

15 September 2017
EMA/CHMP/605853/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 17-20 July 2017

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

Table of contents

1.	Introduction	8
1.1.	Welcome and declarations of interest of members, alternates and experts	8
1.2.	Adoption of agenda	8
1.3.	Adoption of the minutes	8
2.	Oral Explanations	9
2.1.	Pre-authorisation procedure oral explanations.....	9
2.1.1.	etirinotecan pegol - EMEA/H/C/003874	9
2.1.2.	midostaurin - Orphan - EMEA/H/C/004095	9
2.1.3.	padeliporfin - EMEA/H/C/004182	9
2.2.	Re-examination procedure oral explanations	10
2.3.	Post-authorisation procedure oral explanations	10
2.3.1.	Opdivo - nivolumab - EMEA/H/C/003985/II/0029	10
2.4.	Referral procedure oral explanations	10
2.4.1.	Gadolinium-containing contrast agents (GdCA): gadoversetamide – OPTIMARK (CAP) Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intravenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)	10
3.	Initial applications	11
3.1.	Initial applications; Opinions	11
3.1.1.	Bavencio - avelumab - Orphan - EMEA/H/C/004338.....	11
3.1.2.	Dupixent - dupilumab - EMEA/H/C/004390	11
3.1.3.	Entecavir Accord - entecavir - EMEA/H/C/004458	12
3.1.4.	Entecavir Mylan - entecavir - EMEA/H/C/004377	12
3.1.5.	Fanaptum - iloperidone - EMEA/H/C/004149	13
3.1.6.	Lacosamide Accord - lacosamide - EMEA/H/C/004443	13
3.1.7.	Lutathera - lutetium (177Lu) oxodotreotide - Orphan - EMEA/H/C/004123	13
3.1.8.	Onzeald - etirinotecan pegol - EMEA/H/C/003874	14
3.1.9.	Rydapt - midostaurin - Orphan - EMEA/H/C/004095	15
3.1.10.	Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/00439116	
3.1.11.	Tecentriq - atezolizumab - EMEA/H/C/004143	16
3.1.12.	Verkazia ciclosporin - Orphan - EMEA/H/C/004411	17
3.1.13.	Xermelo - telotristat ethyl - Orphan - EMEA/H/C/003937	17
3.2.	Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable)	18
3.2.1.	abaloparatide - EMEA/H/C/004157.....	18
3.2.2.	carmustine - EMEA/H/C/004326	18
3.2.3.	adalimumab - EMEA/H/C/004319	18

3.2.4.	fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781.....	19
3.2.5.	guselkumab - EMEA/H/C/004271.....	19
3.2.6.	neratinib - EMEA/H/C/004030.....	19
3.2.7.	naloxone - EMEA/H/C/004325.....	20
3.2.8.	trastuzumab - EMEA/H/C/004323.....	20
3.2.9.	ritonavir - EMEA/H/C/004549.....	20
3.2.10.	tacrolimus - EMEA/H/C/004435.....	20
3.2.11.	padeliporfin - EMEA/H/C/004182.....	21
3.2.12.	fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363.....	21
3.2.13.	buprenorphine / naloxone - EMEA/H/C/004407.....	21
3.3.	Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable)	22
3.3.1.	tildrakizumab - EMEA/H/C/004514.....	22
3.3.2.	trastuzumab - EMEA/H/C/004361.....	22
3.3.3.	letermovir - Orphan - EMEA/H/C/004536.....	22
3.3.4.	naldemedine - EMEA/H/C/004256.....	22
3.3.5.	brexpiprazole - EMEA/H/C/003841.....	23
3.3.6.	sufentanil - EMEA/H/C/004335.....	23
3.4.	Update on on-going initial applications for Centralised procedure.....	23
3.4.1.	dapivirine - EMEA/H/W/002168, Article 58.....	23
3.4.2.	dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171.....	23
3.4.3.	pegfilgrastim - EMEA/H/C/004262.....	24
3.4.4.	andexanet alfa - EMEA/H/C/004108.....	24
3.4.5.	metreleptin - Orphan - EMEA/H/C/004218.....	24
3.4.6.	nitisinone - EMEA/H/C/004582.....	25
3.4.7.	trastuzumab - EMEA/H/C/004346.....	25
3.4.8.	sodium benzoate - Orphan - EMEA/H/C/004150.....	25
3.4.9.	rotigotine - EMEA/H/C/004286.....	26
3.5.	Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004	26
3.5.1.	Masipro - masitinib - Orphan - EMEA/H/C/004159.....	26
3.5.2.	Adlumiz - anamorelin - EMEA/H/C/003847.....	26
3.5.3.	Human IGG1 monoclonal antibody specific for human interleukin-1 alpha XBiotech - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388.....	26
3.6.	Initial applications in the decision-making phase.....	27
3.7.	Withdrawals of initial marketing authorisation application	27

4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 27

4.1.	Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion	27
-------------	--	-----------

4.1.1.	Prolia - denosumab - EMEA/H/C/001120/X/0059/G.....	27
4.1.2.	Samsca - tolvaptan - EMEA/H/C/000980/X/0024	27
4.1.3.	Signifor - pasireotide - Orphan - EMEA/H/C/002052/X/0030/G.....	28
4.1.4.	Xgeva - denosumab - EMEA/H/C/002173/X/0048/G.....	28
4.1.5.	Xtandi - enzalutamide - EMEA/H/C/002639/X/0029	28
4.2.	Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues	29
4.2.1.	Tasigna - nilotinib - Orphan - EMEA/H/C/000798/X/0088/G	29
4.3.	Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question	30
4.3.1.	Bortezomib Accord - bortezomib - EMEA/H/C/003984/X/0008	30
4.3.2.	Daliresp - roflumilast - EMEA/H/C/002398/X/0031.....	30
4.3.3.	Daxas - roflumilast - EMEA/H/C/001179/X/0035	30
4.3.4.	Humira - adalimumab - EMEA/H/C/000481/X/0164/G	31
4.3.5.	Libertek - roflumilast - EMEA/H/C/002399/X/0032.....	31
4.3.6.	Oncaspar - pegaspargase - EMEA/H/C/003789/X/0008	31
4.3.7.	Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0020.....	32
4.4.	Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008	32
4.5.	Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008	32

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

33

5.1.	Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information.....	33
5.1.1.	Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0048.....	33
5.1.2.	Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0142	33
5.1.3.	Bydureon - exenatide - EMEA/H/C/002020/II/0041	34
5.1.4.	Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016.....	34
5.1.5.	Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0026.....	35
5.1.6.	Humira - adalimumab - EMEA/H/C/000481/II/0163	35
5.1.7.	Keytruda - pembrolizumab - EMEA/H/C/003820/II/0023/G.....	36
5.1.8.	Kineret - anakinra - EMEA/H/C/000363/II/0056	37
5.1.9.	Olumiant - baricitinib - EMEA/H/C/004085/II/0001	37
5.1.10.	Opdivo - nivolumab - EMEA/H/C/003985/II/0029	38
5.1.11.	Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0091.....	38
5.1.12.	Rapamune - sirolimus - EMEA/H/C/000273/II/0164	38
5.1.13.	RoActemra - tocilizumab - EMEA/H/C/000955/II/0066	39

5.1.14.	Sovaldi - sofosbuvir - EMEA/H/C/002798/II/0036	39
5.1.15.	Sutent - sunitinib - EMEA/H/C/000687/II/0065	40
5.1.16.	Vimpat - lacosamide - EMEA/H/C/000863/II/0065/G.....	40
5.1.17.	Xgeva - denosumab - EMEA/H/C/002173/II/0055.....	41
5.1.18.	Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0047	41
5.2.	Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008	42
5.2.1.	Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/02617/II/0072	42
5.2.2.	Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/17	42
5.3.	Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008	42
6.	Ancillary medicinal substances in medical devices	43
6.1.	Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions	43
6.2.	Update of Ancillary medicinal substances in medical devices	43
7.	Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)	43
7.1.	Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)	43
8.	Pre-submission issues	43
8.1.	Pre-submission issue.....	43
8.1.1.	durvalumab - H0004771.....	43
8.2.	Priority Medicines (PRIME).....	43
8.2.1.	List of applications received	43
8.2.2.	Recommendation for PRIME eligibility.....	44
9.	Post-authorisation issues	44
9.1.	Post-authorisation issues	44
9.1.1.	Aranesp (CAP) - darbepoetin alfa – EMEA/H/C/000332/SDA/091; Abseamed (CAP) - epoetin alfa – EMEA/H/C/000727/SDA/029, Binocrit (CAP) - epoetin alfa – EMEA/H/C/000725/SDA/028, Epoetin alfa hexal (CAP) - epoetin alfa – EMEA/H/C/000726/SDA/030; NAP Neorecormon (CAP) - epoetin beta – EMEA/H/C/000116/SDA/055; Biopoin (CAP) - epoetin theta – EMEA/H/C/0001036/SDA/022, Eporatio (CAP) - epoetin theta – EMEA/H/C/0001033/SDA/022; Retacrit (CAP) - epoetin zeta – EMEA/H/C/000872/SDA/046, Silapo (CAP) - epoetin zeta – EMEA/H/C/000760/SDA/039 MIRCERA (CAP) - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/SDA/039; NAP	44
9.1.2.	CHMP request for PRAC advice on Fluoropyrimidines (Capecitabine-Xeloda and 5-FU), EMEA/H/C/0316/LEG-033.1	44
9.1.3.	Vedrop - tocopherol - Orphan - EMEA/H/C/000920/II/0022	45
9.1.4.	Blinicyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0009 & R/0013.....	45
9.1.5.	Opdivo - nivolumab - EMEA/H/C/003985/II/0030	46

9.1.6.	Data collection on adverse events of anti-HIV drugs (D:A:D) study - Evaluation of D:A:D data	46
--------	--	----

10. Referral procedures 46

10.1.	Procedure for Centrally Authorised products under Article 20 Council Regulation (EC) No 726/2004	46
10.2.	Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004 .	46
10.3.	Procedure under Articles 5(2) and 10 of the Regulation (EC) No 726/2004	46
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	46
10.5.	Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC....	46
10.6.	Community Interests - Referral under Article 31 of Directive 2001/83/EC	47
10.6.1.	Gadolinium-containing contrast agents (GdCA): gadoversetamide – OPTIMARK (CAP) Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intravenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)	47
10.7.	Re-examination Procedure under Article 32(4) of Directive 2001/83/EC.....	48
10.7.1.	Alcover 750 mg, 1250 mg, 1750 mg Granulat im Beutel – Sodium oxybate – EMEA/H/A-29(4)/1451	48
10.8.	Procedure under Article 107(2) of Directive 2001/83/EC	48
10.9.	Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) (EC) No 1084/2003	48
10.10.	Procedure under Article 29 Regulation (EC) 1901/2006.....	48
10.11.	Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) No 1234/2008)	48

11. Pharmacovigilance issue 49

11.1.	Early Notification System	49
-------	---------------------------------	----

12. Inspections 49

12.1.	GMP inspections	49
12.2.	GCP inspections	49
12.3.	Pharmacovigilance inspections.....	49
12.4.	GLP inspections	49

13. Innovation Task Force 49

13.1.	Minutes of Innovation Task Force	49
13.2.	Innovation Task Force briefing meetings.....	49
13.3.	Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004	50
13.4.	Nanomedicines activities	50

14.	Organisational, regulatory and methodological matters	50
14.1.	Mandate and organisation of the CHMP	50
14.1.1.	Time schedule of CHMP August written procedure	50
14.1.2.	Pilot phase for abolition of signatures for divergent positions for referral procedures	50
14.1.3.	Confirmation of joint CHMP/PDCO membership for Romania	50
14.1.4.	Update to the CHMP templates on initial Marketing Authorisation	50
14.2.	Coordination with EMA Scientific Committees	51
14.2.1.	Pharmacovigilance Risk Assessment Committee (PRAC)	51
14.2.2.	Committee for Advanced Therapies (CAT)	51
14.2.3.	Paediatric Committee (PDCO)	51
14.2.4.	Committee for Orphan Medicinal Products (COMP)	52
14.2.5.	Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)	52
14.3.	Coordination with EMA Working Parties/Working Groups/Drafting Groups	52
14.3.1.	Scientific Advice Working Party (SAWP)	52
14.3.2.	Quality Working Party (QWP)	52
14.3.3.	Radiopharmaceutical Drafting Group (RadDG)	53
14.3.4.	CHMP Guidelines Consistency Group (GCG)	53
14.3.5.	Blood Product Working Party (BPWP)	53
14.4.	Cooperation within the EU regulatory network	53
14.5.	Cooperation with International Regulators	53
14.6.	Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee	54
14.7.	CHMP work plan	54
14.7.1.	CHMP 2017 Work Plan: mid-year update	54
14.8.	Planning and reporting	54
14.9.	Others	54
15.	Any other business	54
15.1.	AOB topic	54
15.1.1.	Working group on Committees' operational preparedness for human medicines	54
15.1.2.	Revision of the 'Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products'	54
15.1.3.	Bridging the regulator and the payer world	55
16.	List of participants	56
17.	Explanatory notes	62

1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) July 2017 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 17-20 July 2017 (to be published post September 2017 CHMP meeting).

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The CHMP welcomed the new member Ewa Balkowiec Iskra from Poland replacing Piotr Fiedor and the new alternate Tomas Boran from Czech Republic replacing Radka Montoniová.

1.2. Adoption of agenda

CHMP agenda for 17-20 July 2017.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 19-22 June 2017.

The CHMP adopted the CHMP minutes for 19-22 June 2017.

The Minutes of the July 2017 CHMP ORGAM meeting held on 10 July 2017, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. etirinotecan pegol - EMEA/H/C/003874

treatment of breast cancer with brain metastases

Scope: Oral explanation/Opinion, SAG report

Action: Oral explanation to be held on 19 July 2017 at time 09:00

Revised list of experts for the ad hoc expert group meeting adopted via written procedure on 11 July 2017.

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

The oral explanation to be held on 19 July 2017 at time 09:00 was cancelled.

See 3.1

2.1.2. midostaurin - Orphan - EMEA/H/C/004095

Novartis Europharm Ltd; treatment of mastocytosis and treatment of acute myeloid leukaemia

Scope: Oral explanation

Action: Oral explanation to be held on 19 July 2017 at time 11:00

List of Outstanding Issues adopted on 22.06.2017, 21.04.2017. List of Questions adopted on 15.12.2016.

An oral explanation was held on 19 July 2017 at time 09:00

See 3.1

2.1.3. padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Oral explanation

Action: Oral explanation to be held on 18 July 2017 at time 11:00

Oral explanation 20.04.2017. List of Outstanding Issues adopted on 21.04.2017, 15.12.2016. List of Questions adopted on 26.05.2016.

The CHMP agreed that an oral explanation is not needed this time.

See 3.2.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Opdivo - nivolumab - EMEA/H/C/003985/II/0029

Bristol-Myers Squibb Pharma EEIG

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

Scope: Oral explanation

Action: Oral explanation to be held on 19 July 2017 at time 14:00

"Extension of Indication to include the treatment of hepatocellular carcinoma after prior sorafenib therapy in adults for Opdivo.

As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

Moreover, the updated RMP version 8.0 has been submitted."

Request for Supplementary Information adopted on 22.06.2017, 23.03.2017.

An oral explanation was held on 19 July 2017 at time 15:00

See 5.1

2.4. Referral procedure oral explanations

2.4.1. Gadolinium-containing contrast agents (GdCA): gadoversetamide – OPTIMARK (CAP) Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intravenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)

Applicant(s): Guerbert (Optimark); various

Rapporteurs for the Article 31 referral: PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Doris Stenver

PRAC Rapporteur of the re-examination: Ulla Wändel Liminga; PRAC Co-rapporteur of the re-examination: Valerie Strassmann

Rapporteurs for Optimark: CHMP Rapporteur: Patrick Salmon, CHMP Co-rapporteur: Johann Lodewijk Hillege

Scope: Oral explanation

Action: Oral explanation to be held on 18 July 2017 at time 14:00

CHMP opinion following PRAC final recommendation

Four oral explanations were held on 18 July 2017.

See 10.6

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Bavencio - avelumab - Orphan - EMEA/H/C/004338

Merck Serono Europe Limited; treatment of Merkel cell carcinoma (MCC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 22.06.2017. List of Questions adopted on 23.02.2017.

The members discussed the available efficacy and safety data and the different options of marketing authorisations.

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

The Committee adopted a positive opinion recommending the granting of a conditional marketing authorisation by majority (27 out of 30 votes) together with the CHMP assessment report and translation timetable.

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

The divergent position (Johann Lodewijk Hillege, Natalja Karpova, Romaldas Maciulaitis) was appended to the opinion.

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

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.2. Dupixent - dupilumab - EMEA/H/C/004390

sanofi-aventis groupe; treatment of moderate-to-severe atopic dermatitis

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 23.03.2017.

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

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

Furthermore, the CHMP considered that dupilumab is a new active substance, as claimed by

the applicant.

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

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

The CHMP noted the letter of recommendation dated 20 July 2017.

The CHMP adopted the BWP report.

3.1.3. [Entecavir Accord - entecavir - EMEA/H/C/004458](#)

Accord Healthcare Ltd; treatment of chronic hepatitis B virus infection

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 22.06.2017. List of Questions adopted on 15.12.2016.

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

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

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

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

The summary of opinion was circulated for information.

3.1.4. [Entecavir Mylan - entecavir - EMEA/H/C/004377](#)

Mylan S.A.S; treatment of chronic hepatitis B virus infection

Scope: Opinion

Action: For adoption

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

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

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

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

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

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

The CHMP noted the letter of recommendations dated 18 July 2017.

The summary of opinion was circulated for information.

3.1.5. [Fanaptum - iloperidone - EMEA/H/C/004149](#)

Vanda Pharmaceuticals Ltd.; treatment of schizophrenia

Scope: Opinion

Action: For adoption

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

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

The CHMP was reminded of previous discussions and the remaining issues.

The CHMP adopted a negative opinion by consensus, recommending the refusal of the marketing authorisation application. The CHMP adopted the assessment report.

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

The refusal question and answers document was circulated for information.

Post-meeting note: the applicant submitted the request for re-examination on 27.07.2017.

