (OHSS)", "Thromboembolic events, usually with OHSS" and "Hypersensitivity reactions"
- remove the important potential risks of "Breast cancer", "Ovarian cancer", Endometrial cancer", "Congenital anomalies" and "Malignant melanoma""

PRAC Led
Praluent - alirocumab - EMEA/H/C/003882/II/0050/G
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated

RMP version 5.0 in order to amend the list of safety concerns (removing 'cataract (in the context of very low LDL-C)' as important potential risk; 'long-term use (>5 years)' and 'clinical impact of very low LDL-C for extended period of time' as missing information; and consequentially to remove the following additional Pharmacovigilance activities (category 3 studies in the RMP) from the RMP: study R727-CL-1609 (MEA 016), study OBS14697 (MEA 019) and study ALIROC07997 (MEA 017) based on a review of data since the MA was granted including the 1st interim report for study OBS14697, a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low LDL-C levels, in order to fulfil MEA 019.4." Request for Supplementary Information adopted on 31.10.2019.	
PRAC Led **Revestive - teduglutide - EMEA/H/C/002345/II/0050, Orphan** Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 9 in order to update the list of safety concers."	
PRAC Led **Taxotere - docetaxel - EMEA/H/C/000073/II/0134** Aventis Pharma S.A., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 1.1 in order to revise the list of safety concerns in line with the GVP Module V Rev.2 and to complete Part II modules."	
PRAC Led **Torisel - temsirolimus - EMEA/H/C/000799/II/0078** Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 4.0 in order to remove the safety concerns: "missing information", "risk of cardiovascular events in patients with coexisting cardiovascular conditions", "reproductive	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

toxicity" from the RMP and to comply with the Module V, Risk Management Systems Rev 2 (as requested through EMEA/H/C/PSUSA/00002887/201803)." Opinion adopted on 16.01.2020.	
PRAC Led **WS1653** **Enbrel-EMEA/H/C/000262/WS1653/0230** **LIFMIOR-EMEA/H/C/004167/WS1653/0024** Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR, also referred as study B1801309) listed as a category 3 study in the RMP. This is a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety." Request for Supplementary Information adopted on 16.01.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1655** **Aerius-EMEA/H/C/000313/WS1655/0091** **Azomyr-EMEA/H/C/000310/WS1655/0095** **Neoclarityn-EMEA/H/C/000314/WS1655/0089** Merck Sharp & Dohme B.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Koenraad Norga, Lead PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "C.I.13: Submission of the final report from study (EUPAS15038) listed as a category 3 study in the RMP. This is a non-interventional non-imposed PASS study designed to assess the potential risk of desloratadine exposure on seizures, supraventricular tachycardia, and atrial fibrillation or flutter." Request for Supplementary Information adopted on 05.09.2019.	
PRAC Led **WS1713** **Kivexa-EMEA/H/C/000581/WS1713/0083** **Triumeq-EMEA/H/C/002754/WS1713/**	

0075
Trizivir-EMEA/H/C/000338/WS1713/0115
Ziagen-EMEA/H/C/000252/WS1713/0109
ViiV Healthcare B.V., Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "Submission of updated RMPs in order to remove the additional risk minimisation measure of provision of abacavir hypersensitivity education materials for healthcare professionals. Annex II is updated accordingly."

PRAC Led
WS1748
Lacosamide UCB-EMEA/H/C/005243/WS1748/0003
Vimpat-EMEA/H/C/000863/WS1748/0085
UCB Pharma S.A., Lead PRAC Rapporteur: Ulla Wändel Liminga, "To provide an updated RMP to propose changes of due dates for three category 3 studies as follows:
- SP848 due date change from 'Nov2021' to 'Dec2021';
- EP0012 due date change from 'Nov2022' to 'Dec2022';
- EP0034 due date change from 'May2024' to 'Aug2024';
Amended protocols for the studies SP848 and EP0034 in Annex 3 have also been provided."

PRAC Led
WS1755
Cymbalta-EMEA/H/C/000572/WS1755/0083
Duloxetine Lilly-EMEA/H/C/004000/WS1755/0020
Xeristar-EMEA/H/C/000573/WS1755/0086
Yentreve-EMEA/H/C/000545/WS1755/0068
Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "As agreed in the procedure WS-1527G in order to address the foetal outcomes, submission of the final report from study FIJ-MC-B059 'Observational Study to Assess Fetal Outcomes Following Maternal Exposure to Duloxetine' and the revised final report from study Study F1J-MC-B057 'Observational Studies to Assess Maternal and

Fetal Outcomes Following Exposure to Duloxetine'."

PRAC Led
WS1760
Lixiana-EMEA/H/C/002629/WS1760/0024
Roteas-EMEA/H/C/004339/WS1760/0011
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final study report from study ETNA-DUS: a retrospective drug utilisation chart review study listed as a category 3 study in the RMP. The Edoxaban Treatment in Routine Clinical Practice Drug Utilisation Study (ETNA-DUS) was designed to gain insight on how edoxaban is used in real practice. The ETNA-DUS intends to help identify prescription patterns and the effectiveness of the educational programs"

B.5.5. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0014, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Request for Supplementary Information adopted on 08.11.2019.

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0017/G, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

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

WS1659/G
Silodosin Recordati-EMEA/H/C/004964/ WS1659/0001/G
Silodyx-EMEA/H/C/001209/WS1659/ 0036/G
Urorec-EMEA/H/C/001092/WS1659/

0039/G Recordati Ireland Ltd, Lead Rapporteur: Daniela MelchiorriRequest for Supplementary Information adopted on 19.09.2019.	
WS1696/G **Glyxambi-EMEA/H/C/003833/WS1696/0025/G** **Jentadueto-EMEA/H/C/002279/WS1696/0053/G** **Trajenta-EMEA/H/C/002110/WS1696/0040/G** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 16.01.2020.	Positive Opinion adopted by consensus on 16.01.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1698/G **Genvoya-EMEA/H/C/004042/WS1698/0066/G** **Stribild-EMEA/H/C/002574/WS1698/0109/G** **Tybost-EMEA/H/C/002572/WS1698/0052/G** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes,	
WS1699 **Hexacima-EMEA/H/C/002702/WS1699/0093** **Hexaxim-EMEA/H/W/002495/WS1699/0098** **Hexyon-EMEA/H/C/002796/WS1699/0097** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	
WS1703/G **Advagraf-EMEA/H/C/000712/WS1703/0055/G** **Modigraf-EMEA/H/C/000954/WS1703/0034/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe	
WS1715/G **Ebymect-EMEA/H/C/004162/WS1715/0041/G** **Xigduo-EMEA/H/C/002672/WS1715/0052/G** AstraZeneca AB, Lead Rapporteur: Kristina Dunder	
WS1719	

Zalviso-EMEA/H/C/002784/WS1719/0014
Grunenthal GmbH, Lead Rapporteur: Milena Stain, "To update section 4.4 of the SmPC in order to include new prescribing information on other side effects including central sleep apnea (CSA) and drug interactions following a Drug Safety Communication by FDA on 9 April 2019. Section 2 of the Package Leaflet has been updated accordingly."