3.1.6. [Lacosamide Accord - lacosamide - EMEA/H/C/004443](#)

Accord Healthcare Ltd; treatment of epilepsy

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 22.06.2017, List of Questions adopted on 26.01.2017.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 21 July 2017.

3.1.7. [Lutathera - lutetium \(177Lu\) oxodotreotide - Orphan - EMEA/H/C/004123](#)

Advanced Accelerator Applications; treatment of gastro-entero-pancreatic neuroendocrine tumours

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 18.05.2017. List of Questions adopted on 15.09.2016.

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

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

Furthermore, the CHMP considered that 'lutetium (¹⁷⁷Lu) oxodotreotide' is a new active substance, as claimed by the applicant.

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

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

The CHMP noted the letter of undertaking dated 17 July 2017.

The summary of opinion was circulated for information.

3.1.8. [Onzeald - etirinotecan pegol - EMEA/H/C/003874](#)

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

Scope: Oral explanation/Opinion, SAG report

Action: For adoption

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

Revised list of experts for the ad hoc expert group meeting adopted via written procedure on 11 July 2017.

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

See 2.1

The CHMP noted SAG report. According to SAG, the available evidence is not sufficient to establish the efficacy of Onzeald in the proposed indication.

The CHMP noted the letter by the applicant concerning the SAG meeting.

The oral explanation to be held on 19 July 2017 at time 09:00 was cancelled, as the CHMP considered that there was no new data available in addition to what was presented during the oral explanation on 16.05.2017 and the responses to the list of outstanding issues adopted on 18.05.17.

The CHMP considered that the benefit of Onzeald in the treatment of breast cancer that had spread to the brain had not been sufficiently demonstrated.

The claim of effectiveness relied on data from a subgroup of patients from a main study which, overall, failed to convincingly show the effectiveness of Onzeald. The Committee considered that the data from this subgroup, which were not supported by additional studies, were not sufficient to prove the effectiveness of Onzeald in patients whose breast cancer had spread to the brain.

Therefore, the CHMP was of the opinion that the study did not provide enough evidence on the benefits of Onzeald and recommended that the marketing authorisation be refused.

The CHMP adopted a negative opinion by majority (23 out of 28 votes) recommending the refusal of the conditional marketing authorisation application. The CHMP adopted the assessment report.

The Norwegian member was in agreement with the CHMP recommendation and the Icelandic member was not.

The divergent position (Andrea Laslop, Dana Gabriela Marin, Katarina Vucic, Kolbeinn Gudmundsson, Robert Hemmings, David Lyons) was appended to the opinion.

The refusal questions and answers document was circulated for information.

Post-meeting note: the applicant submitted the request for re-examination on 26.07.2017.

3.1.9. Rydapt - midostaurin - Orphan - EMEA/H/C/004095

Novartis Europharm Ltd; treatment of mastocytosis and treatment of acute myeloid leukaemia

Scope: Oral explanation/Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 22.06.2017, 21.04.2017. List of Questions adopted on 15.12.2016.

See 2.1

An oral explanation was held on 19 July 2017 at time 09:00. The presentation focused mainly on efficacy data in different age groups.

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

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

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

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

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

The summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 20 July 2017.

The CHMP adopted the similarity assessment report for Rydapt.

3.1.10. Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391

Janssen-Cilag International N.V.; treatment of human immunodeficiency virus type 1 (HIV-1)

Scope: Opinion

Action: For adoption

Fixed combination application (Article 10b of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 18.05.2017. List of Questions adopted on 26.01.2017.

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

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

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

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

The CHMP noted the letter of recommendation dated 19 July 2017.

The summary of opinion was circulated for information.

3.1.11. Tecentriq - atezolizumab - EMEA/H/C/004143

Roche Registration Limited; treatment of locally advanced or metastatic urothelial carcinoma,
treatment of non-small cell lung carcinoma (NSCLC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.04.2017. List of Questions adopted on 15.09.2016.

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (24 out of 30 votes) together with the CHMP assessment report and translation timetable.

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

The Icelandic Member was in agreement with the CHMP recommendation and the Norwegian Member was not.

The divergent position (Alar Irs, Alexandre Moreau, Daniela Melchiorri, Johann Lodewijk Hillege, Natalja Karpova, Sinan B. Sarac, Svein Rune Andersen) was appended to the

opinion.

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

The summary of opinion was circulated for information.

3.1.12. Verkazia ciclosporin - Orphan - EMEA/H/C/004411

Accelerated assessment

Santen Oy; treatment of severe vernal keratoconjunctivitis (VKC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 22.06.2017, List of Questions adopted on 19.04.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.13. Xermelo - telotristat ethyl - Orphan - EMEA/H/C/003937

Ipsen Pharma; treatment of carcinoid syndrome

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.04.2017. List of Questions adopted on 10.11.2016.

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

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

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

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

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

The summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 18 July 2017.

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

3.2.1. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 01.04.2016.

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

The Committee adopted a 2nd list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues.

3.2.2. carmustine - EMEA/H/C/004326

treatment of brain tumors, multiple myeloma, Hodgkin's disease and non-Hodgkin's lymphomas

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 13.10.2016.

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

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

3.2.3. adalimumab - EMEA/H/C/004319

treatment of rheumatoid arthritis, axial spondyloarthritis, psoriasis, hidradenitis suppurativa (HS), Crohn's disease, ulcerative colitis and uveitis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.03.2017.

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

issues.

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

The CHMP adopted the BWP report.

3.2.4. fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781

treatment of adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

3.2.5. guselkumab - EMEA/H/C/004271

treatment of plaque psoriasis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

The CHMP adopted the BWP report.

3.2.6. neratinib - EMEA/H/C/004030

extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.12.2016.

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

The CHMP agreed to the request for an extension to the clock stop to respond to the list of outstanding issues with a specific timetable

3.2.7. naloxone - EMEA/H/C/004325

intended for emergency use for known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.03.2017.

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

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

3.2.8. trastuzumab - EMEA/H/C/004323

treatment of breast cancer and metastatic gastric cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.01.2017.

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

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

The CHMP adopted the BWP report.

3.2.9. ritonavir - EMEA/H/C/004549

treatment of HIV-1

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

3.2.10. tacrolimus - EMEA/H/C/004435

prophylaxis of transplant rejection and treatment of allograft rejection

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

3.2.11. [padeliporfin - EMEA/H/C/004182](#)

treatment of prostate cancer

Scope: Day 180 list of outstanding issue

Action: Oral explanation to be held on 18 July 2017 at time 11:00

Oral explanation 20.04.2017. List of Outstanding Issues adopted on 21.04.2017, 15.12.2016. List of Questions adopted on 26.05.2016.

See 2.1

The CHMP agreed that oral explanation is not needed this time.

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

3.2.12. [fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363](#)

treatment of adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

3.2.13. [buprenorphine / naloxone - EMEA/H/C/004407](#)

treatment for opioid drug dependence, treatment for opioid drug dependence

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.02.2017.

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

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

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

3.3.1. tildrakizumab - EMEA/H/C/004514

treatment of adults with moderate-to-severe plaque psoriasis

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP adopted the BWP report.

3.3.2. trastuzumab - EMEA/H/C/004361

treatment of metastatic breast cancer, early breast cancer, metastatic gastric cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP adopted the BWP report.

3.3.3. letermovir - Orphan - EMEA/H/C/004536

Accelerated assessment

Merck Sharp & Dohme Limited; prophylaxis of cytomegalovirus (CMV) reactivation and disease

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.4. naldemedine - EMEA/H/C/004256

treatment of opioid-induced constipation (OIC) in adult patients

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application

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

3.3.5. brexpiprazole - EMEA/H/C/003841

treatment of schizophrenia

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The CHMP agreed that SAG should be involved in the future.

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

3.3.6. sufentanil - EMEA/H/C/004335

management of acute moderate to severe pain

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP agreed to the request by the applicant for an extension to the clock stop with a specific timetable.

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

3.4.1. dapivirine - EMEA/H/W/002168, Article 58

reducing the risk of HIV-1 infection via vaginal intercourse in sexually active HIV-uninfected women

Scope: Start of the article 58 procedure

Action: For information

The CHMP noted the start of procedure. See also B.6.1.

3.4.2. dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: Letter from the applicant requesting an additional extension of clock stop to respond to the List of Outstanding Issues adopted on 23.03.2017.

Action: For adoption

List of Outstanding Issues adopted on 23.03.2017, List of Questions adopted on 21.07.2016.

The CHMP agreed to the request by the applicant for an additional extension of clock stop to respond to the List of Outstanding Issues adopted on 23.03.2017.

3.4.3. [pegfilgrastim - EMEA/H/C/004262](#)

treatment of neutropenia

Scope: Letter from the applicant dated 12 July 2017 requesting an additional extension of clock stop to respond to the List of Questions adopted on 13 October 2016.

Action: For adoption

List of Questions adopted on 13.10.2016.

The CHMP did not accept the request by the applicant for an additional extension of clock stop to respond to the List of Questions adopted on 13 October 2016, because it was considered that the requested clock stop extension was excessively long and the applicant's proposal was not realistic .

3.4.4. [andexanet alfa - EMEA/H/C/004108](#)

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: Letter from the applicant dated 7 July 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 15 December 2016

Action: For adoption

List of Questions adopted on 15.12.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 15 December 2016.

3.4.5. [metreleptin - Orphan - EMEA/H/C/004218](#)

Aegerion Pharmaceuticals Limited; treatment of leptin deficiency (lipodystrophy)

Scope: Letter from the applicant dated 17 July 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 18.05.2017.

Action: For adoption

List of Questions adopted on 18.05.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 18.05.2017.

3.4.6. nitisinone - EMEA/H/C/004582

treatment of hereditary tyrosinemia type 1

Scope: Letter from the applicant dated 13 July 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 22 June 2017.

Action: For adoption

List of Questions adopted on 22 June 2017

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 22 June 2017.

3.4.7. trastuzumab - EMEA/H/C/004346

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

Scope: Letter from the applicant dated 12 July 2017 requesting an extension of clock stop to respond to the List of Outstanding Issues adopted on 18.05.2017.

Action: For adoption

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

The CHMP did not accept the request by the applicant for an additional extension of clock stop to respond to the List of Outstanding Issues adopted on 18.05.2017, because it was considered that the requested clock stop extension was excessively long and the applicant's proposal was not realistic .

3.4.8. sodium benzoate - Orphan - EMEA/H/C/004150

Lucane Pharma; treatment of non ketotic hyperglycinemia, urea cycle disorders including carbamoyl-phosphate synthase-1 deficiency, ornithine transcarbamylase deficiency, citrullinaemia type 1, argininosuccinic aciduria, hyperargininaemia, n-acetylglutamate synthase deficiency, ornithine translocase deficiency and lysinuric protein intolerance

Scope: Letter from the applicant dated 18 July 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 22.06.2017.

Action: For adoption

List of Questions adopted on 22.06.2017.

Rejected

The CHMP did not accept the request by the applicant for an additional extension of clock stop to respond to the List of Questions adopted on 22.06.2017.

Another request was made by the applicant to extend the clock-stop and CHMP agreed to this.

3.4.9. rotigotine - EMEA/H/C/004286

treatment of idiopathic Restless Legs Syndrome and Parkinson's disease

Scope: Request by the applicant dated 11 July 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 21 April 2017.

Action: For adoption

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 21 April 2017.

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

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

AB Science; treatment of mastocytosis

Scope: SAG list of questions, re-examination timetable

Letter from the applicant dated 31 May 2017 requesting a re-examination of the Opinion adopted on 18 May 2017 and consultation of a Scientific Advisory Group

Action: For adoption

Opinion adopted on 18.05.2017.

The CHMP discussed the list of questions to the SAG and adopted the re-examination timetable. The final list of questions will be adopted via written procedure after the Plenary.

3.5.2. Adlumiz - anamorelin - EMEA/H/C/003847

Helsinn Birex Pharmaceuticals Ltd; treatment of anorexia, cachexia or unintended weight loss in adult patients with non-small cell lung cancer (NSCLC)

Scope: re-examination timetable

Action: For adoption

Opinion adopted on 18.05.2017.

The CHMP adopted the re-examination timetable.

3.5.3. Human IGG1 monoclonal antibody specific for human interleukin-1 alpha XBiotech - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388

XBiotech Germany GmbH; treatment of metastatic colorectal cancer

Scope: re-examination timetable

Action: For adoption

Opinion adopted on 18.05.2017.

The CHMP adopted the re-examination timetable.

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. Prolia - denosumab - EMEA/H/C/001120/X/0059/G

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application."

Action: For adoption

List of Outstanding Issues adopted on 18.05.2017. List of Questions adopted on 26.01.2017.

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

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

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

4.1.2. Samsca - tolvaptan - EMEA/H/C/000980/X/0024

Otsuka Pharmaceutical Europe Ltd

Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams

Scope: "Extension application to add a new strength of 7.5 mg tablets."

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

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

4.1.3. Signifor - pasireotide - Orphan - EMEA/H/C/002052/X/0030/G

Novartis Europharm Ltd

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension application to introduce two new strengths of the 'powder and solvent for suspension for injection pharmaceutical form' (10 mg and 30 mg) grouped with a type II variation (C.I.6.a) to extend the indication to include 'Treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed' to the intramuscular injection formulations."

Action: For adoption

List of Questions adopted on 21.04.2017.

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

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

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

4.1.4. Xgeva - denosumab - EMEA/H/C/002173/X/0048/G

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application."

Action: For adoption

List of Outstanding Issues adopted on 18.05.2017. List of Questions adopted on 26.01.2017.

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

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

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

4.1.5. Xtandi - enzalutamide - EMEA/H/C/002639/X/0029

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia

Scope: "To add new pharmaceutical form and strengths (film-coated tablets 40 mg and 80 mg) to the currently approved presentations for Xtandi."

Action: For adoption

List of Questions adopted on 21.07.2016.

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

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

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

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

4.2.1. Tasigna - nilotinib - Orphan - EMEA/H/C/000798/X/0088/G

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include treatment of paediatric patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukemia in chronic phase (Ph+ CML-CP), or with Ph+ CML-CP resistant or intolerant to prior therapy including imatinib, based on results from two clinical studies in paediatric patients conducted in accordance with the approved Tasigna Paediatric Investigation Plan (PIP), the Phase I PK study CAMN107A2120 and the Phase II safety and efficacy study CAMN107A2203. An updated RMP version 18.0 was provided as part of the application.

Extension application to add a new strength of 50mg hard capsules.

In addition, the applicant proposes to merge the SmPCs for the 50 mg and 200 mg strengths."

Action: For adoption

List of Questions adopted on 23.03.2017.

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication in terms of age cut-off of the paediatric population. The members discussed the available clinical data and considered the indication in newly diagnosed Ph+ CML patients below 6 years of age requires further justification.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

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

4.3.1. Bortezomib Accord - bortezomib - EMEA/H/C/003984/X/0008

Accord Healthcare Ltd

Rapporteur: Milena Stain, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension application to add a new strength of powder for solution for injection (1 mg) to the currently approved strength (3.5 mg) of Bortezomib Accord."

Action: For adoption

The Committee discussed the issues identified in this application. The Committee noted the questions related quality, clinical aspects and similarity assessment. The applicant should update the similarity report including further quality information and adding a scientific comparison/discussion of the therapeutic indications, mechanism of action and molecular structure of the orphan drugs.

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

4.3.2. Daliresp - roflumilast - EMEA/H/C/002398/X/0031

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: David Lyons, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

The Committee discussed the issues identified in this application. The main discussion related to some quality and clinical aspects.

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

4.3.3. Daxas - roflumilast - EMEA/H/C/001179/X/0035

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: David Lyons, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

The Committee discussed the issues identified in this application. The main discussion

related to some quality and clinical aspects.

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

4.3.4. Humira - adalimumab - EMEA/H/C/000481/X/0164/G

AbbVie Limited.

Rapporteur: Kristina Dunder

Scope: "Extension application to add a new strength/potency of 20 mg for adalimumab solution for injection in pre-filled syringe, grouped with a type II variation (C.I.4.z) to update of sections 4.2 of the SmPC in order to introduce new fixed dose regimen (posology) for the paediatric indications of JIA and Ps. The Package Leaflet and Labelling are updated accordingly.

In addition, the marketing authorisation holder took the opportunity to:

- introduce editorial changes to align wording and layout of the Product Information
- to amend the statement relating to anti-adalimumab antibody development in JIA patients, which will reside in section 5.1 of the Humira SmPCs (20 mg and 40 mg presentations)."

Action: For adoption

The Committee discussed the issues identified in this application. It was concluded that the clinical safety data that the applicant provided in support of the fixed dose is somewhat incomplete. Further information is needed before a final conclusion can be drawn and this information is requested.

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

4.3.5. Libertek - roflumilast - EMEA/H/C/002399/X/0032

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: David Lyons, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

The Committee discussed the issues identified in this application. The main discussion related to some quality and clinical aspects.

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

4.3.6. Oncaspar - pegaspargase - EMEA/H/C/003789/X/0008

Baxalta Innovations GmbH

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

Scope: "Extension application to add a new pharmaceutical form, powder for solution for injection/infusion (750 U/ml)."

Action: For adoption

The Committee noted the issues identified in this application. The identified issues related to the quality part, the pharmacokinetics, the RMP and some regulatory issues.

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

4.3.7. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0020

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Almath Spooner

Scope: "Extension application to add a new strength of film-coated tablets (100 mg Lumacaftor / 125 mg Ivacaftor) for paediatric use (6 to 11 years). The RMP (version 3.1) is updated accordingly.

CHMP assessment report on similarity

CHMP assessment report on significant clinical benefit (additional year of market exclusivity)"

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP noted that there is still substantial concern around a transient drug-induced bronchoconstrictive effect that is not yet sufficiently understood or what the safety implications may be. Although there is no clear evidence that this is a greater risk in the younger age group there is also insufficient assurance this is not the case. The questions to be addressed by the applicant seek a more robust understanding.

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

The CHMP adopted the assessment report on similarity of Orkambi.

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/0048

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC
Rapporteur: Sabine Straus

Scope: "Extension of indication to include the new indication "ADCETRIS is indicated for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) who require systemic therapy", based on data from study C25001 (the 'ALCANZA' study): "A Phase 3 Trial of brentuximab vedotin(SGN-35) Versus Physician's Choice (Methotrexate or Bexarotene) in Patients With CD30-Positive Cutaneous T-Cell Lymphoma". 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. An updated RMP (version 10) has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application. The questions to be addressed by the applicant, are whether the positive benefit-risk established in MF and pcALCL can be extrapolated to other types of CTCL and to the first line treatment setting.

The Committee adopted a request for supplementary information with a specific timetable.

The CHMP adopted the BWP report.

The CHMP adopted the assessment report on similarity of Adcetris.

5.1.2. Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0142

Amgen Europe B.V.

Rapporteur: Martina Weise, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Valerie Strassmann

Scope: "Extension of Indication to include treatment of anaemia in adult patients with low transfusion demand in low or intermediate-1-risk myelodysplastic syndromes for Aranesp; as a consequence, sections 4.1, 4.2,4.8, 5.1 and 5.2 of the SmPC are updated in order to update the safety and efficacy information. The Package Leaflet is updated in accordance. Updated RMP version 8.0 has been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce QRD editorial changes in the SmPC, Annex IIIA and Annex IIIB."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to biometrical and clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.3. Bydureon - exenatide - EMEA/H/C/002020/II/0041

AstraZeneca AB

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of indication for Bydureon to include the add-on use of exenatide in combination with dapagliflozin to patients whose diabetes is not adequately controlled with metformin based on the study D5553C00003 (Duration 8 study); section 4.1 of the SmPC is updated in order to align the indication wording with more recently approved glucose-lowering agents. Section 5.1 of the SmPC is also updated with the results of study D5553C00003 (Duration 8 study). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet and to update the Irish local representative information in the Package Leaflet. Furthermore, the consolidated RMP version 27 has been agreed."

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017.

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

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

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

5.1.4. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include a new indication for Gazyvaro in combination with chemotherapy, followed by Gazyvaro maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance. In addition, the due date for provision of the final clinical study report of study BO21223/GALLIUM listed in the Gazyvaro RMP as Category 3 has been updated.

Furthermore, the PI is brought in line with the missing information of QRD template version 9.1 regarding annex II C. In addition, clarification or editorial changes to the SmPC are proposed for accuracy and clarity." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 18.05.2017, 26.01.2017.

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

The Committee adopted a positive opinion by majority (26 out of 27 votes) together with the CHMP Assessment Report and translation timetable.

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

The divergent position (Johann Lodewijk Hillege) was appended to the opinion.

The summary of opinion was circulated for information.

The CHMP agreed to the request for 1 year of market protection for a new indication.

5.1.5. [Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0026](#)

Gilead Sciences International Ltd

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of Indication to include paediatric patients from 6 of age to less than 12 years of age, with body weight of at least 25kg, infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir, for Genvoya.

As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the analysis of the paediatric study GS-US-292-0106 (Cohort 2) "A Phase 2/3, Open-Label Study of the Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in HIV-1 Infected Antiretroviral Treatment Naive Adolescents and Virologically Suppressed Children".

The Package Leaflet and the Risk Management Plan (v. 3) are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017.

The Committee discussed the issues identified in this application. The Committee concluded that the extension of indication is not adequately supported by the data.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.6. [Humira - adalimumab - EMEA/H/C/000481/II/0163](#)

AbbVie Limited.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wandel Liminga

Scope: "Extension of Indication to include a new indication for Humira for the treatment of paediatric chronic non-infectious anterior uveitis in patients from 2 years of age who have had an inadequate response to or are intolerant to conventional therapy, or in whom

conventional therapy is inappropriate; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet was updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement an alternative format statement for blind/partially sighted patients in the Package Leaflet. Furthermore, the MAH has made some editorial changes to the Package Leaflet.”

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017.

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

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

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

The CHMP noted the letter of recommendation dated 17 July 2017.

The summary of opinion was circulated for information.

5.1.7. [Keytruda - pembrolizumab - EMEA/H/C/003820/II/0023/G](#)

Merck Sharp & Dohme Limited

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: “Grouped application including:

Extension of Indication to add treatment as monotherapy of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy based on the results from study KEYNOTE-045; a phase 3, randomized, active-controlled, multi-site, open-label trial evaluating pembrolizumab administered at 200 mg Q3W versus investigators’ choice of paclitaxel, docetaxel, or vinflunine in patients previously treated with chemotherapy.

Extension of Indication to add treatment as monotherapy of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy based on the results from study KEYNOTE-52; a phase 2, single-arm, multisite, open-label trial of pembrolizumab at 200 mg Q3W in the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. Further, the MAH is taking the opportunity to implement a change to section 4.4 of the SmPC adding possible hypersensitivity and anaphylaxis as part of infusion reactions. In addition, Annex II has been updated to include new Post-authorisation efficacy studies (PAES) as obligations under ‘conditions or restrictions with regard to the safe and effective use of the medicinal product’. An updated RMP version 7.2 was agreed during the procedure.”

Action: For adoption

Request for Supplementary Information adopted on 18.05.2017.

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

The Committee adopted a positive opinion by majority (24 out of 28 votes) together with the CHMP Assessment Report and translation timetable.

The Icelandic CHMP member was in agreement with the CHMP recommendations and the Norwegian CHMP member was not.

The divergent position (Johann Lodewijk Hillege, Alexandre Moreau, Romaldas Maciulaitis, Sinan B. Sarac, Svein Rune Andersen) was appended to the opinion.

The summary of opinion was circulated for information.

5.1.8. Kineret - anakinra - EMEA/H/C/000363/II/0056

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Torbjorn Callreus

Scope: "Extension of indication to include a new indication for Kineret 100 mg/0.67 ml solution for injection in pre-filled syringe for the treatment of active Still's disease, including Systemic Juvenile Idiopathic Arthritis and Adult-Onset Still's Disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 4.0) are updated accordingly.

In addition, the marketing authorisation holder took the opportunity to make some editorial changes in the SmPC and Package leaflet."

Action: For adoption

The Committee discussed the issues identified in this application, which was related to the first line use of the product and severity of disease.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.9. Olumiant - baricitinib - EMEA/H/C/004085/II/0001

Eli Lilly Nederland B.V.; treatment of moderate to severe active rheumatoid arthritis (RA)

Scope: "Update of section 4.4 of the SmPC in order to add a warning on venous thromboembolism based on analyses of the occurrence of venous thromboembolic events in clinical trials with baricitinib. The Package Leaflet is updated accordingly. The RMP version 2.0 has been submitted, as part of this application."

Action: For adoption

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

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

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

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

5.1.10. Opdivo - nivolumab - EMEA/H/C/003985/II/0029

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include the treatment of hepatocellular carcinoma after prior sorafenib therapy in adults for Opdivo.

As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

Moreover, the updated RMP version 8.0 has been submitted."

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017, 23.03.2017.

See 2.3

An oral explanation was held on 19 July 2017 at time 15:00. The presentation mainly related to the clinical trial design and outcome.

The CHMP noted that the applicant withdrew the variation application.

5.1.11. Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0091

Roche Registration Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to include paediatric patients from 3 to less than 18 years of age with Chronic Hepatitis B in the immune-active phase for Pegasys.

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 efficacy and safety information from study YV25718. The Package Leaflet is updated in accordance.

An updated EU RMP (version 8.0) is included in this application."

Action: For adoption

Request for Supplementary Information adopted on 23.02.2017.

The Committee discussed the issues identified in this application, which were related to clinical efficacy and safety outstanding issues.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.12. Rapamune - sirolimus - EMEA/H/C/000273/II/0164

Pfizer Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 6.0) are updated in accordance. In addition the MAH took the opportunity to make very minor formatting

changes in the Labelling.”

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the use of product in target population and its clinical relevance. The CHMP noted the need for similarity assessment, which was requested from the applicant to be submitted with the responses to the RSI.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.13. [RoActemra - tocilizumab - EMEA/H/C/000955/II/0066](#)

Roche Registration Limited

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: “Extension of indication to include an indication in adult patients for the treatment of giant cell arteritis for the subcutaneous formulation of RoActemra. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect information relevant to this indication. The Package Leaflet is updated in accordance.”

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017, 23.03.2017.

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

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

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

The summary of opinion was circulated for information.

5.1.14. [Sovaldi - sofosbuvir - EMEA/H/C/002798/II/0036](#)

Gilead Sciences International Ltd

Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

Scope: “Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to <18 years.

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 on posology, warnings, safety, efficacy and pharmacokinetics.

The Package Leaflet and Risk Management Plan (RMP version 5.2) are updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

Furthermore, the Product Information is brought in line with the latest QRD template version 10.”

Action: For adoption

Request for Supplementary Information adopted on 18.05.2017, 23.02.2017.

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

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

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

The summary of opinion was circulated for information.

5.1.15. Sutent - sunitinib - EMEA/H/C/000687/II/0065

Pfizer Limited

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension of Indication to include adjuvant treatment of patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy for Sutent; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on the study A6181109 ("a randomized double-blind phase 3 study of adjuvant sunitinib vs. placebo in subjects at high risk of recurrent RCC"). The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and Package Leaflet and in addition, to fulfil PAM (FU2 22.5). Furthermore, the PI is brought in line with the latest QRD template version 10. Moreover, updated RMP version 16 has been submitted."

Action: For adoption

The Committee discussed the issues identified in this application which were related to clinical efficacy and safety aspects. The Committee adopted a request for supplementary information with a specific timetable.

The CHMP adopted the similarity assessment report for Sutent.

5.1.16. Vimpat - lacosamide - EMEA/H/C/000863/II/0065/G

UCB Pharma S.A.

Rapporteur: Filip Josephson, Co-Rapporteur: Luca Pani, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to extend the indication for Vimpat to monotherapy and adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adolescents and children aged 4 to less than 16 years with epilepsy. For the treatment initiation pack, the use was only extended to adolescents weighting 50 kg or more as it is not suitable for the weight-based dosing regimen recommended for patients weighing less. Sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2 and 5.3 of the SmPC have been updated including the addition of a warning of the potential for electro-clinical worsening in specific epileptic syndromes. The Package Leaflet was updated in accordance. Moreover, section 6.3 of the SmPC of the syrup is updated to reflect the extension of shelf life after first opening from 4 weeks to 2 months. Furthermore, a 10 mL dosing syringe for the 200 ml and the 465 ml syrup bottles is introduced as additional dosing device for paediatric

population; section 6.5 of the SmPC of the syrup presentations is updated accordingly. Finally, the PI was also brought in line with the latest QRD template version and editorial amendments were made in several sections. The MAH also took the opportunity to introduce a combined SmPC for the film coated tablets. Moreover, updated RMP version 12.2 has been agreed.”

Action: For adoption

Request for Supplementary Information adopted on 18.05.2017, 10.11.2016.

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

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

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

The summary of opinion was circulated for information.

5.1.17. Xgeva - denosumab - EMEA/H/C/002173/II/0055

Amgen Europe B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension of Indication to include “Prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with multiple myeloma and in adults with bone metastases from solid tumours” for Xgeva; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.”

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.18. Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0047

Janssen-Cilag International NV

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Eva A. Segovia

Scope: “Extension of indication to include the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer and in combination with androgen deprivation therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 14.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet”

Action: For adoption

The Committee discussed the issues identified in this application, which were related to clinical efficacy and safety aspects.

The Committee adopted a request for supplementary information with a specific timetable.

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. Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/02617/II/0072

AstraZeneca UK Ltd

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Bart Van der Schueren

Scope: "To replace the strain of a seasonal vaccine against human influenza in line with the EU recommendations for the seasonal influenza vaccine composition for the season 2017/2018."

Action: For information

Request for Supplementary Information adopted on 22.06.2017

The CHMP was updated on HAI tests performed by the WHO.

The CHMP adopted the BWP report.

5.2.2. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/17

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Almath Spooner

PM: Elisa Pedone, EPL: Andrea Taft, QM: Dolores Hernan Perez de la Ossa

Scope: Request by the applicant dated 3 July 2017 requesting an extension of clock stop to respond to the second Request for Supplementary Information adopted on 18.05.2017.

Action: For adoption

Request for Supplementary Information adopted on 18.05.2017, 23.02.2017

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the second Request for Supplementary Information adopted on 18.05.2017

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. durvalumab - H0004771

treatment of patients with locally advanced, unresectable NSCLC whose disease has not progressed following platinum-based chemoradiation therapy

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

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 8 recommendations for eligibility to PRIME: 1 was accepted. 7 were denied. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

- 9.1.1. Aranesp (CAP) - darbepoetin alfa – EMEA/H/C/000332/SDA/091;
Abseamed (CAP) - epoetin alfa – EMEA/H/C/000727/SDA/029,
Binocrit (CAP) - epoetin alfa – EMEA/H/C/000725/SDA/028,
Epoetin alfa hexal (CAP) - epoetin alfa – EMEA/H/C/000726/SDA/030; NAP
Neorecormon (CAP) - epoetin beta – EMEA/H/C/000116/SDA/055;
Biopoin (CAP) - epoetin theta – EMEA/H/C/0001036/SDA/022,
Eporatio (CAP) - epoetin theta – EMEA/H/C/0001033/SDA/022;
Retacrit (CAP) - epoetin zeta – EMEA/H/C/000872/SDA/046,
Silapo (CAP) - epoetin zeta – EMEA/H/C/000760/SDA/039
MIRCERA (CAP) - methoxy polyethylene glycol-epoetin beta -
EMEA/H/C/000739/SDA/039; NAP
-

Applicants: Amgen Europe B.V. (Aranesp), Hexal AG (Epoetin Alfa Hexal), Hospira UK Limited (Retacrit), Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Roche Registration Limited (Neorecormon, Mircera), Ratiopharm GmbH (Eporatio), Sandoz GmbH (Binocrit), Stada Arzneimittel AG (Silapo), Teva GmbH (Biopoin); various

Rapporteur: Martina Weise, Co-Rapporteur: Koenraad Norga (Aranesp), Rapporteur: Alexandre Moreau, Co-Rapporteur: Martina Weise (Abseamed, Binocrit, Biopoin, Eporatio, Epoetin Alfa Hexal, Mircera), Rapporteur: Martina Weise, Co-Rapporteur: Alexandre Moreau (NeoRecormon), Rapporteur: Martina Weise, Co-Rapporteur: Nithyanandan Nagercoil (Retacrit, Silapo)

Scope: DHPC letter and communication plan

Action: For adoption

The CHMP agreed to the DHPC and communication plan.

- 9.1.2. CHMP request for PRAC advice on Fluoropyrimidines (Capecitabine-Xeloda and 5-FU), EMEA/H/C/0316/LEG-033.1
-

Xeloda, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber

Scope: PRAC Advice to CHMP following formal advice from PgWP regarding the proposed SmPC changes for upfront testing of patients for DPYD variants and dose reduction based on patient's genotype to reduce the toxicity of capecitabine and 5-FU y

Action: For adoption

The CHMP endorsed the PRAC advice.

9.1.3. Vedrop - tocofersolan – Orphan - EMEA/H/C/000920/II/0022

Orphan Europe SARL

Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

Scope: "Submission of the final report for the registry of paediatric patients treated with Vedrop (tocofersolan) in Europe for vitamin E deficiency due to digestive malabsorption in congenital or hereditary chronic cholestasis. Consequentially, the remaining specific obligation is fulfilled and Annex II is updated accordingly."

Action: For adoption

The Committee confirmed that the remaining specific obligations on this marketing authorisation had been fulfilled. As the data are still not as comprehensive as a full marketing authorisation would require, the MAH shall therefore continue to provide yearly updates on any new information concerning efficacy and safety of the product in patients with congenital chronic cholestasis or hereditary cholestasis as a condition (specific obligation) to the marketing authorisation under exceptional circumstances.

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

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

9.1.4. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0009 & R/0013

MAH: Amgen Europe B.V.

Rapporteur: Pierre Demolis

Scope: "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information with the data from the study 103311. This study is fulfilling the specific obligation for the conditional MA. The SO is removed from annex II. The Package Leaflet is updated accordingly.

The MAH takes this opportunity to amend the format of the preparation instructions to improve clarity. The content is not impacted."

Rapporteur: Pierre Demolis, Co-Rapporteur: Daniela Melchiorri

Scope: Renewal

Action: For adoption

Request for Supplementary Information adopted on 26.01.2017.

The Committee discussed the issues identified in this application.

The Committee adopted a 2nd request for supplementary information.

The CHMP agreed to harmonise the timetable for the renewal and the type II variation II/09.

The CHMP agreed to consult the SAG Oncology and adopted a list of question to this group.

9.1.5. Opdivo - nivolumab - EMEA/H/C/003985/II/0030

Bristol-Myers Squibb Pharma EEIG

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

Scope: Letter from the applicant dated 04 July 2017 requesting an extension of clock stop to respond to Request for supplementary information adopted on 23.03.2017

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Request for supplementary information adopted on 23.03.2017.

9.1.6. Data collection on adverse events of anti-HIV drugs (D:A:D) study - Evaluation of D:A:D data

Action: For adoption

The CHMP adopted the data merger report.

10. Referral procedures

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

No items

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

No items

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

No items

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

No items

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

No items

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

10.6.1. Gadolinium-containing contrast agents (GdCA): gadoversetamide – OPTIMARK (CAP) Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intravenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)

Applicant(s): Guerbert (Optimark); various

Rapporteurs for the Article 31 referral: PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Doris Stenver

PRAC Rapporteur of the re-examination: Ulla Wändel Liminga; PRAC Co-rapporteur of the re-examination: Valerie Strassmann

Rapporteurs for Optimark: CHMP Rapporteur: Patrick Salmon, CHMP Co-rapporteur: Johann Lodewijk Hillege

Scope: Oral explanation/Opinion

Action: For adoption

CHMP opinion following PRAC final recommendation

See 2.4

Four oral explanations were held on 18 July 2017. The companies invited to take part in the oral explanations were Bayer, Bracco, GE Healthcare and Guerbet. The presentations focused on data in relation to gadolinium deposition in brain and other tissues and the overall benefit-risk profiles of these products

The CHMP was updated on discussions at the PRAC and discussed the grounds for the PRAC recommendation and the conditions for lifting the suspension.