WS1723
Advate-EMEA/H/C/000520/WS1723/0103
ADYNOVI-EMEA/H/C/004195/WS1723/0009
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1725
Infanrix hexa-EMEA/H/C/000296/WS1725/0267
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1730/G
Filgrastim Hexal-EMEA/H/C/000918/WS1730/0053/G
Zarzio-EMEA/H/C/000917/WS1730/0054/G
Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1741
Revatio-EMEA/H/C/000638/WS1741/0087
Viagra-EMEA/H/C/000202/WS1741/0103
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege

WS1752
Nuwiq-EMEA/H/C/002813/WS1752/0034
Vihuma-EMEA/H/C/004459/WS1752/0016
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1753/G
Prezista-EMEA/H/C/000707/WS1753/0103/G
Rezolsta-EMEA/H/C/002819/WS1753/0036/G
Symtuza-EMEA/H/C/004391/WS1753/0022/G
Janssen-Cilag International NV, Lead

Rapporteur: Johann Lodewijk Hillege

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

MabThera - rituximab - EMEA/H/C/000165/II/0165 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Change in the posology section as 8 cycles of MabThera should be used in combination with 6-8 (previously 8) cycles of CHOP chemotherapy." Request for Supplementary Information adopted on 17.10.2019, 25.07.2019. Withdrawal request submitted on 08.01.2020.	The MAH withdrew the procedure on 08.01.2020.

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

CRYSVITA - burosumab - EMEA/H/C/004275/II/0007/G, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 21.11.2019, 12.09.2019.	Request for an extension to the clock-stop to respond to the Request for Supplementary Information adopted on 21.11.2019 - adopted via written procedure on 15.01.2019.
WS1700/G Humalog-EMEA/H/C/000088/WS1700/0180/G Liprolog-EMEA/H/C/000393/WS1700/0141/G Eli Lilly Nederland B.V., Informed Consent of Humalog, Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 14.11.2019, 24.10.2019.	Request for an extension to the clock-stop – for adoption via written procedure .

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

remimazolam - EMEA/H/C/005246 indicated for procedural sedation
duvelisib - EMEA/H/C/005381, Orphan Verastem Europe GmbH, Treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) and relapsed or refractory follicular lymphoma (FL)
glucagon - EMEA/H/C/005391 for the treatment of severe hypoglycaemia in

adults, adolescents, and children aged 2 years and over with diabetes mellitus	
istradefylline - EMEA/H/C/005308 indicated as an adjunctive treatment to levodopa-based regimens in patients with Parkinson's disease	
azathioprine - EMEA/H/C/005055 indicated for the prophylaxis of transplant rejection, and an immunosuppressant antimetabolite, indicated in patients who are intolerant to glucocorticosteroids, and chronic inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), relapsing multiple sclerosis, generalised myasthenia gravis	
moxetumomab pasudotox - EMEA/H/C/005322, Orphan AstraZeneca AB, relapsed or refractory hairy cell leukaemia (HCL) after receiving at least two prior systemic therapies	
pemigatinib - EMEA/H/C/005266, Orphan Incyte Biosciences Distribution B.V., treatment of locally advanced or metastatic cholangiocarcinoma	
netarsudil / latanoprost - EMEA/H/C/005107 reduction of elevated intraocular pressure	
valoctocogene roxaparvovec - EMEA/H/C/004749, Orphan, ATMP BioMarin International Limited, treatment of haemophilia A	**Accelerated review**

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

SIRTURO - bedaquiline - EMEA/H/C/002614/X/0036/G, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength (20 mg tablets) grouped with a type II variation (C.I.6) to extend the existing SIRTURO indication to include paediatric patients aged from 5 years to less than 18 years of age and weighing more than 15 kg, based on the results of the Week 24 analysis of Cohort 2 (paediatric subjects aged ≥5 to <12 years) of Study TMC207-C211. Sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 and the Product Leaflet are updated to	

support the extended indication. The RMP (version 4.4) is updated in accordance."

Ultomiris - ravulizumab - EMEA/H/C/004954/X/0004/G

Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Agnes Gyurasics"Extension application to add a new strength (1100 mg in 11 ml vial, concentration 100 mg/ml) for Ultomiris concentrate for solution for infusion, grouped with a Type II application (B.II.z) for a new presentation (300 mg in 3 ml vial, concentration 100 mg/ml) "

Xarelto - rivaroxaban - EMEA/H/C/000944/X/0074/G

Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to introduce a new pharmaceutical form, granules for oral suspension, 1 mg/ml. Extension of indication to include treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children, and adolescents aged less than 18 years following initiation of standard anticoagulation treatment for Xarelto 15 and 20 mg tablets.
As a consequence, sections 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly.
In addition, sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC is updated for all other dose strengths (2.5/10/ and 15/20 mg initiation packs) of Xarelto and corresponding sections of the Package Leaflet. Section 4.4 has been updated with regards to sodium content according to Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668).
The RMP version 12.1 has also been submitted."

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

cabazitaxel - EMEA/H/C/005178

treatment of adult patients with metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen
List of Questions adopted on 19.09.2019.

glasdegib - EMEA/H/C/004878, Orphan

Pfizer Europe MA EEIG, treatment of newly diagnosed de novo or secondary acute myeloid leukaemia
List of Questions adopted on 19.09.2019.

fingolimod - EMEA/H/C/005191
treatment of multiple sclerosis
List of Questions adopted on 19.09.2019.

fingolimod - EMEA/H/C/005282
treatment of multiple sclerosis
List of Questions adopted on 19.09.2019.

Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/X/0081/G
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Extension application to introduce a new strength (45/200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (33.75/150 and 45/200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 90/400 mg film-coated tablets. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information."
List of Questions adopted on 17.10.2019.

imlifidase - EMEA/H/C/004849, Orphan
Hansa Biopharma AB, indicated for desensitization treatment of highly sensitized adult kidney transplant patients with positive crossmatch against an available deceased donor
List of Questions adopted on 27.06.2019.

insulin aspart - EMEA/H/C/005033
treatment of diabetes mellitus
List of Questions adopted on 17.10.2019.

teriparatide - EMEA/H/C/005087
treatment of osteoporosis
List of Questions adopted on 19.09.2019.

teriparatide - EMEA/H/C/005388
treatment of osteoporosis

List of Questions adopted on 19.09.2019.

luspatercept - EMEA/H/C/004444, Orphan
Celgene Europe BV, - treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anaemia; - the treatment of adult patients with beta-thalassaemia (β-thalassaemia)-associated anaemia who require RBC transfusions.
List of Questions adopted on 19.09.2019.

Sovaldi - sofosbuvir - EMEA/H/C/002798/X/0059/G
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Extension application to introduce a new strength (200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (150 and 200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to < 12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 400 mg film-coated tablets.
The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information."
List of Questions adopted on 17.10.2019.

Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/X/0042
Indivior Europe Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5, 4/1, 8/2, and 16/4 mg) and a new route of administration (either sublingual or buccal administration)"
List of Questions adopted on 25.07.2019.

ivosidenib - EMEA/H/C/005056, Orphan
Agios Netherlands B.V., Treatment of adult patients (≥ 18 years old) with relapsed or refractory acute myeloid leukaemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation

List of Questions adopted on 29.05.2019.

bupivacaine / meloxicam - EMEA/H/C/005205
for application into the surgical site to reduce postoperative pain for application into the surgical site to reduce postoperative pain
List of Questions adopted on 25.07.2019.

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

Kolbam - cholic acid - EMEA/H/C/002081/S/0031, Orphan
Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Agni Kapou

Vyndaqel - tafamidis - EMEA/H/C/002294/S/0055, Orphan
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ghania Chamouni

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

Aripiprazole Sandoz - aripiprazole - EMEA/H/C/004008/R/0014
Sandoz GmbH, Generic, Generic of Abilify, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins

Brinavess - vernakalant - EMEA/H/C/001215/R/0037
Correvio, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst

Cresemba - isavuconazole - EMEA/H/C/002734/R/0027, Orphan
Basilea Pharmaceutica Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Adam Przybylkowski

Duloxetine Zentiva - duloxetine - EMEA/H/C/003935/R/0009
Zentiva k.s., Generic, Generic of Cymbalta, Yentreve, Rapporteur: Kristina Dunder, PRAC Rapporteur: Maria del Pilar Rayon

Fexeric (EXP) - ferric citrate coordination complex - EMEA/H/C/003776/R/0016
Akebia Europe Limited c/o Matheson,

See agenda item 9.1

Rapporteur: Romaldas Mačiulaitis, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Kimmo Jaakkola

Intuniv - guanfacine - EMEA/H/C/003759/R/0022
Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Maria del Pilar Rayon

Pemetrexed Lilly - pemetrexed - EMEA/H/C/004114/R/0011
Eli Lilly Nederland B.V., Generic, Generic of Alimta, Rapporteur: Alar Irs, PRAC Rapporteur: Ghania Chamouni

Praluent - alirocumab - EMEA/H/C/003882/R/0055
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Brigitte Keller-Stanislawski

Pregabalin Accord - pregabalin - EMEA/H/C/004024/R/0015
Accord Healthcare S.L.U., Generic, Generic of Lyrica, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Liana Gross-Martirosyan

Raxone - idebenone - EMEA/H/C/003834/R/0020, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Amelia Cupelli

VPRIV - velaglucerase alfa - EMEA/H/C/001249/R/0045, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

Zalviso - sufentanil - EMEA/H/C/002784/R/0016
Grunenthal GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Adam Przybylkowski

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

Latuda - lurasidone -

EMEA/H/C/002713/II/0029
Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of indication for the treatment of schizophrenia in adolescent from 13 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) takes the opportunity to update the PI according to the excipient guideline and update the list of local representatives in the Package Leaflet. The RMP version 8 has also been submitted."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Lynparza - olaparib - EMEA/H/C/003726/II/0035
AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include the use of Lynparza tablets in combination with bevacizumab for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy with bevacizumab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. The PL is updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza hard capsules are revised based on updated safety data analysis.
Furthermore, the PI is brought in line with the latest QRD template version 10.1. The RMP version 19 has also been submitted."

Lynparza - olaparib - EMEA/H/C/003726/II/0036
AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include the use of Lynparza tablets as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene mutations (germline and/or

somatic) who have progressed following a prior new hormonal agent. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The PL is updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza hard capsules are revised based on updated safety data analysis.
The RMP version 20 has also been submitted."

Olumiant - baricitinib - EMEA/H/C/004085/II/0016

Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Adam Przybylkowski, "Extension of indication to include a new indication in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated.
The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Minor editorial changes were brought to the Labelling. Furthermore, the Annex II is brought in line with the latest QRD template version 10.1.
The RMP version 8.1 has also been submitted."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0033

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to include the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumours express PD-L1 for Tecentriq based on the results of the pivotal study GO29431 (IMpower110), comparing atezolizumab monotherapy to platinum-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adenuric - febuxostat -
EMEA/H/C/000777/II/0056
Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop

Alprolix - eftrenonacog alfa -
EMEA/H/C/004142/II/0028, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop

Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) -
EMEA/H/C/002333/II/0087
GSK Vaccines S.r.l, Rapporteur: Kristina Dunder

Buvidal - buprenorphine -
EMEA/H/C/004651/II/0005
Camurus AB, Rapporteur: Peter Kiely

Cometriq - cabozantinib -
EMEA/H/C/002640/II/0037, Orphan
Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik

Erelzi - etanercept -
EMEA/H/C/004192/II/0024/G
Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege

Hizentra - human normal immunoglobulin -
EMEA/H/C/002127/II/0112/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

HyQvia - human normal immunoglobulin -
EMEA/H/C/002491/II/0054
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus

ILARIS - canakinumab -
EMEA/H/C/001109/II/0068/G
Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus

Myozyme - alglucosidase alfa -
EMEA/H/C/000636/II/0080/G
Genzyme Europe BV, Co-Rapporteur: Koenraad Norga

Nulojix - belatacept -
EMEA/H/C/002098/II/0065/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson

Ogivri - trastuzumab -
EMEA/H/C/004916/II/0011/G
Mylan S.A.S, Rapporteur: Koenraad Norga

Omnitrope - somatropin -
EMEA/H/C/000607/II/0062/G
Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege

Ovaleap - follitropin alfa -
EMEA/H/C/002608/II/0032
Theramex Ireland Limited, Rapporteur: Paula Boudewina van Hennik

Ozempic - semaglutide -
EMEA/H/C/004174/II/0011
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege

Remicade - infliximab -
EMEA/H/C/000240/II/0225/G
Janssen Biologics B.V., Rapporteur: Kristina Dunder

Remsima - infliximab -
EMEA/H/C/002576/II/0080/G
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola

RoActemra - tocilizumab -
EMEA/H/C/000955/II/0093/G
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

Rotarix - rotavirus vaccine (live, oral) -
EMEA/H/C/000639/II/0116/G
GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren

Skilarence - dimethyl fumarate -
EMEA/H/C/002157/II/0019
Almirall S.A, Rapporteur: Janet Koenig

TAKHZYRO - lanadelumab -
EMEA/H/C/004806/II/0012/G, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder

WS1758
Infanrix hexa-
EMEA/H/C/000296/WS1758/0270
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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

Cablivi - caplacizumab - EMEA/H/C/004426/II/0021, Orphan
Ablynx NV, Rapporteur: Filip Josephson, "Submission of the results of the study ALX-0681-MS-01, a Modelling/Simulation study performed for the paediatric population as part of the approved Paediatric Investigation Plan (EMEA-001157-PIP-01-11-M02) for Cablivi"

Cometriq - cabozantinib - EMEA/H/C/002640/II/0036, Orphan
Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Submission of PK results from the clinical study ADVL1211 (an open-label trial to evaluate toxicity, tolerability, pharmacokinetics and pharmacodynamics of cabozantinib in children with refractory or relapsed malignant solid tumours (MEA 019))."