The CHMP discussed further the PRAC recommendation and possible divergent views.

The CHMP, having considered the PRAC recommendation, adopted an opinion by majority (19 out of 31 votes) recommending that the marketing authorisations for products containing gadodiamide, gadopentetic acid and gadoversetamide for intravenous use should be suspended. Furthermore, the CHMP recommended that the marketing authorisations for medicinal products containing intravenous gadobutrol, gadoteric acid, gadoteridol, gadoxetic acid, gadobenec acid, intra-articular gadoteric acid and intra-articular gadopentetic acid should be varied.

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

The divergent positions (Agnes Gyurasics, Alar Irs, Andrea Laslop, Bruno Sepodes, Daniela Melchiorri, David Lyons, John Joseph Borg, Kristina Dunder, Natalja Karpova, Romaldas Maciulaitis, Tomas Boran, Ewa Balkowiec Iskra, Svein Rune Andersen, Kolbeinn Gudmundsson) were appended to the opinion.

DHPC and communication plan were adopted via written procedure on 18.08.2017.

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

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

D&A Pharma

Rapporteur: Andrea Laslop, Co-Rapporteur: Fatima Ventura,

Scope: Appointment of re-examination rapporteurs, draft timetable, SAG involvement

Letter from the applicant dated 30 June 2017 requesting a re-examination of the Opinion adopted on 22 June 2017 and consultation of a Scientific Advisory Group

Action: For adoption

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

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

The CHMP appointed a re-examination Rapporteur and a re-examination Co-Rapporteur.

The CHMP noted the draft re-examination timetable.

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

The CHMP noted the July 2017 Early Notification System.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

The CHMP noted the minutes.

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Time schedule of CHMP August written procedure

Action: For information

The CHMP noted the time schedule of the CHMP August written procedure.

14.1.2. Pilot phase for abolition of signatures for divergent positions for referral procedures

The proposal is to start new process from September onwards.

Action: For information

The CHMP agreed to the proposal for abolition of signatures for divergent positions for referral procedures. The new process might be extended to other divergent positions in the future.

14.1.3. Confirmation of joint CHMP/PDCO membership for Romania

Romania - Simona Badoi and Dana Gabriela Marin

Action: For adoption

The CHMP appointed Simona Badoi and Dana Gabriela Marin as joint CHMP/PDCO members.

14.1.4. Update to the CHMP templates on initial Marketing Authorisation

Update to the Rapporteurs' D80 AR overview guidance document to add guidance specific to biosimilars (including a revised Benefit/Risk balance section). When adopted, the changes will be implemented in all relevant templates on initial MA.

Action: For adoption

The CHMP noted the update on the assessment report templates. Any comments should be sent **by 1st September 2017**. In the absence of comments the document will be considered adopted.

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 3-6 July 2017

Action: For information

The CHMP noted the Summary of recommendations and advice of PRAC meeting held on 3-6 July 2017.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for July 2017

Action: For adoption

The CHMP adopted the EURD list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 12-14 July 2017

Action: For information

The CHMP noted the minutes.

Revision of Procedural advice on the evaluation of Advanced Therapy Medicinal Product in accordance with Article 8 of Regulation (EC) NO 1394/2007

Action: For information

The CHMP noted the revision. Comments should be sent by 31 July 2017.

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at July 2017 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 18-21 July 2017

Action: For information

The CHMP noted the information.

Advice from the CHMP and PDCO task force on how to address issues related to therapeutic equivalence for orally inhaled products for children

Action: For adoption

No comments from members were received on the CHMP PDCO advice.

The CHMP adopted the advice.

EMA/FDA/Health Canada workshop on paediatric pulmonary hypertension (PAH) – meeting highlights

Action: For information

The CHMP noted the information.

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 11-13 July 2017

Action: For information

The CHMP noted the report.

14.2.5. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 17-19 July 2017.

Action: For information

The CHMP noted the report.

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 3-6 July 2017. Table of conclusions

Action: For information

The CHMP noted the report.

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

14.3.2. Quality Working Party (QWP)

Chair: Keith Pugh

Election of QWP Vice Chair, the term of the current Chair ending in July 2017.

Action: For adoption

The CHMP elected Blanka Hirschlerova (CZ) as vice-chair of the QWP.

Guideline on Manufacture of the Finished Dosage Form (EMA/CHMP/QWP/BWP/245074)

Action: For adoption

The CHMP adopted the guideline. The guideline replaces the note for guidance on the manufacture of the finished dosage form (CPMP/QWP/486/95). The note for guidance has been updated to reflect the requirements as laid down in the current legislation (Directive

2001/83/EC, and to follow the format and content of the Common Technical Document (CTD) Module 3 dossier. It also addresses current manufacturing practices in terms of complex supply chains and worldwide manufacture. In addition, the content and principles of the ICH Q8 guideline are also taken into account.

14.3.3. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

Guideline on core SmPC and Package Leaflet for (68Ge-68Ga) generator (EMA/313282/2017)

Action: For adoption

Overview of comments 'Guideline on core SmPC and Package Leaflet for (68Ge/68Ga)' (EMA/313283/2017)

Action: For information

The CHMP adopted the guideline and noted the overview of comments. The purpose of this core SmPC and package leaflet is to provide applicants and regulators with harmonised guidance on the information to be included in the Summary of product characteristics (SmPC) for (68Ge/68Ga) generator. This guideline should be read in conjunction with the core SmPC and package leaflet for Radiopharmaceuticals, the QRD product information templates and the guideline on Summary of Product Characteristics.

14.3.4. CHMP Guidelines Consistency Group (GCG)

Chair: Barbara van Zwieten-Boot

Nomination of new member to the GCG

Action: For adoption

The CHMP appointed Andreas Kirisits (AT) as new member to the GCG.

14.3.5. Blood Product Working Party (BPWP)

Chair: Jacqueline Kerr

BPWP 2017 work plan has been modified with a change of date of face-to-face meeting in November 2017.

Action: For adoption

The CHMP adopted the revised BPWP 2017 work plan

14.4. Cooperation within the EU regulatory network

None

14.5. Cooperation with International Regulators

None

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

None

14.7. CHMP work plan

14.7.1. CHMP 2017 Work Plan: mid-year update

Action: For information

The CHMP noted the status update of work plan activities. Members were invited to send any comments over the summer.

14.8. Planning and reporting

None

14.9. Others

None

15. Any other business

15.1. AOB topic

15.1.1. Working group on Committees' operational preparedness for human medicines

Scope: CHMP representatives to this Cross-Committee working group

Action: For information

The CHMP was updated on recent discussions.

15.1.2. Revision of the 'Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products'

CHMP Rapporteur: Harald Enzmann

Scope: Final revised guideline to be published

Action: For adoption

The CHMP adopted the revised guideline. The revision is intended to further assist stakeholders in the transition from non-clinical to early clinical development and in identifying factors influencing risk for new investigational medicinal products (IMPs). The document includes considerations on quality aspects, non-clinical and clinical testing strategies, study design and on conduct of FIH/early CTs. Strategies for mitigating and managing risks are

given, including principles on the calculation of the starting dose to be used in humans, the subsequent dose escalations, the criteria for maximum dose and the conduct of the trial inclusive of multiple parts.

15.1.3. Bridging the regulator and the payer world

Scope: presentation

Action: For information

The CHMP noted the update.

16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/ experts following evaluation of declared interests for the 17 – 20 July 2017 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Tomas Boran	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Hanne Lomholt Larsen	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Eleftheria Nikolaidi	Member	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Luca Pani	Alternate	Italy	No interests declared	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	3.1.11. Tecentriq - atezolizumab - EMEA/H/C/004143 5.1.4. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016 5.1.11. Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0091 5.1.13. RoActemra - tocilizumab - EMEA/H/C/000955/II/0066 9.1.1. Neorecormon (CAP) - epoetin beta – EMEA/H/C/000116/SD A/055; MIRCERA (CAP) - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/SD A/039
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Aldona Paluchowska	Alternate	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Eva Malikova	Member – via Adobe	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Member	Spain	No participation in final deliberations and voting on:	<p>3.1.11. Tecentriq - atezolizumab - EMEA/H/C/004143</p> <p>5.1.4. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016</p> <p>5.1.11. Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0091</p> <p>5.1.13. RoActemra - tocilizumab - EMEA/H/C/000955/II/0066</p> <p>9.1.1. Neorecormon (CAP) - epoetin beta – EMEA/H/C/000116/SD A/055; MIRCERA (CAP) - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/SD A/039</p>
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No interests declared	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	3.2.4. - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781 3.2.12. - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Kristina Bech Jensen	Expert - in person*	Denmark	No interests declared	
Örn Gudmundsson	Expert - in person*	Iceland	No interests declared	
Ulla Wändel Liminga	Expert - in person*	Sweden	No interests declared	
Valerie Strassmann	Expert - in person*	Germany	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Maria Escudero Galindo	Expert - in person*	Spain	No participation in final deliberations and voting on:	3.1.4. Entecavir Mylan - entecavir - EMEA/H/C/004377 3.4.3. - pegfilgrastim - EMEA/H/C/004262 3.4.7. - trastuzumab - EMEA/H/C/004346 3.4.9. - rotigotine - EMEA/H/C/004286
Valerie Lescrainier	Expert - in	Belgium	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
	person*			
Peter Kiely	Expert - in person*	Ireland	No interests declared	
Sylvan Gueho	Expert - in person*	France	No interests declared	
Pierre Demolis	Expert - via telephone*	France	No interests declared	
Barbara Spruce	Expert - via telephone*	UK	No restrictions applicable to this meeting	
Benoy Daniel	Expert – via telephone*	UK	No interests declared	
Jan-Willem van der Laan	Expert - via telephone*	Netherlands	No interests declared	
Ingrid Wang	Expert - via telephone*	Norway	No interests declared	
June Raine	Expert - via telephone*	UK	No interests declared	
John Clements	Expert - via telephone*	UK	No restrictions applicable to this meeting	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Patrick Batty	Expert - via telephone*	UK	No interests declared	
Ingrid Bourges	Expert - via telephone*	Belgium	No restrictions applicable to this meeting	
João Freire	Expert - via telephone*	Portugal	No restrictions applicable to this meeting	
Anabel Cortés Blanco	Expert - via telephone*	Spain	No interests declared	
Susanne Brendler-Schwaab	Expert - via Adobe*	Germany - BfArM	No interests declared	
Janet Schriever	Expert - via Adobe*	Germany - BfArM	No interests declared	
Ralf Meyer	Expert – via Adobe*	Germany - BfArM	No interests declared	
Tobias Lamkemeyer	Expert - via Adobe*	Germany - BfArM	No interests declared	
Tim Leest	Expert - via Adobe*	Belgium	No restrictions applicable to this meeting	
Coraline Claeys	Expert - via Adobe*	Belgium	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

17. 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 *(section 5.3)*

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 Pharmacovigilance 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/

15 September 2017
EMA/CHMP/628544/2017

Annex to July 2017 CHMP Minutes

Pre submission and post authorisations issues

A. PRE SUBMISSION ISSUES	3
A.1. ELIGIBILITY REQUESTS	3
A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications	3
A.3. PRE-SUBMISSION ISSUES FOR INFORMATION	3
B. POST-AUTHORISATION PROCEDURES OUTCOMES	3
B.1. Annual re-assessment outcomes	3
B.1.1. Annual reassessment for products authorised under exceptional circumstances	3
B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES	3
B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal	3
B.2.2. Renewals of Marketing Authorisations for unlimited validity	3
B.2.3. Renewals of Conditional Marketing Authorisations	5
B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES	6
B.4. EPARs / WPARs	11
B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES	12
B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects	12
B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects	17
B.5.3. CHMP-PRAC assessed procedures	33
B.5.4. PRAC assessed procedures	47
B.5.5. CHMP-CAT assessed procedures	52
B.5.6. CHMP-PRAC-CAT assessed procedures	52
B.5.7. PRAC assessed ATMP procedures	52
B.5.8. Unclassified procedures and worksharing procedures of type I variations	52
B.5.9. Information on withdrawn type II variation / WS procedure	54
B.5.10. Information on type II variation / WS procedure with revised timetable	54
B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION	54
B.6.1. Start of procedure for New Applications: timetables for information	54
B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information	56
B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information	56
B.6.4. Annual Re-assessments: timetables for adoption	58

B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed	58
B.6.6. VARIATIONS – START OF THE PROCEDURE.....	59
B.6.7. Type II Variations scope of the Variations: Extension of indication	59
B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects	60
B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects.....	62
B.6.10. CHMP-PRAC assessed procedures.....	72
B.6.11. PRAC assessed procedures	79
B.6.12. CHMP-CAT assessed procedures	81
B.6.13. CHMP-PRAC-CAT assessed procedures.....	81
B.6.14. PRAC assessed ATMP procedures	81
B.6.15. Unclassified procedures and worksharing procedures of type I variations	81
B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY.....	83
B.7.1. Yearly Line listing for Type I and II variations.....	83
B.7.2. Monthly Line listing for Type I variations.....	83
B.7.3. Opinion on Marketing Authorisation transfer (MMD only)	83
B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)	84
B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)	84
B.7.6. Notifications of Type I Variations (MMD only)	84

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)84

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)84

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES84

E.1. PMF Certification Dossiers:	84
E.1.1. Annual Update.....	84
E.1.2. Variations	84
E.1.3. Initial PMF Certification.....	84
E.2. Time Tables – starting & ongoing procedures: For information	84

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver84

F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended	84
F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health.....	84

G. ANNEX G.....84

G.1. Final Scientific Advice (Reports and Scientific Advice letters):	84
G.2. Ongoing procedures	85
G.3. PRIME.....	85
G.3.1. List of procedures concluding at 17-20 July 2017 CHMP plenary:	85
G.3.2. List of procedures starting in July 2017 for August 2017 CHMP adoption of outcomes.....	85

H. ANNEX H - Product Shared Mailboxes – e-mail address.....85

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for July 2017: For adoption	Adopted.
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A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications

Final Outcome of Rapporteurship allocation for July 2017: For adoption	Adopted.
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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

Elaprase - idursulfase - EMA/H/C/000700/S/0070 MAH: Shire Human Genetic Therapies AB, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus together with the CHMP assessment report <and translation timetable>. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
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B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Amyvid - florbetapir (18F) - EMA/H/C/002422/R/0026 MAH: Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Valerie Strassmann	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members
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	were in agreement with the CHMP Opinion.
Betmiga - mirabegron - EMA/H/C/002388/R/0026 MAH: Astellas Pharma Europe B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Dolores Montero Corominas Request for Supplementary Information adopted on 18.05.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMA/H/C/002333/R/0053 MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Qun-Ying Yue	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Ibandronic acid Accord - ibandronic acid - EMA/H/C/002638/R/0013 MAH: Accord Healthcare Limited, Generic, Generic of Bondronat, Rapporteur: Alar Irs, PRAC Rapporteur: Doris Stenver Request for Supplementary Information adopted on 18.05.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Imatinib Teva - imatinib - EMA/H/C/002585/R/0028 MAH: Teva B.V., Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Lyxumia - lixisenatide - EMA/H/C/002445/R/0023 MAH: sanofi-aventis groupe, Rapporteur: Kristina Dunder, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Qun-Ying Yue	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Ryzodeg - insulin degludec / insulin aspart -	Positive Opinion adopted by consensus together

EMA/H/C/002499/R/0024 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Qun-Ying Yue	with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Tresiba - insulin degludec - EMA/H/C/002498/R/0027 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Qun-Ying Yue	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Zaltrap - aflibercept - EMA/H/C/002532/R/0037 MAH: sanofi-aventis groupe, Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
B.2.3. Renewals of Conditional Marketing Authorisations	
Adcetris - brentuximab vedotin - EMA/H/C/002455/R/0051, Orphan MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus. Request for Supplementary Information adopted on 20.07.2017.	Request for Supplementary Information adopted.
Blincyto - blinatumomab - EMA/H/C/003731/R/0013, Orphan MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva Jirsová Request for Supplementary Information adopted on 20.07.2017.	Request for Supplementary Information adopted.
Lartruvo - olaratumab - EMA/H/C/004216/R/0004, Orphan MAH: Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be

	<p>granted.</p> <p>The Marketing Authorisation remains conditional.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Ninlaro - ixazomib - EMA/H/C/003844/R/0003, Orphan MAH: Takeda Pharma A/S, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.</p> <p>The Marketing Authorisation remains conditional.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Venclyxto - venetoclax - EMA/H/C/004106/R/0005, Orphan MAH: AbbVie Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty</p> <p>Request for Supplementary Information adopted on 20.07.2017.</p>	<p>Request for Supplementary Information adopted.</p>

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

<p>Signal detection</p> <p>PRAC recommendations on signals adopted at the PRAC meeting held on 3-6 July 2017 PRAC:</p>	<p>Noted.</p>
<p>Aranesp - Darbepoetin alfa - EMA/H/C/000332; MAH: Amgen Europe B.V.; Rapporteur: Martina Weise, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Valerie Strassmann,</p> <p>Abseamed - Epoetin alfa - EMA/H/C/000727; MAH: Medice Arzneimittel Pütter GmbH & Co. KG; &</p> <p>Binocrit - Epoetin alfa - EMA/H/C/000727; MAH: Sandoz GmbH; &</p> <p>Epoetin alfa Hexal - Epoetin alfa - EMA/H/C/000726; MAH: Hexal AG; Rapporteur: Alexandre Moreau, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ghania Chamouni,</p> <p>NeoRecormon – Epoetin beta - EMA/H/C/000116; MAH: Roche Registration Limited; Rapporteur: Martina Weise, Co-Rapporteur: Alexandre Moreau,</p>	<p>Adopted.</p>

PRAC Rapporteur: Valerie Strassmann,

Biopoin – Epoetin theta -

EMA/H/C/001036; MAH: TEVA GmbH;

Eporatio – Epoetin theta -

EMA/H/C/001033; ratiopharm GmbH;

Rapporteur: Alexandre Moreau,

Co-Rapporteur: Martina Weise, PRAC

Rapporteur: Ghania Chamouni,

Retacrit – Epoetin zeta -

EMA/H/C/000872; MAH: Hospira UK Ltd; &

Silapo – Epoetin zeta -

EMA/H/C/000760; MAH: STADA

Arzneimittel AG;

Rapporteur: Martina Weise, Co-Rapporteur:

Nithyanandan Nagercoil, PRAC Rapporteur:

Valerie Strassmann,

Mircera – Methoxy polyethylene

glycol-epoetin beta - EMA/H/C/000739;

MAH: Roche Registration Limited; Rapporteur:

Alexandre Moreau, Co-Rapporteur: Martina

Weise, PRAC Rapporteur: Ghania Chamouni,

Signal of severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) –

PRAC recommendation on a variation, DHPC letter and Communication plan (DHPC and Communication plan are being finalised via written procedure): **For adoption**

Faslodex - Fulvestrant –

Adopted.