Darzalex - daratumumab - EMEA/H/C/004077/II/0035, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4 - Update of section 5.1 of the SmPC in order to update efficacy information based on interim results from phase III studies of 3 approved combination treatments of daratumab (D) in relapsed or refractory MM patients MMY3003 (DRd vs Rd) and MMY3004 (DVd vs Vd) and in newly diagnosed MM patients MMY3007 (DVd vs Vd). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet ."

Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0007/G
Sanofi Pasteur, Rapporteur: Bart Van der Schueren, "C.I.13: Submission of the final report from studies CYD63 and CYD64 listed as a category 3 study in the RMP. These are booster studies to evaluate the safety and immunogenicity of a booster dose of dengue vaccine administered in a subset of subjects who received third dose of dengue vaccine 4-5 years before, in Phase II studies."

Dovato - dolutegravir / lamivudine - EMEA/H/C/004909/II/0008
ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC

in order to update the safety and efficacy information following the week 48 results from TANGO study (204862); TANGO (204862) is an on-going 200-week, Phase III, randomized, open-label, active controlled, multicenter, parallel-group study, evaluating the efficacy, safety, and tolerability of switching to Dovato in HIV-1 infected adults who are virologically suppressed. The RMP version has not been submitted."	
Dovato - dolutegravir / lamivudine - EMEA/H/C/004909/II/0009 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 5.1 in order to update the safety and efficacy following the week 96 results from 204861 (GEMINI-1) and 205543 (GEMINI-2) studies listed as a specific category 3 study in the RMP; these are two identical pivotal ongoing, randomized, double-blind, parallel group, 148-week, phase III studies to evaluate the efficacy, safety, and tolerability of dolutegravir plus 3TC compared to dolutegravir plus tenofovir/emtricitabine in HIV-1-infected treatment naïve patients. The RMP version has not been submitted."	
Feraccru - ferric maltol - EMEA/H/C/002733/II/0024 Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "To update sections 4.4 and 5.1 of the SmPC in order to update safety and efficacy information based on final results from study ST 10-01-304 this is a phase 3b, randomized, controlled, multicentre study with oral ferric maltol (Feraccru) or intravenous iron (ferric carboxymaltose; FCM), for the treatment of iron deficiency anaemia in subjects with inflammatory bowel disease."	
Fexinidazole Winthrop - fexinidazole - EMEA/H/W/002320/II/0002 sanofi-aventis groupe, Rapporteur: Fátima Ventura, "Update of section 4.5 of the SmPC with data on pharmacokinetic interactions, based on results obtained from five in vitro pharmacokinetics study reports and the Drug Drug Interaction phase I study (INT15307), the latter mentioned in the RMP as "other study" in post-opinion development plan ."	
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0084, Orphan	

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC in order to include the information based on results from study VX14-661-110, which is a Phase 3, multicenter, open label, rollover study for Studies 103, 106, 107, 108, 109, 111, 112, and 114 designed to evaluate the long-term safety and tolerability of TEZ/IVA treatment in combination with ivacaftor for 96 weeks in cystic fibrosis (CF) subjects 12 years and older, homozygous or heterozygous for the F508del CFTR mutation."

Kisqali - ribociclib - EMEA/H/C/004213/II/0020

Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and include safety information on toxic epidermal necrolysis. The Package Leaflet is updated accordingly."

Kisqali - ribociclib - EMEA/H/C/004213/II/0022

Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on the final OS analysis from study CLEE011F2301 (MONALEESA-3), a randomised double-blind, placebo-controlled, multicentre phase III clinical study in the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer who had received no or only one line of prior endocrine treatment, in combination with fulvestrant versus fulvestrant alone."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0031

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Submission of the final report from the Phase 3b study M16-156 (A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir GLE)/Pibrentasvir (PIB) in Treatment-Naïve Adults in Brazil with Chronic Hepatitis C Virus (HCV) Genotype 1 – 6 Infection)."

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0123

Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, "Update of section 4.8 of the SmPC in order to update the safety information regarding neutropenia and

agranulocytosis following update to the Pradaxa Company Core Data Sheet. The Package Leaflet are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make Minor Linguistic Changes to the several language versions of the Product Information."

Pravafenix - fenofibrate / pravastatin sodium - EMEA/H/C/001243/II/0028/G

Laboratoires SMB s.a., Rapporteur: Jean-Michel Race, "Grouping of variations following a request from PRAC as part of PSUSA/00001363/201804:
- Update of section 4.8 of the SmPC to add 'dermatomyosis', 'lichenoid eruption' and 'erythematous lupus syndrome' as new adverse drug reactions.
- Update of sections 4.4 and 4.5 of the SmPC to include a new warning regarding the concomitant use with glecaprevir/pibrentasvir
- Update of sections 4.4 and 4.5 of the SmPC to amend the current warning regarding co-administration with fusidic acid and the risk of rhabdomyolysis.
The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include 'hepatitis' as an adverse drug reaction in section 4.8 of the SmPC as it is already included in section 4 of the Package Leaflet and to bring the PI in line with version 10 and 10.1 of the QRD template."

Qutenza - capsaicin - EMEA/H/C/000909/II/0049

Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to update the safety information on adverse reactions frequencies based on latest clinical data pooling; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version."

RoActemra - tocilizumab - EMEA/H/C/000955/II/0091

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for RoActemra 162 mg solution for injection in pre-filled pen in order to align with the approved

indications for RoActemra 162 mg solution for injection in pre-filled syringe to include active systemic juvenile idiopathic arthritis (sJIA) and juvenile idiopathic polyarthritis; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder took the opportunity to make minor editorial changes in sections 3, 4.2, 4.4 and 5.1 of the SmPC for RoActemra 162 mg solution for injection in pre-filled syringe and the Annex II.”	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0021 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, “C.I.13: Submission of the final report from studyZoster-063, listed as a category 3 study in the RMP version 2.0. The study was conducted to investigate the impact of reactogenicity on health-related quality of life in subjects ≥50 YOA following Shingrix vaccination.”	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0008 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely, “Update of SmPC 5.1 'Pharmacodynamic Properties' of the Skyrizi SmPC. The change pertains to the addition of information on retreatment after withdrawal of risankizumab to the summary of the IMMhance clinical study (M15-992).”	
SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0040 Bracco International B.V., Rapporteur: Alexandre Moreau, “Update of annex II.D to amend the description and due date of study BR1-145 (ANX 002), an observational study of SonoVue/Lumason- enhanced urosonography in paediatric subjects with known or suspected vesicoureteral reflux to assess subject management decision and changes during a follow-up period of at least 12-months among children undergoing SonoVue/Lumason-enhanced Voiding Urosonography (VUS) (VUS group) in comparison with children undergoing Voiding cystourethrography (VCUG) (VCUG group) for assessment of VUR, following the adoption of the final draft protocol by CHMP. In addition, the Marketing authorisation holder	

(MAH) took the opportunity to implement some formatting changes (hyperlink on Appendix V) in the SmPC and in the Package Leaflet."

SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0041

Bracco International B.V., Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC to add 'Kounis syndrome' as a new adverse drug reaction based on a review of post-marketing cases and of the literature. The Package Leaflet is updated accordingly."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0032

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4 and 4.8 of the SmPC in order to include erythema multiforme as an adverse drug reaction following the review of the MAH internal safety data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity of this procedure to add the event frequency of Stevens-Johnson syndrome to align with the approved text in the SmPC."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0033

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.1 of the SmPC in order to reflect the final Overall Survival (OS) analysis from study D5160C00007 (FLAURA) as recommended by the CHMP in the context of procedure No EMEA/H/C/004124/II/0019. In addition, results from a biomarker analysis from FLAURA study has also been provided as recommended by the CHMP. The MAH also took the opportunity of this variation to add the respective strength and pharmaceutical form to the correspondent Marketing Authorisation Number in the SmPC and Labelling."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0034

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 5.1 of the SmPC in order to include updated overall survival data from study IMvigor 211 (GO29294), a phase III study to investigate the efficacy and safety of atezolizumab compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure of

platinum-containing chemotherapy."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0035

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the results of study GO29664, (iMATRIX) evaluate the safety and pharmacokinetics of Tecentriq in paediatric (<18, n=69) and young adult patients (18-30 years, n=18) with relapsed or progressive solid tumours as well as with Hodgkin's and non-Hodgkin's lymphoma. This study was agreed under the Paediatric Investigational Plan EMEA-001638-PIP01-14-M02 (EMA decision: P/0207/2019). The Package Leaflet is updated accordingly."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0036

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Submission of the final report from study GO28915 (OAK) listed as a category 3 study in the RMP. This is a Phase III, open-label multicenter, randomized study to investigate the efficacy and safety of atezolizumab (anti−PD-L1 antibody) compared with docetaxel in patients with NSCLC after failure with platinum-containing chemotherapy. In addition, the MAH submitted integrated analyses of the potential relationship of ADA and safety we based on studies IMvigor210, IMvigor211, OAK, POPLAR, IMpower150, IMpower130, IMpower131, IMpower132, IMpower133 and IMpassion130 as recommended by the CHMP."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0037

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to amend the information regarding immunogenicity further to the assessment of the effect of atezolizumab neutralising antibodies on the pharmacokinetics and efficacy endpoints including OS, PFS and ORR on the NSCLC studies POPLAR, OAK, IMpower 150, IMpower 130, IMPower 131 and IMpower 132 as well as on studies IMvigor 211 (UC), IMmotion 151 (RCC), IMpower 133 (SCLC) and IMpassion 130 (TNBC), as recommended by the CHMP."

Translarna - ataluren - EMEA/H/C/002720/II/0056/G, Orphan

PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "C.I.13: Submission of final results of 8 in vitro genotoxicity studies (not included as post-authorisation measures in the RMP) conducted with four identified organic impurities present in the Translarna (ataluren) drug substance."

Tygacil - tigecycline - EMEA/H/C/000644/II/0110

Pfizer Europe MA EEIG, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4 and 4.8 of the SmPC in order to add a recommendation regarding monitoring of coagulation parameters prior to and during tigecycline treatment and to update the frequency of the existing adverse drug reaction hypofibrinogenaemia from `Not known' to `Rare', based on post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) and to bring the PI in line with the latest QRD template version 10.1."

Tygacil - tigecycline - EMEA/H/C/000644/II/0111

Pfizer Europe MA EEIG, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.5 of the SmPC in order to add drug interaction information regarding the concomitant use of tigecycline and calcineurin inhibitors, based on pharmacovigilance data."

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0054

MCM Vaccine B.V., Rapporteur: Bart Van der Schueren, "Update of section 4.8 of the Vaxelis SmPC in order to add Hypotonic Hyporesponsive Episode to the list of post-marketing adverse events, based on a cumulative assessment of post-marketing data from the Marketing authorisation holder (MAH) global safety database. The Package Leaflet is updated accordingly. In addition, the MAH made minor

editorial changes to the PI."

VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0001
Bayer AG, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to remove the warning related to drug-drug interactions between larotrectinib and CYP2 substrates based on the results of study PH-40955 investigating the inductive potential of Larotrectinib on the expression of cytochrome P450 (CYP) enzymes. The Package Leaflet is updated accordingly."

Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0074
Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.2 and 5.2 of the SmPC in order to add the possibility to crush the tablets for patients unable to swallow whole tablets based on final results from study EP093-155; this is an interventional study to investigate and compare the relative bioavailability and bioequivalence of a crushed tablet and an intact tablet of ESL (800 mg); The Package Leaflet is updated accordingly."

WS1749
AZILECT-EMEA/H/C/000574/WS1749/ 0084
Rasagiline ratiopharm- EMEA/H/C/003957/ WS1749/0016
Teva B.V., Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final report from study TV1030-CNS-50024 listed as a category 3 study in the RMP. This is a non-interventional retrospective cohort study which was conducted using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagilline mesylate in patients with Parkinson's disease."

B.6.10. CHMP-PRAC assessed procedures

Baraclude - entecavir - EMEA/H/C/000623/II/0064
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the completion of the two paediatric studies AI463028 (Evaluation of

the pharmacokinetics, safety, tolerability and efficacy of Entecavir (ETV) in pediatric subjects with chronic hepatitis B virus (HBV) infection who are HBeAg-Positive) and AI463189 (A Comparative Study of the Antiviral Efficacy and Safety of Entecavir (ETV) versus Placebo in Pediatric Subjects with Chronic Hepatitis B Virus (HBV) Infection who are HBeAg-Positive) and section 5.3 to reflect the outcome of study AI463080 (Randomized, Observational Study of Entecavir to Assess Long-term Outcomes Associated with Nucleoside/Nucleotide Monotherapy for Patients with Chronic HBV Infection: The REALM Study). Section 5.2 of the SmPC is also updated to remove information on the pharmacokinetics of entecavir in lamivudine-experienced paediatric patients, at the request of the CHMP. The RMP version 15 has also been submitted, which implements Revision 2 of the EU-RMP template. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to make minor editorial changes to the PI."	
Bavencio - avelumab - EMEA/H/C/004338/II/0013 Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of section 5.1 of the SmPC in order to update efficacy information following results from study EMR100070-003 Part B listed as a specific obligation in the Annex II; this is a Phase II, open-label, multicenter trial to investigate the clinical activity and safety of avelumab (MSB0010718C) in subjects with Merkel cell carcinoma. With this submission the company is also taking the opportunity to update annex-II proposing deletion of the specific obligation and proposing the switch from conditional to full marketing authorisation. The package leaflet and the RMP (version 2.1) are updated accordingly."	
Benlysta - belimumab - EMEA/H/C/002015/II/0076 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information based on the final results from study BEL115467 listed as a imposed PASS in the	