EMA/H/C/000540; MAH: AstraZeneca UK

Ltd; Rapporteur: Filip Josephson,

Co-Rapporteur: Tuomo Lapveteläinen, PRAC

Rapporteur: Ulla Wändel Liminga,

Signal of anaphylactic reactions: **For adoption**

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its July 2017 meeting:

EMA/H/C/PSUSA/00000425/201611
(bosentan)

CAPS:

Stayveer (EMA/H/C/002644) (bosentan),

MAH: Marklas Nederlands BV, Rapporteur:

Alexandre Moreau

Tracleer (EMA/H/C/000401) (bosentan), MAH:

Actelion Registration Limited, Rapporteur:

Alexandre Moreau

NAPS:

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s):

KLIMURTAN - ELPEN PHARMACEUTICAL CO. INC., PRAC Rapporteur: Caroline Laborde, "20 November 2015 - 19 November 2016"

Update of section 4.5 of the SmPC to add the interaction between bosentan and tadalafil. In addition, the following interactions which could have clinical relevance and which are already mentioned in bosentan SmPC should be added to the package leaflet: warfarin, simvastatin, ketoconazole and sildenafil.

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

EMA/H/C/PSUSA/00001730/201611

(indacaterol)

CAPS:

Hirobriz Breezhaler (EMA/H/C/001211) (indacaterol), MAH: Novartis Europharm Ltd, Rapporteur: Hanne Lomholt Larsen

Onbrez Breezhaler (EMA/H/C/001114) (indacaterol), MAH: Novartis Europharm Ltd, Rapporteur: Hanne Lomholt Larsen

Oslif Breezhaler (EMA/H/C/001210) (indacaterol), MAH: Novartis Europharm Ltd, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, "1-Dec-2013 to 30-Nov-2016"

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends, the variation to the terms of the marketing authorisations for the above mentioned medicinal products, concerning the following change:

To remove the additional risk minimisation measures, as information in the educational materials for Health Care professionals is sufficiently described in relevant sections of the SmPC and no new safety information has arisen regarding the incorrect use of the products containing indacaterol alone. Consequently Annex II.D and the RMP are updated (RMP Version 10.2 is agreed).

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

EMA/H/C/PSUSA/00001838/201612

(lenalidomide)

CAPS:

Revlimid (EMA/H/C/000717) (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "27/12/2015 - 26/12/2016"

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:

Update of sections 4.2, 4.4 and 4.8 of the SmPC to introduce dose modifications in case of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), to add a relevant warning and to include DRESS in the list of adverse reactions with a frequency unknown. The Package leaflet is updated accordingly.

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

<p>EMA/H/C/PSUSA/00002451/201612 (plerixafor) CAPS: Mozobil (EMA/H/C/001030) (plerixafor), MAH: Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "16-Dec-2013 – 15-Dec-2016"</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change(s): Update of section 4.4 and 4.8 of the SmPC to add information on the post marketing cases reported of splenomegaly and splenic rupture. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMA/H/C/PSUSA/00010028/201612 (concentrate of proteolytic enzymes enriched in bromelain) CAPS: NexoBrid (EMA/H/C/002246) (concentrate of proteolytic enzymes enriched in bromelain), MAH: MediWound Germany GmbH, Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, "Update of section 4.4 and 4.8 of the SmPC to add serious allergic reactions including anaphylactic reaction with a frequency not known and to add a warning on hypersensitivity reactions. The Package leaflet is updated accordingly."</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following changes: Update of section 4.4 and 4.8 of the SmPC to add serious allergic reactions including anaphylactic reaction with a frequency not known and to add a warning on hypersensitivity reactions. The Package leaflet is updated accordingly.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMA/H/C/PSUSA/00010128/201612 (ponatinib) CAPS: Iclusig (EMA/H/C/002695) (ponatinib), MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "14 June 2016 – 13 December 2016"</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.2 of the SmPC to update the recommendations for dose modifications for neutropenia and thrombocytopenia that are unrelated to leukaemia as well as for pancreatic adverse events. No changes to the package leaflet are required. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMA/H/C/PSUSA/00010322/201612</p>	<p>The CHMP, having considered in accordance with</p>

<p>(olaparib)</p> <p>CAPS:</p> <p>Lynparza (EMA/H/C/003726) (olaparib), MAH: AstraZeneca AB, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Carmela Macchiarulo, "16 June 2016 to 15 December 2016"</p>	<p>Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):</p> <p>Update of section 4.8 of the SmPC to add the adverse reaction rash with a frequency common and hypersensitivity and dermatitis with a frequency uncommon. The Package leaflet is updated accordingly.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMA/H/C/PSUSA/00010379/201701</p> <p>(nivolumab)</p> <p>CAPS:</p> <p>Opdivo (EMA/H/C/003985) (nivolumab), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "04 July 2016 - 03 January 2017"</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:</p> <p>Update of sections 4.4 and 4.8 of the SmPC to add Vogt-Koyanagi-Harada-Syndrome. The Package leaflet needs no update.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMA/H/C/PSUSA/00010391/201612</p> <p>(lutetium (177Lu) chloride)</p> <p>CAPS:</p> <p>EndolucinBeta (EMA/H/C/003999) (lutetium (177Lu) chloride), MAH: ITG Isotope Technologies Garching GmbH, Rapporteur: Patrick Salmon</p> <p>LuMark (EMA/H/C/002749) (lutetium, isotope of mass 177), MAH: I.D.B. Holland B.V., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, "06.07.2016 to 19.12.2016"</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisations for the above mentioned medicinal products, concerning the following changes:</p> <p>Update of section 4.4 of the SmPC to introduce warnings in relation to myelosuppression, renal irradiation and haematological disorders and of section 4.8 of the SmPC to introduce anaemia, thrombocytopenia, leukopenia and lymphopenia as new ADRs with frequency 'very common' as well as a description of dry mouth in association with prostate cancer therapy including Lutetium (177Lu)-labelled radioligands.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned</p>

	recommendation of the CHMP.
EMA/H/C/PSUSA/00010460/201612 (blinatumomab) CAPS: Blinicyto (EMA/H/C/003731) (blinatumomab), MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, "24 May 2016 - 02 December 2016"	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:</p> <p>Update of section 4.8 of the SmPC to add Cranial nerve disorders with a frequency uncommon ($\geq 1/1000$ to $< 1/100$). The Package leaflet is updated accordingly.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>

B.4. EPARs / WPARs

Fotivda - tivozanib - EMA/H/C/004131 Applicant: EUSA Pharma (UK) Limited, treatment of adult patients with advanced renal cell carcinoma (RCC), New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Imraldi - adalimumab - EMA/H/C/004279 Applicant: Samsung Bioepis UK Limited (SBUK), treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	adopted.
Kisqali - ribociclib - EMA/H/C/004213 Applicant: Novartis Europharm Ltd, treatment of breast cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Mavenclad - cladribine - EMA/H/C/004230 Applicant: Merck Serono Europe Limited, treatment of highly active relapsing-remitting multiple sclerosis (MS), Known active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Maviret - glecaprevir / pibrentasvir - EMA/H/C/004430 Applicant: AbbVie Limited, indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.

Nitisinone MendeliKABS - nitisinone - EMEA/H/C/004281	adopted.
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Applicant: MendeliKABS Europe Ltd, treatment of hepatorenal tyrosinemia type 1, Generic, Generic of Orfadin, Generic application (Article 10(1) of Directive No 2001/83/EC)

Qinprezo (WD) - vosaroxin - EMEA/H/C/004118, Orphan	adopted.
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Applicant: Sunesis Europe Ltd, treatment acute myeloid leukaemiaNew active substance (Article 8(3) of Directive No 2001/83/EC)

WPAR

Rixathon – rituximab - EMEA/H/C/003903	adopted.
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Applicant: Sandoz GmbH, treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Riximyo - rituximab - EMEA/H/C/004729	adopted.
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Applicant: Sandoz GmbH, treatment of Non-Hodgkin's lymphoma (NHL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis), , Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Vosevi - sofosbuvir / velpatasvir / voxilaprevir - EMEA/H/C/004350	adopted.
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Applicant: Gilead Sciences International Limited, treatment of chronic hepatitis C virus in adults (HCV) infection in adults, New active substance (Article 8(3) of Directive No 2001/83/EC)

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Advate - octocog alfa - EMEA/H/C/000520/II/0082/G	Request for Supplementary Information adopted with a specific timetable.
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MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus

Request for Supplementary Information adopted on 20.07.2017, 23.02.2017.

Advate - octocog alfa -	Request for Supplementary Information adopted
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EMEA/H/C/000520/II/0085 MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.07.2017.	with a specific timetable.
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0001 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.07.2017, 21.04.2017.	Request for Supplementary Information adopted with a specific timetable.
Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0006/G, Orphan MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop Opinion adopted on 20.07.2017. Request for Supplementary Information adopted on 09.06.2017.	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ciambra - pemetrexed - EMEA/H/C/003788/II/0002/G MAH: Menarini International Operations Luxembourg S.A., Generic, Generic of Alimta, Rapporteur: Juris Pokrotnieks Opinion adopted on 06.07.2017. Request for Supplementary Information adopted on 06.04.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0061/G MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder Opinion adopted on 13.07.2017.	Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cosentyx - secukinumab - EMEA/H/C/003729/II/0024 MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen Opinion adopted on 06.07.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0036/G MAH: Merck Sharp & Dohme Limited, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 20.07.2017. Request for Supplementary Information adopted on 09.06.2017.	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Envarsus - tacrolimus - EMEA/H/C/002655/II/0008/G MAH: Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg	Request for Supplementary Information adopted with a specific timetable.

Request for Supplementary Information adopted on 20.07.2017, 16.03.2017.

**Fabrazyme - agalsidase beta -
EMA/H/C/000370/II/0099/G**

MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Gardasil 9 - human papillomavirus vaccine
[types 6, 11, 16, 18, 31, 33, 45, 52, 58]
(recombinant, adsorbed) -
EMA/H/C/003852/II/0019/G**

MAH: MSD Vaccins, Rapporteur: Kristina Dunder

Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Imatinib Actavis - imatinib -
EMA/H/C/002594/II/0013**

MAH: Actavis Group PTC ehf, Generic, Generic of Glivec, Rapporteur: Hrefna Gudmundsdottir

Request for Supplementary Information adopted on 06.07.2017.

Request for Supplementary Information adopted with a specific timetable.

**Inflectra - infliximab -
EMA/H/C/002778/II/0050/G**

MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey

Opinion adopted on 29.06.2017.

Request for Supplementary Information adopted on 05.05.2017.

Positive Opinion adopted by consensus on 29.06.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Jakavi - ruxolitinib -
EMA/H/C/002464/II/0034**

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson

Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Kadcyla - trastuzumab emtansine -
EMA/H/C/002389/II/0034**

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac

Request for Supplementary Information adopted on 29.06.2017.

Request for Supplementary Information adopted with a specific timetable.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0026/G**

MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri

Opinion adopted on 13.07.2017.

Request for Supplementary Information adopted on 01.06.2017, 21.04.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0030**

Request for Supplementary Information adopted with a specific timetable.

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Daniela Melchiorri
Request for Supplementary Information adopted
on 06.07.2017.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0031/G**

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Daniela Melchiorri
Request for Supplementary Information adopted
on 13.07.2017.

Request for Supplementary Information adopted
with a specific timetable.

**Memantine ratiopharm - memantine -
EMA/H/C/002671/II/0008**

MAH: ratiopharm GmbH, Generic, Generic of
Ebixa, Rapporteur: Bart Van der Schueren
Opinion adopted on 20.07.2017.
Request for Supplementary Information adopted
on 01.06.2017.

Positive Opinion adopted by consensus on
20.07.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Myozyme - alglucosidase alfa -
EMA/H/C/000636/II/0063/G**

MAH: Genzyme Europe BV, Rapporteur:
Alexandre Moreau
Request for Supplementary Information adopted
on 20.07.2017.

Request for Supplementary Information adopted
with a specific timetable.

**Pemetrexed Fresenius Kabi - pemetrexed -
EMA/H/C/003895/II/0002**

MAH: Fresenius Kabi Oncology PLC, Generic,
Generic of Alimta, Rapporteur: Bjorg Bolstad
Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on
06.07.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Perjeta - pertuzumab -
EMA/H/C/002547/II/0030**

MAH: Roche Registration Limited, Rapporteur:
Sinan B. Sarac
Request for Supplementary Information adopted
on 29.06.2017.

Request for Supplementary Information adopted
with a specific timetable.

**Plavix - clopidogrel -
EMA/H/C/000174/II/0127/G**

MAH: Sanofi Clir SNC, Rapporteur: Bruno
Sepodes
Request for Supplementary Information adopted
on 20.07.2017.

Request for Supplementary Information adopted
with a specific timetable.

**Praluent - alirocumab -
EMA/H/C/003882/II/0024/G**

MAH: sanofi-aventis groupe, Rapporteur: Johann
Lodewijk Hilleg
Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on
13.07.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

Privigen - human normal immunoglobulin -

Positive Opinion adopted by consensus on

EMA/H/C/000831/II/0118 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 06.07.2017.	06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ratiograstim - filgrastim - EMA/H/C/000825/II/0053/G MAH: ratiopharm GmbH, Rapporteur: Outi Mäki-Ikola Opinion adopted on 06.07.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Remicade - infliximab - EMA/H/C/000240/II/0205 MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 20.07.2017.	Request for Supplementary Information adopted with a specific timetable.
Remsima - infliximab - EMA/H/C/002576/II/0042/G MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey Opinion adopted on 29.06.2017. Request for Supplementary Information adopted on 05.05.2017.	Positive Opinion adopted by consensus on 29.06.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tevagrastim - filgrastim - EMA/H/C/000827/II/0063/G MAH: TEVA GmbH, Duplicate, Duplicate of Biograstim, Rapporteur: Outi Mäki-Ikola Opinion adopted on 06.07.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMA/H/C/003982/II/0012/G MAH: MCM Vaccine B.V., Rapporteur: Bart Van der Schueren Opinion adopted on 20.07.2017.	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vihuma - simoctocog alfa - EMA/H/C/004459/II/0001/G MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.07.2017. Request for Supplementary Information adopted on 15.06.2017.	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xultophy - insulin degludec / liraglutide -	Positive Opinion adopted by consensus on

EMA/H/C/002647/II/0019 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder Opinion adopted on 20.07.2017. Request for Supplementary Information adopted on 01.06.2017.	20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Yervoy - ipilimumab - EMA/H/C/002213/II/0048/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 06.07.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1143 Aflunov-EMA/H/C/002094/WS1143/0033 Foclivia-EMA/H/C/001208/WS1143/0028 MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 20.07.2017. Request for Supplementary Information adopted on 15.06.2017, 05.05.2017.	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1159 Neulasta-EMA/H/C/000420/WS1159/0095 Ristempa-EMA/H/C/003910/WS1159/0011 MAH: Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings Opinion adopted on 06.07.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1186/G Fertavid-EMA/H/C/001042/WS1186/0036/G Puregon-EMA/H/C/000086/WS1186/0094/G MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 13.07.2017.	Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Arzerra - ofatumumab - EMA/H/C/001131/II/0050, Orphan MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a recommendation to permanently discontinue Arzerra in case of anaphylactic reaction and revise the adverse drug reaction profile based on cumulative safety	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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pool data analysis from clinical trials, the company safety database and updated company core data sheet.

The Package Leaflet is updated accordingly."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 15.06.2017.

Arzerra - ofatumumab -

EMA/H/C/001131/II/0051, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, "Update to sections 4.6 and 5.3 of the SmPC based on a cumulative review of data from completed non-clinical safety studies, cases reported in the pharmacovigilance database related to pregnancy and foetal exposure while receiving ofatumumab therapy.

Update to the section 4.5 of the SmPC based on results from clinical study OMB11360 investigating pharmacokinetic interactions between ofatumumab and bendamustine.

Updates to sections 4.2, 5.1 and 5.2 of the SmPC were made to simplify them and ease their understanding. Editorial updates were made to sections 4.4 and 4.8.

Furthermore, the MAH took the opportunity to combine the SmPCs of the different strengths (100 mg and 1000 mg concentrate for solution for infusion), to introduce editorial changes and to bring the PI in line with the latest QRD template version 10. In addition, the list of local representatives in the Package Leaflet has been updated."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 15.06.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) -

EMA/H/C/002333/II/0054

MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add the adverse reactions "injection site reactions (including extensive swelling of the vaccinated limb)" and "injection site nodule which may persist for more than one month" with a frequency not known. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

10.0.”

Opinion adopted on 06.07.2017.

Blincyto - blinatumomab -

EMA/H/C/003731/II/0009, Orphan

MAH: Amgen Europe B.V., Rapporteur:

Alexandre Moreau, “Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information with the data from the study 103311. This study is fulfilling the specific obligation for the conditional MA. The SO is removed from annex II. The Package Leaflet is updated accordingly.

The MAH takes this opportunity to amend the format of the preparation instructions to improve clarity. The content is not impacted.”

Request for Supplementary Information adopted on 20.07.2017, 26.01.2017.

Request for Supplementary Information adopted with a specific timetable.