Annex II; this is a Randomized, Double-Blind, Placebo-Controlled 52-Week Study to Assess Adverse Events of Special Interest in Adults with Active, Autoantibody-Positive Systemic Lupus Erythematosus Receiving Belimumab; the Package Leaflet is updated accordingly. The RMP version 36 has also been submitted. The MAH took the opportunity to make the following minor updates to the RMP: - Updated information on transplant study, updated information on BEL116543, added information on paediatric continuation study in Module SIV. - Updated exposure information and information for BEL116543 in Module SIV.2. - Update data on revised rates of pregnancy and lactation in Module SIV.3. - Correction of an error within Annex 3 and provision of the the updated protocol Amendment 7 of a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of belimumab plus Standard of Care versus Placebo plus standard of Care in Adult Subjects with Active Lupus Nephritis (BEL114054). This RMP also includes changes being reviewed in procedure II/0062, related to the use of Benlysta in paediatric patients, and BEL116027, evaluating the safety and efficacy of temporary discontinuation of belimumab. In addition, the Marketing authorisation holder took the opportunity make minor editorial changes to the Annex II and the label.”	
Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0088 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.2 and 5.1 of the SmPC in order to reflect the final data of Study V72_38OB listed as category 3 in the RMP; this is an observational effectiveness study of the impact of Bexsero vaccination; the Package Leaflet is updated accordingly. The RMP version 7.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some rewording in section 5.1 of the SmPC and to bring the PI in line with the latest QRD template version 10.1 and to amend minor typos detected in the European	

annexes.”

Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0027

Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Liana Gross-Martirosyan, “Update of sections 4.8 and 5.1 of the Biktarvy SmPC to reflect pooled efficacy and safety data from the final clinical study reports of two antiretroviral therapy-naive adult studies through 144 weeks of treatment, GS-US-380-1489 (A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Abacavir [ABC]/Dolutegravir [DTG]/Lamivudine [3TC] in HIV-1 Infected, Antiretroviral Treatment-Naive Adults) and GS-US-380-1490 (A Phase 3, Randomized, Double-Blinded Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naive Adults). Both studies are listed as Category 3 studies in the RMP and this submission therefore fulfils MEA 001 and MEA 002. The RMP version 2.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor editorial changes to the PI and update Annex II with regards to PSUR requirements.”

Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0106

GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, “Update of sections 4.4 and 5.1 of the SmPC based on final results from study HPV-019 listed as a category 3 study in the RMP (in fulfilment of MEA080); this is a safety and immunogenicity study of Cervarix in HIV-positive female subjects aged 15-25 years as compared to HPV-4, which was already submitted in P46-95. In addition, the Marketing authorisation holder (MAH) took the opportunity to reflect an update in section 4.2 of the SmPC to indicate that limited clinical data is now available in 4-6 years old children based on study HPV-073 following assessment in P46-90; this is a safety and immunogenicity study of

Cervarix in girls aged 4-6 years, as an alternative to the current adolescent HPV vaccination schedule. The RMP version 21 has also been submitted to reflect the availability of the final results of the HPV-019 and HPV-073 studies, and the use of Cervarix in HIV-infected subjects or subjects with known immune deficiencies has been removed as missing information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0038, Orphan

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Submission of final CSR for study MO28543/GREEN to fulfil the post authorization commitment [MEA] 005 , the RMP is updated with the deletion of the study under PhV plan, (RMP version 6.1)"

Herceptin - trastuzumab - EMEA/H/C/000278/II/0158

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final report from study BO29159 (MetaPHER) a post-authorization safety measure Category 3 Non-Imposed Post-Approval Safety Study (NI-PASS), following approval of the Herceptin SC line extension procedure EMEA/H/C/278/X/60 to generate and evaluate additional safety and tolerability data for the approved triplet regimen (Herceptin+Perjeta+docetaxel) in the advanced breast cancer setting. In addition, bioanalytical supportive studies are presented. An updated version of the Herceptin Risk Management Plan (version 21) has also been submitted."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0058, Orphan

Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.5 and 4.6 of the SmPC following the results from study CLL1017 (MEA 012.2). The PL is updated accordingly."

Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0026/G, Orphan

Alexion Europe SAS, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel

Liminga, "Grouping consisting of the following variations: - Update of sections 4.2, 4.4, 4.8, 5.1 of the Summary of Product Characteristics (SmPC) in order to update the clinical information based on the pooled safety and efficacy analysis of already submitted studies (Studies LAL-CL04, LAL-CL03, LAL-CL06, LAL-CL08 and LAL-CL02) and updated population PK analyses in children and adults. The Package Leaflet has been amended accordingly. The ATC code has been added to the SmPC. The RMP version 4 has also been submitted. Annex II is also updated to remove the specific obligation related to the provision of fstudy LAL-CL08. - Submission of the final report from study LAL-EA01 An open-label study with sebelipase alfa (1 mg/kg every other week for up to 78 weeks or until drug commercialization) in United States (US) patients who did not otherwise qualify for an active sebelipase alfa trial (expanded access protocol)"	
Kisqali - ribociclib - EMEA/H/C/004213/II/0021 Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on ILD/pneumonitis and related dose modification recommendations. The Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted."	
Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0016, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study VX14-661-110 listed as a category 3 study in the RMP; this is a Phase 3, multicenter, open label, rollover study for Studies 103, 106, 107, 108, 109, 111, 112, and 114 designed to evaluate the long-term safety and tolerability of TEZ/IVA treatment for 96 weeks in cystic fibrosis (CF) subjects 12 years and older, homozygous or heterozygous for the F508del CFTR mutation. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD	

template version 10.1. The RMP version 2.2 has also been submitted."

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0146

GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from a hospital-based surveillance study assessing the impact of Synflorix immunisation program in Kenya on pneumonia, invasive pneumococcal disease (IPD) and replacement disease. This submission is made to fulfil post-authorisation measure MEA 021.8, and propose an update of the Risk Management Plan (RMP) accordingly. Review the safety concerns listed in the Synflorix RMP in alignment with the recommendations from EU-RMP with GVP module V revision 2 was also carried out, considering the closure of MEA 021.8 and the RMP principle that safety concerns can be removed or reclassified when the safety profile and risks are well-characterised, the MAH revised the Synflorix RMP and removed all well-characterised risks.
The RMP version 18 has been submitted."

Talzenna - talazoparib - EMEA/H/C/004674/II/0001

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with severe renal impairment and update pharmacokinetic information based on the results from PK study MDV3800-01 (C3441001) listed as a category 3 study in the RMP. The RMP version 1.0 has also been submitted. In addition, the MAH took the opportunity to make minor changes through the product information and to bring the PI in line with the latest QRD template version 10.1."

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0023

Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and

immunogenicity information based on final results from study B1971033 listed as a category 3 study in the RMP (MEA007); this is a duration of immunity study to assess persistence of hSBA response for up to 48 months after completion of vaccination with Trumenba and the immunogenicity, safety, and tolerability of a booster dose of Trumenba; The RMP version 3 has also been submitted, including changes related to this variation, changes agreed during another ongoing variation (II-13) and editorial changes. In addition, the Marketing authorisation holder (MAH) took the opportunity to include editorial changes in Annex II, in the labelling and in the Package Leaflet."	
Velphoro - iron - EMEA/H/C/002705/II/0021 Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "Update of section 5.1 of the SmPC in order to add information related to the results of the VERIFIE study. This was a non-interventional voluntary PASS trial, which aimed to investigate the short and long-term real-life safety, effectiveness, and adherence of Velphoro in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis. It was listed as an additional pharmacovigilance activity (EMEA/H/C/002705/MEA/002), a category 3 study in the RMP. Furthermore, minor editorial wording changes in section 4.2 to provide consistent information between the SmPC and that already existing in the Labelling and PL were introduced. The RMP version 8.0 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 10.1."	
Voncento - human coagulation factor viii / human von willebrand factor - EMEA/H/C/002493/II/0042 CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Submission of an updated RMP version 7 in order to: - align with the revision of the GVP module V - reflect the completion of the post-marketing study (PMS) in patients with Von Willebrand	

Disease (VWD)
- request a waiver to the post-authorisation safety study (category 3 study) in patients with haemophilia A due to feasibility reasons."

Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0034
Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of section 4.2 of the SmPC in order to change the wording "transfer from basal insulin" to "transfer from any insulin regimen", based on data from study NN9068-4184 (DUAL II Japan: A double-blinded trial comparing the efficacy and safety of insulin degludec/liraglutide and insulin degludec both in combination with metformin in Japanese subjects with type 2 diabetes mellitus inadequately controlled with basal or pre-mix/combination insulin therapy and oral anti-diabetic drugs) as well as data from the post-marketing setting. In addition, the MAH took the opportunity to make a minor correction in SmPC section 5.1 and to implement changes in the annexes in accordance with QRD template 10.1.
The MAH provided an updated RMP version 9.0 as part of the application."

B.6.11. PRAC assessed procedures

PRAC Led
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0030
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik, PRAC-CHMP liaison: Andrea Laslop, "C.I.11 b : Submission of an updated RMP version 5.0 as a PDCO commitment (PIP modification request) to stop enrollment in arm 2 Previously Untreated Patient (PUP) of clinical trial CSL627_3001 (remains ongoing). Completion of Arms 1 and 3 (Previously Treated Patient) is also reflected. Updated information on registries/noninterventional study (NIS) to reflect only those considered additional pharmacovigilance activities, category 3 (addition of registry American Thrombosis and Hemostasis Network [ATHN] 8 removal of registries ATHN 2 and Dutch Hemophilia Registry as well as the AFSTYLA NIS); also to demonstrate how PUP data will be

complemented. Clinical trials CSL627_1001 and 3002 removed from Table Part VII-2 as both studies have not been listed in a previous Pharmacovigilance Plan. Data have been updated to the DLP of 03 July 2019 to be consistent with Periodic Safety Update Report No. 5.”	
PRAC Led **Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0040** Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, “To update the RMP for Ameluz to version 11.1 based on the new RMP template (GVP module V, rev.2), as well as the implementation of changes assessed and agreed by PRAC in the recently finalised PSUSA procedure (EMEA/H/C/002204/PSUSA/00010006/20180614).”	
PRAC Led **Betmiga - mirabegron - EMEA/H/C/002388/II/0033** Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “Final study report of the PASS Study 178-CL-114 – An evaluation of Cardiovascular Events in Users of Mirabegron and Other Treatments for Overactive Bladder.”	
PRAC Led **Celsentri - maraviroc - EMEA/H/C/000811/II/0061** ViiV Healthcare B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, “Submission of the final report from study A4001067 (POEM): An International, Multicenter, Prospective Observational Study of the Safety of Maraviroc Used With Optimized Background Therapy In Treatment-Experienced HIV-1 Infected Patients. Study A4001067 (POEM) is a non-interventional PASS (Post-Authorisation Safety Study) listed as a category 3 study in the RMP. The updated EU-RMP (v12.0) is also included in this variation application.”	
PRAC Led	

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0086

UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (UP0038) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study with the aim to evaluate the effectiveness of Cimzia risk minimisation educational materials for healthcare professionals and patients."

PRAC Led

Fampyra - fampridine - EMEA/H/C/002097/II/0046

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC in order to update the existing contraindication for renal impaired patients, update the frequency of seizure to uncommon and reflect safety information based on from final results from study 218MS401 (LIBERATE) listed as category 3 study in the RMP; Study 218MS401 was a Phase IV prospective, noninterventional, multicentre, observational study in MS patients who began Fampyra treatment in the postmarketing setting. The Package Leaflet is updated accordingly. An updated RMP version 13.1 has also been submitted to align with the RMP Rev. 2 template."

PRAC Led

Firmagon - degarelix - EMEA/H/C/000986/II/0035

Ferring Pharmaceuticals A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "This Type II variation procedure (C.I.13) contains a revised Post Authorisation Safety Study (PASS) report. Study identifier: "FE 200486 CS39. Prospective Observational Safety Study in Patients with Advanced Prostate Cancer Treated with FIRMAGON (Degarelix) or a GnRH Agonist"
This variation does not lead to any changes of the Summary of Product Characteristics, Labelling or Package Leaflet"

PRAC Led

Flixabi - infliximab -
EMEA/H/C/004020/II/0052
Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP to replace the prospective observational cohort study of Flixabi in patients with Crohn's disease (CD) (SB2-G42-CD), with real-world data from PERFUSE, CREDIT and CEDUR studies."

PRAC Led
Kineret - anakinra -
EMEA/H/C/000363/II/0073
Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from study (Sobi.ANAKIN-302) listed as a category 3 study in the RMP. This is a non-interventional, post-authorisation safety study to evaluate long-term safety of anakinra (Kineret) in patients with systemic juvenile idiopathic arthritis. The RMP version 5.1 has also been submitted to reflect the completion of the study."

PRAC Led
Myozyme - alglucosidase alfa -
EMEA/H/C/000636/II/0079
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from study ALGMYC07390, Prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions (MEA 053 resulting from variation EMEA/H/C/000636/II/0052) to test the effectiveness of the approved Safety Information Packet (SIP)."