Cosentyx - secukinumab -

EMA/H/C/003729/II/0020

MAH: Novartis Europharm Ltd, Rapporteur:

Tuomo Lapveteläinen, “Update of section 4.5 of the SmPC in order to revise general information on CYP450/CYP3A4 as a result of data provided by the clinical drug-drug interaction study A2110.”

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 01.06.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Cyanokit - hydroxocobalamin -

EMA/H/C/000806/II/0031

MAH: SERB SA, Rapporteur: Alexandre Moreau, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on renal disorders and to update the safety information on skin and subcutaneous tissue disorders, renal and urinary disorders following a safety signal on renal disorders and based on a safety review including review of clinical data, preclinical data, literature and cumulative review of renal disorders cases occurring after hydroxocobalamin administration. The package leaflet is updated accordingly.”

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 18.05.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Dacogen - decitabine -

EMA/H/C/002221/II/0031, Orphan

MAH: Janssen-Cilag International N.V.,

Rapporteur: Alexandre Moreau, “Update of

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

section 6.6. of the SmPC in order to update the recommendation.
reconstitution procedure by narrowing the concentration range of the diluted solution of Dacogen from '0.1 mg/ml-1.0 mg/ml' to '0.15 mg/ml-1.0 mg/ml' due to an update of Chapter 5.1.10 'Guidelines for using the test for bacterial endotoxins' in edition 8.8 of the European Pharmacopoeia."
Opinion adopted on 20.07.2017.

**Edurant - rilpivirine -
EMA/H/C/002264/II/0025**

MAH: Janssen-Cilag International NV,
Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in order to include Pharmacokinetics data of drug-drug interactions between simeprevir and rilpivirine, based on final result from study TMC435-TiDP16-C114; this is a Phase I, 2-panel, open-label, randomized, cross-over study in healthy subjects to investigate the potential drug-drug interaction between simeprevir and RPV.

In addition, the drug-drug interaction information for telaprevir is removed from the SmPC as this product is no longer available since its marketing authorization was not renewed.

The Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10."

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 11.05.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Elonva - corifollitropin alfa -
EMA/H/C/001106/II/0034**

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Paula Boudewina van Hennik,
"Update of section 4.5 of the SmPC to add information pertaining to potential hCG cross-reactivity resulting in a false positive pregnancy test.

In addition, the MAH is taking the opportunity to implement changes in the annexes in line with the QRD templates (versions 9.1 and 10) and to propose combined versions of the SmPCs and Package Leaflets for the different strengths."

Request for Supplementary Information adopted on 20.07.2017, 18.05.2017.

Request for Supplementary Information adopted with a specific timetable.

**Emend - aprepitant -
EMA/H/C/000527/II/0055**

Request for Supplementary Information adopted with a specific timetable.

MAH: Merck Sharp & Dohme Limited,
 Rapporteur: Filip Josephson, "Update of sections 4.2 of the SmPC in order to replace the nomogram for the paediatric formulation provided in ml/kg with purely weight-based dosing instructions (in mg/kg) This is based on data that were already submitted as part of the paediatric application X/49. 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 10.0."
 Request for Supplementary Information adopted on 20.07.2017.

**Empliciti - elotuzumab -
 EMEA/H/C/003967/II/0006**

MAH: Bristol-Myers Squibb Pharma EEIG,
 Rapporteur: Paula Boudewina van Hennik,
 "Update of section 5.2 of the SmPC to update the volume of distribution and elimination of elotuzumab based on an updated analysis of study HuLuc63-1701."
 Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Esbriet - pirfenidone -
 EMEA/H/C/002154/II/0043, Orphan**

MAH: Roche Registration Limited, Rapporteur: Greg Markey, "Update of sections 4.2 and 5.2 of the SmPC in order to update the existing safety information with revised recommendations for patients with moderate renal impairment based on the totality of data from clinical studies; the Package Leaflet is updated accordingly."
 Request for Supplementary Information adopted on 29.06.2017.

Request for Supplementary Information adopted with a specific timetable.

**Forsteo - teriparatide -
 EMEA/H/C/000425/II/0046**

MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of section 5.1 of the SmPC of the SmPC based on the results of study B3D-EW-GHDW (VERO), a phase 4 multi-centre, prospective, randomized, parallel, double-blind, double-dummy, active controlled study comparing the effect of teriparatide for injection versus risedronate on the incidence of fractures and low bone mass. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct the formatting throughout the Product Information and to bring Annex II in line with the latest QRD template version 10."

Request for Supplementary Information adopted with a specific timetable.

Request for Supplementary Information adopted on 20.07.2017.

Galafold - migalastat -
EMA/H/C/004059/II/0010, Orphan
MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study AT1001-041: A phase 3 open label extension study to assess the safety and efficacy of 150 mg migalastat HCl QOD in subjects with Fabry disease who have completed Studies AT1001-011, AT1001- 012 or FAB-CL-205, listed as a category 3 study in the RMP."
Request for Supplementary Information adopted on 13.07.2017.

Request for Supplementary Information adopted with a specific timetable.

Giotrif - afatinib -
EMA/H/C/002280/II/0023
MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add the adverse reaction nail disorders with a frequency common based on the results of study 1200.131 and supportive evidence from EGFR TKJ comparator studies. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes to the polish product information."
Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Harvoni - ledipasvir / sofosbuvir -
EMA/H/C/003850/II/0053
MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to revise information related to the Cytochrome P450 3A (CYP3A) mediated drug-drug interaction potential of ledipasvir based on final results from study GS-US-337-1887, listed as a category 3 study in the RMP"
Request for Supplementary Information adopted on 13.07.2017.

Request for Supplementary Information adopted with a specific timetable.

Hetlioz - tasimelteon -
EMA/H/C/003870/II/0008, Orphan
MAH: Vanda Pharmaceuticals Ltd., Rapporteur: Greg Markey, "Update of sections 4.4, 4.5 of the SmPC, based on in vitro studies and pooled analyses from clinical studies, with cautionary statements regarding the coadministration of Hetlioz with strong CYP1A2 inhibitors and removal, from the Risk Management Plan (RMP),

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

of the commitment to conduct a human CYP2C19 Drug-Drug Interaction Study to evaluate the single-dose pharmacokinetics of tasimeleone 20 mg alone and in combination with a CYP2C19 inhibitor, omeprazole, at steady-state. Section 5.2 is also updated with data of the pooled analyses of the clinical studies and the in vitro studies."

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 06.04.2017.

**Humira - adalimumab -
EMA/H/C/000481/II/0168**

MAH: AbbVie Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update information on the long-term safety, tolerability, and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa after finalisation of phase III open-label extension study M12-555."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 15.06.2017.

**Humira - adalimumab -
EMA/H/C/000481/II/0169**

MAH: AbbVie Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update the clinical data section based on interim data from the OLE Study M11-327 in non-infectious uveitis (A Multicenter Open-Label Study of the Long-term Safety and Efficacy of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Non-infectious Intermediate, Posterior, or Panuveitis)"

Request for Supplementary Information adopted on 20.07.2017.

**Imnovid - pomalidomide -
EMA/H/C/002682/II/0025, Orphan**

MAH: Celgene Europe Limited, Rapporteur: Robert James Hemmings, "Submission of a biomarker analysis report following a recommendation from CHMP in MAA procedure (EMA/H/C/2682/0000) to present the biomarker analysis report based on clinical studies CC-4047-MM-008 and CC-4047-MM-010."

Request for Supplementary Information adopted on 06.07.2017.

Intelence - etravirine -

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted with a specific timetable.

Request for Supplementary Information adopted with a specific timetable.

Positive Opinion adopted by consensus on

EMA/H/C/000900/II/0050

MAH: Janssen-Cilag International NV,
Rapporteur: Joseph Emmerich, "Update of sections 4.3, 4.4 and 4.5 of the SmPC to include additions to the drug-drug interaction (DDI) information of etravirine with hepatitis C virus (HCV) direct-acting antivirals (DAAs) elbasvir/grazoprevir, daclastavir and simeprevir and human immunodeficiency virus (HIV) protease inhibitors (PIs) atazanavir/cobicistat and darunavir/cobicistat, following the same changes in medicinal products containing these active substances. Section 4.9 of the SmPC is also updated with regard to treatment of etravirine overdose. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes, to align the PL with SmPC regarding co-administration of etravirine with anti-HIV medicines efavirenz, nevirapine, rilpivirine, indinavir, nelfinavir, to update the list of local representative for the Netherlands in the PL and to align the PI with the latest the QRD template (version 10.0)."
Opinion adopted on 13.07.2017.

13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Invega - paliperidone -**EMA/H/C/000746/II/0056/G**

MAH: Janssen-Cilag International NV,
Rapporteur: Kristina Dunder, "Update of section 4.2 and 4.9 of the SmPC in order to add 3 mg every other day dosing for patients with moderate and severe renal impairment and to delete the recommendation for gastric lavage in accordance with current best practices for management of overdose, respectively. Furthermore, the MAH is proposing the deletion of the Invega 1.5 mg strength (all presentations) which has never been marketed in the EU. In addition, the details of the local representatives for Latvia, the Netherlands, Estonia and Lithuania are updated in the PL. The Company also proposes to combine the SmPCs for the different Invega strengths (3mg, 6mg, 9mg, 12mg) and to align the package leaflet to the latest QRD template (version 10.0)."
Opinion adopted on 20.07.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Kadcyla - trastuzumab emtansine -**EMA/H/C/002389/II/0033**

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Submission of the final clinical study results from study TDM4788g/ BO22589

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(MARIANNE) listed as a specific obligation in Annex II.D; this is an interventional randomised, 3-arm, phase III study to evaluate the efficacy and safety of trastuzumab emtansine combined with pertuzumab, or trastuzumab emtansine combined with pertuzumab-placebo versus trastuzumab plus taxane, as first line treatment in HER2-positive progressive or recurrent locally advanced breast cancer or previously untreated metastatic breast cancer.

As a result of this submission, Annex II of the product information is affected."

Opinion adopted on 13.07.2017.

Lenvima - lenvatinib -

EMA/H/C/003727/II/0008, Orphan

MAH: Eisai Europe Ltd., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wandel Liminga, "Submission of Clinical Study Report for Study E78080-J081-208"

Request for Supplementary Information adopted on 20.07.2017, 06.04.2017.

Request for Supplementary Information adopted with a specific timetable.

Norvir - ritonavir -

EMA/H/C/000127/II/0146

MAH: AbbVie Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.6 of the SmPC in order to update the safety information on pregnancy and lactation based on the company's core data sheet information."

Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Norvir - ritonavir -

EMA/H/C/000127/II/0147

MAH: AbbVie Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.3 and 4.5 of the SmPC in order to add a contraindication regarding the interaction between ritonavir and venetoclax based on the company's core data sheet. The Package Leaflet is updated accordingly to also include some minor editorial updates."

Opinion adopted on 20.07.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Ofev - nintedanib -

EMA/H/C/003821/II/0016, Orphan

MAH: Boehringer Ingelheim International GmbH, Rapporteur: David Lyons, "Update of section 4.4 of the SmPC to amend the current warning on the hepatic function to include low body weight, Asian origin, female sex and age as factors of increased risk of liver enzymes elevations, update of section 4.8 of the SmPC to revised the

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

frequency of the ADR 'drug-induced liver injury' (DILI) from 'not known' to 'uncommon' and update of section 5.2 of the SmPC to amend the current information related to the mean exposure to nintedanib by race, based on a review of clinical trials and post-marketing data on DILI and on the exposure safety relationship between nintedanib plasma exposure and liver enzyme elevations. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make a small correction in section 5.2 of the SmPC."

Opinion adopted on 20.07.2017.

**Pradaxa - dabigatran etexilate -
EMA/H/C/000829/II/0103**

MAH: Boehringer Ingelheim International GmbH,
Rapporteur: Hanne Lomholt Larsen, "Update of sections 4.2, 4.4 and 5.1 to reflect the final study results of the phase IV study 1160.204 (The RE-CIRCUIT Trial), " A Randomised Evaluation of dabigatran etexilate Compared to warfarin in pulmonary vein ablation: assessment of an uninterrupted periprocedural anticoagulation strategy"

Request for Supplementary Information adopted on 20.07.2017.

Request for Supplementary Information adopted with a specific timetable.

**Pyramax - pyronaridine / artesunate -
EMA/H/W/002319/II/0015**

MAH: Shin Poong Pharmaceutical Co., Ltd.,
Rapporteur: Joseph Emmerich, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the main efficacy and safety results from the final report from study SP-C-013-11 listed as a category 3 study in the RMP. This is a phase IIIb/IV comparative, randomised, multi-centre, open label, parallel 3-arm clinical study to assess the safety and efficacy of repeated administration of pyronaridine-artesunate, dihydroartemisinin-piperaquine or artemether-lumefantrine or artesunate-amodiaquine over a 2-year period in children and adult patients with acute uncomplicated Plasmodium sp. malaria. In addition, the SOH took the opportunity to make some editorial changes to the product information."

Opinion adopted on 13.07.2017.

Request for Supplementary Information adopted

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 11.05.2017.

Selincro - nalmefene -

EMA/H/C/002583/II/0020/G

MAH: H. Lundbeck A/S, Rapporteur: Harald Enzmann, "Update of section 4.7 of the SmPC to add new information regarding effects on ability to drive and use machines, based on clinical study and post-marketing data.

Update of section 4.8 of the SmPC in order to add the adverse drug reaction "diarrhoea" with frequency "common", based on clinical study and post-marketing data.

The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 01.06.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Sirturo - bedaquiline -

EMA/H/C/002614/II/0021, Orphan

MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC in order to add delamanid as an example of a drug that prolongs the QT interval following the review of the global safety database for all serious cases received from 28 December 2012 to 30 September 2016.

The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Opinion adopted on 29.06.2017.

Request for Supplementary Information adopted on 18.05.2017, 06.04.2017.

Positive Opinion adopted by consensus on 29.06.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tafinlar - dabrafenib -

EMA/H/C/002604/II/0024

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to include some warning on a drug-drug interaction between dabrafenib and rifampicin (a CYP3A4/CYP2C8 inducer) and between dabrafenib and rabeprazole (a pH elevating agent), based on the final results of study 200072, a phase I open-label fixed sequence study to evaluate the effects of potent CYP3A4 inducer (rifampicin) and of a pH elevating agent (rabeprazole) on the repeat dose pharmacokinetics of dabrafenib in subjects with

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

BRAFV60 mutation positive tumours, to fulfil MEA 005."

Opinion adopted on 06.07.2017.

Tagrisso - osimertinib -

EMA/H/C/004124/II/0014/G

MAH: AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.3 of the SmPC to include information regarding CNS distribution based on non-clinical data."

Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tagrisso - osimertinib -

EMA/H/C/004124/II/0015

MAH: AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.2 of the SmPC to include data from studies performed to investigate human plasma protein binding (Study No. BS001265-53-AZD9291), the assessment of non-specific incubational binding in transporter inhibition assays (Study No. BS000760-92) and the implications on transporter DDI risk assessment. In addition, the MAH took the opportunity to implement minor updates and editorial changes in the SmPC and to update the address of the MAH and manufacturer in SmPC section 7, the labelling and the Package Leaflet." Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tarceva - erlotinib -

EMA/H/C/000618/II/0052

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC in order to include recommendations on Epidermal Growth Factor Receptor (EGFR) mutation status testing, to be in line with current technical and scientific progress.

In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes and to bring the PI in line with the latest QRD template version 10. Moreover, the MAH took the opportunity to make minor correction of section 4.2 of the SmPC.

Furthermore, the Annex II has been corrected, as requested by the EMA, to include Educational Material as an additional risk minimisation measure, which has been already in place in the RMP."

Request for Supplementary Information adopted on 20.07.2017.

Request for Supplementary Information adopted with a specific timetable.

Torisel - temsirolimus -

EMA/H/C/000799/II/0066, Orphan

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP

<p>MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Submission of the further analysis of a possible association of corticosteroid (pre-)treatment and frequency and severity of hypersensitivity/infusion reactions in study 3066K1-4438-WW (B1771007), as requested by the CHMP during procedures EMEA/H/C/799/MEA 023.1 and EMEA/H/C/799/MEA 024.1."</p> <p>Opinion adopted on 06.07.2017.</p> <p>Request for Supplementary Information adopted on 16.03.2017.</p>	<p>Members were in agreement with the CHMP recommendation.</p>
<p>Victrelis - boceprevir - EMA/H/C/002332/11/0042</p> <p>MAH: Merck Sharp & Dohme Limited, Rapporteur: Joseph Emmerich, "Update of section 4.4 of the SmPC to add a warning regarding HBV reactivation observed in patients with HCV/HBV co-infection treated with some direct-acting antivirals not given in combination with peginterferon alfa and ribavirin. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial updates in the Product Information."</p> <p>Opinion adopted on 29.06.2017.</p>	<p>Positive Opinion adopted by consensus on 29.06.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Xarelto - rivaroxaban - EMA/H/C/000944/11/0050</p> <p>MAH: Bayer AG, Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.4 and 5.1 of the Summary of Product Characteristics (SmPC) to reflect information on posology in patients with non valvular atrial fibrillation and information on safety and efficacy in patients who undergo PCI (percutaneous coronary intervention) with stent placement based on the final results of study 16523 (PIONEER AF-PCI): An Open-label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose- Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention. The package Leaflet is updated accordingly. In addition, the marketing authorisation holder took the opportunity to update the telephone number of local representatives for UK in the Package Leaflet. Correction was also made in Annex IIIA to remove the recording of blood type in the patient alert card."</p> <p>Opinion adopted on 20.07.2017.</p>	<p>Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>

Request for Supplementary Information adopted on 22.06.2017, 21.04.2017.

**Xeplion - paliperidone -
EMA/H/C/002105/II/0035**

MAH: Janssen-Cilag International NV,
Rapporteur: Kristina Dunder, "Update of section 4.2 of the SmPC in order to add a dosage conversion table to provide guidance for healthcare professionals when switching patients from paliperidone ER tablets to paliperidone palmitate long acting injection (PP1M). The Package Leaflet is updated accordingly."

Request for Supplementary Information adopted on 20.07.2017.

Request for Supplementary Information adopted with a specific timetable.