PRAC Led
Naglazyme - galsulfase -
EMEA/H/C/000640/II/0081
BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Fátima Ventura, "Submission of an updated RMP version 6.0 in order to update the safety specification plan based on a review of the

preclinical, clinical, post-marketing and literature data. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Naglazyme RMP to the latest EU RMP template.”
PRAC Led **Rebif - interferon beta-1a - EMEA/H/C/000136/II/0144** Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, “C.I.11 for RMP: Submission of an updated RMP version 11 in order to comply with the Good Pharmacovigilance Practices (GVP) Module 5 RMP revision 2 requirements, and to ensure the appropriate time needed for effective review and analysis of all RMP Sections”
PRAC Led **Retacrit - epoetin zeta - EMEA/H/C/000872/II/0094** Pfizer Europe MA EEIG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, “Pfizer’s biosimilar epoetin zeta list of safety concerns has been aligned to the Innovator’s Eprex (reference product, INN epoetin alfa).”
PRAC Led **RoActemra - tocilizumab - EMEA/H/C/000955/II/0094** Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of the final report from study WA22480 (ARTIS) listed as a category 3 study in the RMP. This is a phase IV, prospective observational cohort study using Sweden registers to provide long term safety data from the use of tocilizumab in Sweden for RA patients.”
PRAC Led **Saxenda - liraglutide - EMEA/H/C/003780/II/0025** Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final report from study NN8022-4241 Drug Utilization Study, listed as a category 3 study in the RMP. An updated RMP

version 31 has also been submitted."

PRAC Led

SIRTURO - bedaquiline - EMEA/H/C/002614/II/0038, Orphan

Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "To update the RMP (new version 4.3) to revise the Summary of Safety Concerns for Sirturo in response to a request received from PRAC/CHMP in the context of the assessment of the Renewal of the Conditional Marketing Authorisation of SIRTURO (EMEA/H/C/002614/R/0035). As requested by the PRAC/CHMP, data on co-administration of bedaquiline and HIV-protease inhibitors are also summarised. No changes are proposed to the Product Information of SIRTURO."

PRAC Led

Teysuno - tegafur / gimeracil / oteracil - EMEA/H/C/001242/II/0042

Nordic Group B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 9 in order to update safety specifications (re-classifying and removing risks from the list of important safety concerns as outlined in PSUSA/2875/201801)."

PRAC Led

Trulicity - dulaglutide - EMEA/H/C/002825/II/0048

Eli Lilly Nederland B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of the final study report from study B010, investigating the Utilisation of Dulaglutide in European Countries: A Cross-Sectional, Multi-Country and Multi-Source Drug Utilisation Study Using Electronic Health Record Databases. Study B010 is listed as a category 3 study in the RMP (MEA 001). An updated RMP version 5.1 was submitted."

PRAC Led

WS1742

Ebymect-EMEA/H/C/004162/WS1742/0043

Edistride-EMEA/H/C/004161/WS1742/0037

Forxiga-EMEA/H/C/002322/WS1742/0056
Xigduo-EMEA/H/C/002672/WS1742/0054
AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Update of SmPC section 4.4 (Special warning and precaution for use) of Forxiga, Edistride, Xigduo and Ebymect based on the final results of a Post-Authorization Safety Study (listed as a category 3 study in the RMPs): meta-analysis across studies D1690C00018, D1690C00019 and D1693C00001 (DECLARE), for analysis of lower limb amputation and relevant preceding adverse events. These three studies include T2DM patients with established CVD or with CVD risk factors treated with dapagliflozin or placebo in clinical trial settings. The Package Leaflets (PL) are updated accordingly.
In addition, the applicant took the opportunity to implement a minor editorial change in section 8 of the Edistride 5 mg SmPC.
The updated dapagliflozin RMP version 19 and dapagliflozin/metformin fixed dose combination (FDC) RMP version 12 have also been submitted."

PRAC Led
WS1747
Enbrel-EMEA/H/C/000262/WS1747/0231
LIFMIOR-EMEA/H/C/004167/WS1747/0025
Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP (version 7.0) in line with the latest GVP Module V RMP template (rev. 2) and revision of the list of safety concerns. In addition, the MAH took the opportunity to implement outcomes of previous procedures (type II variation EMEA/H/C/WS/1270 and PSUR EMEA/H/C/PSUSA/001295/201902) to remove or consolidate risks. The MAH is also removing the addendum to RMP version 6.3., making clinical and post-marketing data updates in the RMP and reflecting the completion of post-authorisation studies."

PRAC Led
WS1761
Anoro Ellipta-EMEA/H/C/002751/

WS1761/0029
Incruse Ellipta-EMEA/H/C/002809/ WS1761/0028
Laventair Ellipta-EMEA/H/C/003754/ WS1761/0032
Rolufta Ellipta-EMEA/H/C/004654/ WS1761/0013
GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of the final report from study WWE117397 listed as a category 3 study in the RMP. This was a retrospective longitudinal non-interventional observational study of new users of inhaled umeclidinium/vilanterol (UMEC/VI) or new users of inhaled umeclidinium (UMEC) or new users or long-acting bronchodilators (LABD) in the primary care setting. The primary objective of the study was to report the proportion of patients with a possible off-label use and characterize them in new users of UMEC/VI, UMEC, or other LABD. The second objective was to quantify incidence of major cardiovascular and cerebrovascular events, mortality and pneumonia, and rates of exacerbations of COPD during follow-up in new users of UMEC/VI or UMEC. The tertiary objective was in new users of UMEC/VI or UMEC with 12 or more months of follow-up following initiation, to describe treatment patterns and adherence."

B.6.12. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0036, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0037, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0015, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Yescarta - axicabtagene ciloleucel -

EMEA/H/C/004480/II/0018, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0019, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

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

WS1729
Juluca-EMEA/H/C/004427/WS1729/0020
Tivicay-EMEA/H/C/002753/WS1729/0056
Triumeq-EMEA/H/C/002754/WS1729/0077
ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson

WS1735/G
Comtan-EMEA/H/C/000171/WS1735/0055/G
Comtess-EMEA/H/C/000170/WS1735/0059/G
Corbilta-EMEA/H/C/002785/WS1735/0020/G
Entacapone Orion-EMEA/H/C/002440/WS1735/0018/G
Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS1735/0029/G
Stalevo-EMEA/H/C/000511/WS1735/0090/G
Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola

WS1771/G
AZILECT-EMEA/H/C/000574/WS1771/0085/G
Rasagiline ratiopharm-EMEA/H/C/003957/ WS1771/0017/G
Teva B.V., Lead Rapporteur: Bruno Sepodes

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. Timetables – 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):

Information related to Scientific Advice cannot be released at the present time as these contain commercially confidential information.

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

Some information related to PRIME cannot be released at the present time as these contain commercially confidential information.

G.3.1. List of procedures concluding at 27-30 January 2020 CHMP plenary:

G.3.2. List of procedures starting in January 2020 for February 2020 CHMP adoption of outcomes

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