WS1092

Ebymect-EMA/H/C/004162/WS1092/0017

Edistride-EMA/H/C/004161/WS1092/0013

Forxiga-EMA/H/C/002322/WS1092/0032

Xigduo-EMA/H/C/002672/WS1092/0028

MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.4 and 5.1 of the SmPC in order to reflect the results of the Phase 3 study D5553C00003: 28-week safety and efficacy, randomised, double-blind comparison of simultaneous administration of exenatide once weekly 2 mg and dapagliflozin once daily 10 mg to exenatide once weekly 2 mg alone and dapagliflozin once daily 10 mg alone in patients with type 2 diabetes with inadequate glycaemic control on metformin.

The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflets for Ebymect and Edistride and to introduce minor editorial changes throughout the Product Informations."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 23.03.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1136

Descovy-EMA/H/C/004094/WS1136/0017

Genvoya-EMA/H/C/004042/WS1136/0031

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Odefsey-EMA/H/C/004156/WS1136/001**3**

MAH: Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, "Update of sections 4.4, 4.8. 5.1 and 5.2 of the SmPC in order to provide 48 weeks data from Study GS-US-292-1249; this is a Phase 3b open-label study of the efficacy and safety of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide single-tablet regimen in HIV-1/Hepatitis B co-infected adults. The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to make minor administrative changes in the SmPC and the Package Leaflet."

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 05.05.2017.

WS1144/G**Afinitor-EMA/H/C/001038/WS1144/005
2/G****Votubia-EMA/H/C/002311/WS1144/004
2/G**

MAH: Novartis Europharm Ltd, Lead Rapporteur: Harald Enzmann, "Update of sections 4.4 and 5.1 of the SmPC in order to include new safety information on stomatitis and its management based on final results from study CRAD001JUS226: a phase II, single arm study of the use of steroid-based mouthwash to prevent stomatitis in postmenopausal women with advanced or metastatic hormone receptor positive breast cancer being treated with everolimus plus exemestane

Update of section 4.6 of the SmPC in order to add new information on breast-feeding based on pre-clinical data.

The Package Leaflets were updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to bring the Afinitor PI in line with the latest QRD template version 10."

Opinion adopted on 29.06.2017.

Request for Supplementary Information adopted on 27.04.2017.

Positive Opinion adopted by consensus on 29.06.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1167**Ebymect-EMA/H/C/004162/WS1167/002****1**

Request for Supplementary Information adopted with a specific timetable.

Edistride-EMEA/H/C/004161/WS1167/0016

Forxiga-EMEA/H/C/002322/WS1167/0036

Xigduo-EMEA/H/C/002672/WS1167/0032

MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.8 and 5.1 of the SmPC in order to add information regarding two initial combination studies (MB102021 and MB102034) in treatment-naïve patients of dapagliflozin 5 mg + metformin and dapagliflozin 10 mg + metformin, respectively, compared to each component separately.

In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10."

Request for Supplementary Information adopted on 20.07.2017.

WS1178

Aluvia-EMEA/H/W/000764/WS1178/0102

Kaletra-EMEA/H/C/000368/WS1178/0164

MAH: AbbVie Limited, Lead Rapporteur: Joseph Emmerich, "Update of sections 4.3 and 4.5 of the SmPC in order to add new contraindications and interaction information of lopinavir/ritonavir with venetoclax, with elbasvir/grazoprevir and with ombitasvir/paritaprevir/ritonavir with or without dasabuvir based on the company's core data sheet; the package Leaflet is updated accordingly. In addition, the MAH/SOH is taking the opportunity to update section 4.5 of the SmPC to reflect information already contained in section 4.3 for drug-drug interactions with astemizole, terfenadine, pimozone, ergot alkaloids and cisapride."

Opinion adopted on 20.07.2017.

Positive Opinion adopted by consensus on

20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1179

Invega-EMEA/H/C/000746/WS1179/0055

Trevicta-EMEA/H/C/004066/WS1179/0010

Xeplion-EMEA/H/C/002105/WS1179/0034

MAH: Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder, "Update of section 4.6 (Fertility, pregnancy and lactation) of the SmPC in order to add new information concerning a retrospective observational cohort study with risperidone and risk of congenital malformations. Nationally approved products are also affected by this variation."

Request for Supplementary Information adopted

Request for Supplementary Information adopted with a specific timetable.

on 20.07.2017.

WS1189

ANORO-EMA/H/C/002751/WS1189/0017
Laventair-EMA/H/C/003754/WS1189/0019

MAH: Glaxo Group Ltd, Lead Rapporteur:
Nithyanandan Nagercoil, "Update of section 4.8 of the SmPC and relevant section of the PL to add "dysphonia" with rare frequency."
Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1191

Incruse-EMA/H/C/002809/WS1191/0016
Rolufta-EMA/H/C/004654/WS1191/0001

MAH: Glaxo Group Ltd, Lead Rapporteur:
Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC and relevant section of the PL to add "Eye pain" with a rare frequency."
Opinion adopted on 13.07.2017.

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Adcetris - brentuximab vedotin - EMA/H/C/002455/II/0043, Orphan

MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of sections 4.8 and 5.1 of the SmPC to reflect the final study results from study C25007: a single-arm study of brentuximab vedotin in patients with relapsed or refractory hodgkin lymphoma who are not suitable for stem cell transplantation or multiagent chemotherapy. The submission of the clinical study report fulfils SOB 011 of the conditional marketing authorisation for Adcetris Annex II is updated accordingly."
Opinion adopted on 20.07.2017.
Request for Supplementary Information adopted on 18.05.2017, 23.02.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Aranesp - darbepoetin alfa - EMA/H/C/000332/II/0141

MAH: Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on severe cutaneous conditions including Erythema multiforme and Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) following a request for cumulative review triggered by EMA signal

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

adopted by PRAC on 09 February 2017. The Package Leaflet is updated accordingly. The RMP version 7 has also been submitted.”
Opinion adopted on 20.07.2017.

Dificlir - fidaxomicin -

EMA/H/C/002087/II/0028

MAH: Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, “C.I.11: Submission of an updated RMP version 7 in order to remove the post-authorization measure (PAM) MEA003 (concerning clinical study 2819-CL-2001 in patients with Clostridium difficile Infection who will receive a second course of fidaxomicin) due to the non-feasibility of the study.”

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 05.05.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Edurant - rilpivirine -

EMA/H/C/002264/II/0024

MAH: Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPC in order to include information: use of rilpivirine in combination with a background regimen for the treatment of HIV-1 infection during pregnancy and postpartum, without dose adjustment following final results from study TMC114HIV3015 listed as a category 3 study in the RMP. This is a single arm, open-label trial to assess the pharmacokinetics of darunavir/ritonavir, etravirine, and rilpivirine in HIV-1-infected pregnant women.

The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce the latest renewal date in section 9 of the SmPC and the physical address of the Netherlands Local Operating Company in the PIL section 6.”

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 09.06.2017, 06.04.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Jinarc - tolvaptan -

EMA/H/C/002788/II/0006

MAH: Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “Update of section 5.1 of the SmPC

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

based on final results from study 156-08-271 (TEMPO 4:4) listed as a PAES in Annex II. This study is a Multicenter, Open-label, Extension Study (Extension of Trial 156-04-251) to Evaluate the Long-term Safety and Efficacy of Oral Tolvaptan Tablet Regimens in Patients With Autosomal Dominant Polycystic. It provides data for Jinarc treatment of autosomal dominant polycystic kidney disease (ADPKD) over 5 years. Reference to submission of this study is being deleted from Annex II.

In addition, the Marketing authorisation holder (MAH) took the opportunity to add the current ATC code applicable for tolvaptan as it has been assigned by WHO.

The RMP version 13.1 has also been submitted to reflect the completion of the 156-08-271 study." Opinion adopted on 06.07.2017.
Request for Supplementary Information adopted on 05.05.2017.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0028**

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Daniela Melchiorri, PRAC
Rapporteur: Sabine Straus, "Update sections 4.4 and 4.8 of the SmPC to include the risk of myocarditis that has been reported in patients treated with pembrolizumab. The Package Leaflet has been updated accordingly. An updated RMP version 10.0 was provided as part of the application."
Opinion adopted on 20.07.2017.
Request for Supplementary Information adopted on 22.06.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0029**

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Daniela Melchiorri, PRAC
Rapporteur: Sabine Straus, "Submission of the final study report for non-clinical study "Anti-Murine PD-1 Antibody (muDX400 L-005571333): Exploratory Multiple-Dose Subcutaneous Immunotoxicity Study in Mice with Hepatitis B Vaccine (L-005552770)". An updated RMP version 11.0 was agreed during the procedure."
Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Latuda - lurasidone -

Positive Opinion adopted by consensus on

EMA/H/C/002713/II/0016

MAH: Sunovion Pharmaceuticals Europe Ltd,
Rapporteur: Filip Josephson, PRAC Rapporteur:
Qun-Ying Yue, "Submission of the final CSR for
Study D1001057, an extension of study of
SM-13496 evaluating the long-term safety and
efficacy of lurasidone (40 mg/day or 80 mg/day)
in Pan-Asian (Japanese, Korean, Taiwanese and
Malaysian) subjects with schizophrenia.
The RMP is being updated (ver. 5.0) with
information relative to this study and also
information relative to Study D1050301, which
has already been assessed in P46/006."
Opinion adopted on 06.07.2017.

06.07.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Lemtrada - alemtuzumab -
EMA/H/C/003718/II/0017**

MAH: Genzyme Therapeutics Ltd, Duplicate,
Duplicate of Lemtrada (WD), Rapporteur: Hanne
Lomholt Larsen, PRAC Rapporteur: Torbjorn
Callreus, "Update of sections 4.2, 4.4, 4.8 and
5.1 of the SmPC in order to update the safety and
long term use information in the posology
following final results from study CAMMS03409 -
An Extension Protocol For Multiple Sclerosis
Patients Who Participated in Genzyme-Sponsored
Studies of Alemtuzumab (ongoing at the time of
the initial MAA) to evaluate the long term safety
and efficacy of alemtuzumab in MS patients who
received alemtuzumab during prior
company-sponsored studies. The RMP version
3.0 has also been submitted. The PL has been
updated accordingly.

In addition, the Marketing authorisation holder
(MAH) took the opportunity to bring the PI in line
with the latest QRD template version 10.0 and to
introduce editorial corrections in the PI."

Request for Supplementary Information adopted
on 20.07.2017, 21.04.2017.

Request for Supplementary Information adopted
with a specific timetable.

**Mozobil - plerixafor -
EMA/H/C/001030/II/0032, Orphan**

MAH: Genzyme Europe BV, Rapporteur: Paula
Boudewina van Hennik, PRAC Rapporteur:
Sabine Straus, "Update of sections 4.2 and 5.2 of
the SmPC in order to reflect the results of the
completed study MSC12830 (MOZ11809),
entitled "A Phase 4, Multicenter, Randomized,
Comparator Trial Evaluating the Standard
Weight-Based Dose (0.24 mg/kg) Compared to a
Fixed Dose (20 mg) of Plerixafor Injection in

Request for Supplementary Information adopted
with a specific timetable.

Combination with G-CSF to Mobilize and Collect
≥5 x 10⁶ CD34+ cells/kg in ≤4 Days and to
Evaluate the Difference in Total Systemic
Exposure in Patients with Non-Hodgkin's
Lymphoma Weighing ≤70 kg" listed as a category
3 study in the RMP.

The Package Leaflet is updated accordingly. The
RMP version 9.0 has also been submitted.

In addition, the Marketing authorisation holder
(MAH) took the opportunity to update the list of
local representatives in the Package Leaflet."

Request for Supplementary Information adopted
on 06.07.2017.

Ninlaro - ixazomib -

EMA/H/C/003844/II/0002, Orphan

MAH: Takeda Pharma A/S, Rapporteur: Greg
Markey, PRAC Rapporteur: Ulla Wändel Liminga,
"Update of sections 4.8 and 5.1 of the SmPC to
reflect the final overall survival analysis of
C16010 China continuation study, a phase III
study comparing ixazomib plus lenalidomide and
dexamethasone versus placebo plus lenalidomide
in patients with relapsed and/or refractory
multiple myeloma, in order to fulfil SOB (Specific
Obligation) 002. Annex II.E and the RMP (version
2.0) are updated accordingly. In addition the
Marketing Authorisation Holder (MAH) took the
opportunity to make a small correction in sections
4.7 and 9 of the SmPC and to the German
translations."

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted
on 05.05.2017.

Positive Opinion adopted by consensus on
06.07.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

Odomzo - sonidegib -

EMA/H/C/002839/II/0011

MAH: Sun Pharmaceutical Industries Europe
B.V., Rapporteur: Paula Boudewina van Hennik,
PRAC Rapporteur: Patrick Batty, "Submission of
the final results from studies CLDE225C2301 and
CLDE225X2104.

Study CLDE225C2301 is a phase II, multi-center,
open-label, single-arm study of the efficacy and
safety of oral LDE225 in patients with Hhpathway
activated relapsed medulloblastoma.

Study CLDE225X2104 is a Phase I/II study of
LDE225 in pediatric patients with recurrent or
refractory medulloblastoma or other tumors
potentially dependent on the Hedgehog-signaling

Positive Opinion adopted by consensus on
06.07.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

pathway and adult patients with recurrent or refractory medulloblastoma. The RMP has been updated accordingly. The product information remains unchanged.”

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 09.06.2017.

**Olumiant - baricitinib -
EMA/H/C/004085/II/0001**

MAH: Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, “Update of section 4.4 of the SmPC in order to add a warning on venous thromboembolism based on analyses of the occurrence of venous thromboembolic events in clinical trials with baricitinib. The Package Leaflet is updated accordingly. The RMP version 2.0 has been submitted, as part of this application.”

Opinion adopted on 20.07.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Olysio - simeprevir -
EMA/H/C/002777/II/0031**

MAH: Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Julie Williams, “Update of section 5.1 of the SmPC in order to update the efficacy information following results from study HPC3002 A Prospective 3-year Follow-up Study in Subjects Previously Treated in a Phase IIb or Phase III Study with a TMC435-containing Regimen for the Treatment of Hepatitis C Virus (HCV) Infection listed as a category 3 study in the RMP and in fulfilment of MEA005. The RMP version 4.2 has also been submitted which includes updates of changes already agreed in procedures EMA/H/C/002777/II/0021, EMA/H/C/002777/II/0027 and EMA/H/A-20/1438/C/2777/0019.”

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 18.05.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Perjeta - pertuzumab -
EMA/H/C/002547/II/0029**

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC, annex II and relevant sections of the PL in order to update information on cardiac safety and reflect the results from study BERNICE

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(WO29217) listed as a specific obligation in the Annex II; BERNICE is an ongoing Multicenter, Multinational, Phase II Study to Evaluate Perjeta in Combination with Herceptin and Standard Neoadjuvant Anthracycline-Based Chemotherapy in Patients with HER2- Positive, Locally Advanced, Inflammatory, or Early-Stage Breast Cancer.

The RMP v.9 has also been submitted."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 22.06.2017.

**Praxbind - idarucizumab -
EMA/H/C/003986/II/0007**

Request for Supplementary Information adopted with a specific timetable.

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the final results from a study 1321.3 titled "A Phase III, case series clinical study of the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g idarucizumab (BI 655075) in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures. RE-VERSE-AD (A study of the RE-VERSAl Effects of Idarucizumab on Active Dabigatran) trial" listed as a category 3 study in the RMP (MEA 001).

The RMP version 3.0 has also been submitted.

In addition, the Marketing authorisation holder took the opportunity to update the immunogenicity section in 5.1 of SmPC and to bring the PI in line with the latest QRD template version 10."

Request for Supplementary Information adopted on 20.07.2017.

**Privigen - human normal immunoglobulin -
EMA/H/C/000831/II/0119**

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC to include the PATH (IgPro20_3003) study results (safety & efficacy study with chronic inflammatory demyelinating polyneuropathy (CIDP) patients). Minor changes are also introduced to section 4.2 of the SmPC. In addition, the MAH took the opportunity to make some editorial changes to sections 4.3 and 5.2 of

the SmPC. The Package leaflet and the RMP (finally agreed version 5.1) were updated accordingly.”
Opinion adopted on 06.07.2017.

**Sivextro - tedizolid phosphate -
EMA/H/C/002846/II/0019**

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Bruno Sepodes, PRAC Rapporteur:
Dolores Montero Corominas, “Update of section 4.8 of the SmPC of the concentrate for solution for infusion formulation, in order to add information from BAY119-2631/16121, a Phase 3 randomized, double-blind, multi-centre study comparing the efficacy and safety of intravenous to oral 6-day tedizolid phosphate and intravenous to oral 10 day linezolid for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and change the reported expected frequency of the adverse reaction “infusion site phlebitis” from “uncommon” to “common”. The Package Leaflet is updated accordingly. An updated RMP (version 3.0) has also been submitted, proposing to collect safety information regarding tedizolid phosphate by conducting three investigator initiated studies and deleting the original proposed long term safety study. The MAH also took the opportunity to make minor editorial corrections throughout the product information.”

Request for Supplementary Information adopted on 06.07.2017.

Request for Supplementary Information adopted with a specific timetable.

**Sylvant - siltuximab -
EMA/H/C/003708/II/0023, Orphan**

MAH: Janssen-Cilag International NV,
Rapporteur: Concepcion Prieto Yerro, PRAC
Rapporteur: Brigitte Keller-Stanislawski,
“Submission of the final report from study CANTO328SMM2001 listed as a category 3 study in the RMP This is a ‘Phase 2, Randomized, Double-blind, Placebo-controlled, Multicenter Study of Siltuximab (Anti IL-6 Monoclonal Antibody) in Subjects with High-risk Smoldering Multiple Myeloma’ to evaluate immunogenicity data. No changes to the PI are proposed. The RMP is being updated accordingly.”
Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) -
EMA/H/C/000973/II/0117**

Request for Supplementary Information adopted with a specific timetable.

MAH: GlaxoSmithkline Biologicals SA,
 Rapporteur: Kristina Dunder, PRAC Rapporteur:
 Qun-Ying Yue, "Update of sections 4.2, 4.4 and
 5.1 of the SmPC in order to reflect the results
 from study10PN-PD-DIT-072, a phase III, open,
 controlled, multi-centric study to evaluate the
 immunogenicity, safety and reactogenicity of
 Synflorix in children at an increased risk of
 pneumococcal infection. The Package Leaflet is
 updated accordingly. An updated RMP version 16
 has also been submitted. This submission fulfils
 the post-authorisation measure MEA 065."
 Request for Supplementary Information adopted
 on 06.07.2017.
 Clockstop extension of, responses expected
 12.09.2017. Adopted.
 Letter from the applicant dated 17.07.2017
 requesting a clock stop extension. **For
 information.**

**Tagrisso - osimertinib -
 EMEA/H/C/004124/II/0016**

MAH: AstraZeneca AB, Rapporteur: Jorge
 Camarero Jiménez, PRAC Rapporteur: Sabine
 Straus, "Provision of the final CSR for Study Aura
 17; a phase II, open label, single-arm study to
 assess the safety and efficacy of AZD9291 in Asia
 pacific patients with locally advanced/metastatic
 non-small cell lung cancer whose disease has
 progressed with previous epidermal growth
 factor receptor tyrosine kinase inhibitor therapy
 and whose tumours harbour a T790M mutation
 within the epidermal growth factor receptor
 gene). An updated RMP version 7.0 was agreed
 during the procedure."
 Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on
 06.07.2017. The Icelandic and Norwegian CHMP
 Members were in agreement with the CHMP
 recommendation.

**Tamiflu - oseltamivir -
 EMEA/H/C/000402/II/0128**

MAH: Roche Registration Limited, Rapporteur:
 Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka,
 "Update of section 4.6 of the SmPC in order to
 reflect the final study results from
 non-interventional safety study BV29684, which
 assessed the safety of oseltamivir exposure in
 pregnant women, and was listed as a category 3
 study in the RMP (MEA099). The RMP version
 15.0 has also been updated to reflect the study
 results."
 Request for Supplementary Information adopted
 on 20.07.2017.

Request for Supplementary Information adopted
 with a specific timetable.

Tyverb - lapatinib -**EMA/H/C/000795/II/0048/G**

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel

Liminga, "1) C.I.4 (type II): Update of sections 4.4, 4.8, and 5.1 of the SmPC in order to add a warning on concentration-dependent increase of the QTc interval, concomitant use of CYP3A4 inhibitors, a strengthened recommendation of ECG monitoring (section 4.4), to add to the tabulated list of adverse reactions 'Ventricular arrhythmias/Torsades de Pointes, electrocardiogram QT prolonged' (frequency Not known)(section 4.8) and to update safety information (section 5.1) following the submission of study report EGF114271 (a phase IV placebo controlled single sequence crossover study to evaluate the effect of repeat oral doses of lapatinib on cardiac repolarization in patients with advanced cancer). The Package Leaflet is updated accordingly.

2) C.I.4 (type II): Update of section 4.8 of the SmPC reflecting, in the tabulated list of adverse reactions, that amongst serious cutaneous reactions, Stevens - Johnson syndrome and Toxic Epidermal Necrolysis has been observed (frequency Not known), further to the review of the Novartis safety database. 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 and update the list of local representatives. Moreover, the MAH took the opportunity to update Annex II to delete an Annex II condition related to study EGF114299, fulfilled with procedure ANX. 28.2. The RMP (version 32) is updated to upgrade QTc prolongation, severe cutaneous reactions and food effect from important potential risks to important identified risks and to introduce template-related changes and study milestones updates."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 23.03.2017, 10.11.2016.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Uptravi - selezipag -**EMA/H/C/003774/II/0009**

MAH: Actelion Registration Ltd., Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams,

"Update of section 4.5 of the SmPC to add

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

information on the effect of selexipag administration on the pharmacokinetics of midazolam, its metabolite 1-hydroxymidazolam and the CYP3A4 metabolism, based on data from the completed clinical pharmacology study AC-065-114, a single-centre, open-label, randomized, two-treatment crossover Phase 1 study investigating the effect of selexipag on the pharmacokinetics of midazolam and its metabolite 1-hydroxymidazolam in healthy male subjects. An updated RMP (version 5.1) has also been submitted, to add the results of study AC-065-114, reclassify 'hyperthyroidism' as an important identified risk and update the PASS timelines and protocol versions in accordance with the current EXPOSURE protocol version 3 and the EDUCATE protocol version 2."

Opinion adopted on 06.07.2017.

Vedrop - tocopherol -

See 9.1. of the main agenda

EMA/H/C/000920/II/0022

MAH: Orphan Europe SARL, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "Submission of the final report for the registry of paediatric patients treated with Vedrop (tocopherol) in Europe for vitamin E deficiency due to digestive malabsorption in congenital or hereditary chronic cholestasis. Consequentially, the remaining specific obligation is fulfilled and Annex II is updated accordingly."

Xalkori - crizotinib -

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

EMA/H/C/002489/II/0049/G

MAH: Pfizer Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Submission of the final results related of the Non-Interventional Post-Authorisation Safety Study (PASS) A8081049 "A cross-sectional study to evaluate the effectiveness of XALKORI (PF_02341066, also referred to as crizotinib) Therapeutic Management Guide among physicians prescribing XALKORI in Europe" and PASS A8081050 "A cross-sectional study to evaluate the effectiveness of XALKORI Patient Information Brochure among non-small cell lung cancer (NSCLC) patients receiving XALKORI treatment in Europe".

In the light of the results from PASS study A8081049, the MAH is proposing to update Annex II to remove the XALKORI TMG from the Educational Materials. The MAH is also taking the

opportunity to state “monotherapy” in section 4.1 of the SmPC as requested by CHMP and to bring the PI in line with the latest QRD template.”
Opinion adopted on 06.07.2017.

Xarelto - rivaroxaban -

EMA/H/C/000944/II/0052/G

MAH: Bayer AG, Rapporteur: Kristina Dunder,
PRAC Rapporteur: Qun-Ying Yue, “Group of variations consisting of:

1) C.1.4. To add the authorised indications “Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults” to Xarelto 10 mg based on Einstein Choice trial (A randomised phase III clinical study to evaluate efficacy and safety of Reduced-dosed rivaroxaban and standard-dosed rivaroxaban versus ASA in the long-term prevention of recurrent symptomatic venous thromboembolism in patients with symptomatic deep-vein thrombosis and/or pulmonary embolism) in section 4.1 of the SmPC 10 mg.

Consequently:

- Changes in sections 4.2, 4.8 and 5.1 for Xarelto 10mg, 15mg and 20 mg are made in order to update the posology, efficacy and safety information.

- Annex III is updated to include Xarelto 10 mg into Patient alert card to support management of bleeding when the 10 mg is treated for long-term prevention of recurrent VTE

- RMP (version 10) is updated

2) B.II.e.5.a.1- to add a new pack size of 14 film coated tablets in blister (PP/alu) for Xarelto 10 mg

3) B.II.e.5.a.1- to add a new pack size of 28 film coated tablets in blister (PP/alu) for Xarelto 10 mg

4) B.II.e.5.a.1- to add a new pack size of 98 film coated tablets in blister (PP/alu) for Xarelto 10 mg

5) B.II.e.1.b.1 to change immediate packaging of the finished product for 10 mg film coated tablets to introduce HDPE bottle with screw cap including new presentation (pack containing 100 film coated tablets for 10 mg strength)

6) C.1.4 To add information on interactions with SSRIs and SNRIs in section 4.5 and a related warning in section 4.4 of the SmPC based on post-hoc analyses to investigate bleeding risk for

Request for Supplementary Information adopted with a specific timetable.

rivaroxaban in patients with and without use of SSRI or SNRIs from the pivotal studies.

In addition, MedDRA terminology is updated in the adverse drug reactions table in section 4.8 of the SmPC

7) C.1.11.z To delete from the summary of safety concerns: "Patients undergoing major orthopaedic surgery other than elective hip or knee replacement surgery" and "Remedial pro-coagulant therapy for excessive haemorrhage". Part II - Modules SVIII: Summary of the safety concerns, Part III, Section 1 Safety Concerns and overview of planned pharmacovigilance action were amended accordingly. In addition, Part II, Safety Specification, module SIV, Populations not studied in clinical trials: "Patients undergoing major orthopaedic surgery other than elective hip or knee replacement surgery" and "Remedial pro-coagulant therapy for excessive haemorrhage" was updated.

Request for Supplementary Information adopted on 20.07.2017, 18.05.2017.

**Xgeva - denosumab -
EMA/H/C/002173/II/0051**

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "To update to the Risk Management Plan (RMP) with addition of the important potential risk 'hypercalcemia several months after the last dose in patients with GCTB' and the modification of the important identified risk 'hypercalcemia following treatment discontinuation in patients with growing skeletons' to 'hypercalcemia in patients with growing skeletons several months after the previous dose'; the MAH is also taking the opportunity to implement a minor correction to the RMP for correction or to add clarification."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 22.06.2017, 26.01.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Zavesca - miglustat -
EMA/H/C/000435/II/0056, Orphan**

MAH: Actelion Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Submission of 8th Niemann-Pick type C (NP-C) Registry report and update of Annex II-D to delete the NP-C Registry listed as an obligation to the marketing authorisation.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

The RMP version 12.1 has also been submitted to reflect the above changes.

In addition, the Marketing authorisation holder took the opportunity to introduce minor changes and bring the Product Information and Annex A in line with the latest QRD template version 10."

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 21.04.2017.

WS1117/G

Stocrin-EMA/H/C/000250/WS1117/0110/G

Sustiva-EMA/H/C/000249/WS1117/0139/G

MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "C.I.4 (Type II) - Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to add a warning and update the safety information on QTc prolongation based on the final results from study AI266959; this is an interventional study to determine the concentration-electrocardiographic effects of efavirenz in healthy subjects enriched for cyp2b6 polymorphisms; the Package Leaflet is updated accordingly. The RMP version 8 has also been submitted.

Request for Supplementary Information adopted with a specific timetable.

C.I.4 (Type II) – Update of sections 4.4 and 4.8 to add catatonia as a Psychiatric symptom following an assessment of catatonia cases reported in the literature and via the United States (US) Food and Drug Administration Adverse Event Reporting System (FAERS)."

Request for Supplementary Information adopted on 06.07.2017, 06.04.2017.

WS1182

AMGEVITA-EMA/H/C/004212/WS1182/001

SOLYMBIC-EMA/H/C/004373/WS1182/001

MAH: Amgen Europe B.V., Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Ulla Wandel Liminga, "Submission of the final report from study/studies 20130258, An open-label, single-arm extension study to evaluate the long-term safety and efficacy of ABP 501 in subjects with moderate to severe rheumatoid arthritis, listed as a category 3 study in the RMP (MEA002). No changes of the PI are proposed,

Request for Supplementary Information adopted with a specific timetable.

the RMP is updated accordingly.”
Request for Supplementary Information adopted
on 06.07.2017.

B.5.4. PRAC assessed procedures

<p>PRAC Led</p> <p>Aclasta - zoledronic acid - EMA/H/C/000595/II/0069</p> <p>MAH: Novartis Europharm Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of the final 5-year report from study (ZOL446H2422) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against oral bisphosphonates and untreated population controls.” Request for Supplementary Information adopted on 06.07.2017.</p>	<p>Request for Supplementary Information adopted with a specific timetable.</p>
<p>PRAC Led</p> <p>Inovelon - rufinamide - EMA/H/C/000660/II/0041, Orphan</p> <p>MAH: Eisai Ltd, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, “Submission of the final clinical study report for study E2080-E044-401, the European registry of anti-epileptic drug use in patients with Lennox-Gastaut Syndrome (LAG), listed as a category 3 study in the RMP, in order to fulfil MEA 002.1. This is a non-interventional EU registry study entering patients (aged ≥4 years) with LGS who required a modification in anti-epileptic therapy (either the addition of another AED or the change of one drug to another) to evaluate the long-term safety of rufinamide.” Opinion adopted on 06.07.2017. Request for Supplementary Information adopted on 05.05.2017.</p>	<p>Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>PRAC Led</p> <p>NovoEight - turoctocog alfa - EMA/H/C/002719/II/0020</p> <p>MAH: Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of an amended protocol for PASS study NN7008-3553, category</p>	<p>Request for Supplementary Information adopted with a specific timetable.</p>

3 study in the RMP.

Submission of an updated RMP version 3 to update the timelines of the milestones in order to integrate the required additional pharmacovigilance activities, which include a change in the Last Patient Last Visit (LPLV) date and a change in the Clinical Trial Report (CTR) finalisation date. In addition, the duration of the trial has been amended from 4 to 7 years.”
Request for Supplementary Information adopted on 06.07.2017.

PRAC Led

**Rebif - interferon beta-1a -
EMA/H/C/000136/II/0129**

MAH: Merck Serono Europe Limited, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Filip Josephson, “Submission of an updated RMP version 9.0 in order to upgrade the important potential risk “Immunogenicity/safety risk associated with the formation of neutralizing antibodies” to important identified risk”
Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led

**Retacrit - epoetin zeta -
EMA/H/C/000872/II/0077**

MAH: Hospira UK Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise, “Submission of the final report from the registry based healthcare database study linked to PASCO (PMS-830-07-0043)) listed as a category 3 study in the RMP. This is an observational study on the incidence of thromboembolic events in patients with renal anaemia treated with erythropoietin-zeta as compared with erythropoietin-alpha and other erythropoiesis-stimulating agents.”
Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led

**Revlimid - lenalidomide -
EMA/H/C/000717/II/0095, Orphan**

MAH: Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, “Submission of the final results of the non-interventional, observational category 3 post-authorisation safety study (Study CC-5013-PASS-001) in subjects treated with lenalidomide to further characterise the safety

Request for Supplementary Information adopted with a specific timetable.

profile of lenalidomide plus dexamethasone in the treatment of relapsed and/or refractory (R/R) MM in a real-world setting.”
Request for Supplementary Information adopted on 20.07.2017.

PRAC Led
Silapo - epoetin zeta -
EMA/H/C/000760/II/0045
MAH: STADA Arzneimittel AG, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise, “Submission of the final report from the registry based healthcare database study linked to PASCO (PMS-830-07-0043)) listed as a category 3 study in the RMP. This is an observational study on the incidence of thromboembolic events in patients with renal anaemia treated with erythropoietin-zeta as compared with erythropoietin-alpha and other erythropoiesis-stimulating agents. In addition, an updated RMP (version 11) is submitted to reflect the outcome of the study.”
Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led
Tysabri - natalizumab -
EMA/H/C/000603/II/0101
MAH: Biogen Idec Ltd, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of the final clinical study report for TYGRIS, a post-marketing safety observational cohort program designed to obtain long-term safety data (approximately 5 years) in subjects with MS treated with natalizumab, and comprising parallel studies 101MS402 (United States and Canada) and 101MS403 (Rest of World). The application included an updated RMP version 23.”
Opinion adopted on 06.07.2017.
Request for Supplementary Information adopted on 06.04.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led
Yervoy - ipilimumab -
EMA/H/C/002213/II/0049
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP (version 17) in order to amend the

Request for Supplementary Information adopted with a specific timetable.

study objectives and milestones for two studies:

- study CA184332, a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy in a community setting, a category 3 study in the RMP (MEA 029): to submit the final study report with 2-years of follow-up
- study CA184338, a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy, a category 3 study in the RMP (MEA 030): to submit the final study report with 4-years of follow-up."

Request for Supplementary Information adopted on 06.07.2017.

PRAC Led

WS1163

Harvoni-EMA/H/C/003850/WS1163/0051

Sovaldi-EMA/H/C/002798/WS1163/0041

MAH: Gilead Sciences International Ltd, Lead
PRAC Rapporteur: Julie Williams, PRAC-CHMP
liaison: Greg Markey, "To provide updated RMPs for Sovaldi and Harvoni following the CHMP opinion, endorsing a PRAC recommendation, issued on 15 December 2016 (EMA/CHMP/847450/2016) on the Article 20 procedure for Direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free). The PRAC requested 'hepatitis B reactivation' to be considered as important identified risk for all direct-acting antivirals. In addition, 'emergence of hepatocellular carcinoma' and 'recurrence of hepatocellular carcinoma' have been included as important potential risks. 'Patients with previous HCC' have been reflected as missing information in the RMP of the DAAs, since this population was excluded from existing clinical trials. The requested studies have also been reflected in the RMPs."
Opinion adopted on 06.07.2017.
Request for Supplementary Information adopted on 05.05.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led

WS1169

Exviera-EMA/H/C/003837/WS1169/0028

Viekirax-EMA/H/C/003839/WS1169/0032

2

MAH: AbbVie Limited, Lead Rapporteur: Filip

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Josephson, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "To provide updated RMPs for Exviera and Viekirax following the CHMP opinion, endorsing a PRAC recommendation, issued on 15 December 2016 (EMA/CHMP/847450/2016) on the Article 20 procedure for Direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free). The PRAC requested 'hepatitis B reactivation' to be considered as important identified risk for all direct-acting antivirals. In addition, 'emergence of hepatocellular carcinoma' and 'recurrence of hepatocellular carcinoma' have been included as important potential risks. 'Patients with previous HCC' have been reflected as missing information in the RMP of the DAAs, since this population was excluded from existing clinical trials. The requested studies have also been reflected in the RMPs."

Opinion adopted on 06.07.2017.

Request for Supplementary Information adopted on 05.05.2017.

PRAC Led

WS1188

Humalog-EMA/H/C/000088/WS1188/01

57

Liprolog-EMA/H/C/000393/WS1188/012

0

MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report of a non-interventional post-authorisation safety study EUPAS 13422. This study is aimed to evaluate the impact of additional risk minimisation measures on healthcare professionals and on patients' understanding and their behaviour regarding the risk of hypoglycaemia and/or hyperglycaemia due to medication errors associated with administration of Humalog 200 U/ml KwikPen."

Request for Supplementary Information adopted on 06.07.2017.

Request for Supplementary Information adopted with a specific timetable.

PRAC Led

WS1198

Ebymect-EMA/H/C/004162/WS1198/002

2

Edistride-EMA/H/C/004161/WS1198/00

17

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Forxiga-EMA/H/C/002322/WS1198/003

7

Xigduo-EMA/H/C/002672/WS1198/0033

MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Implement the outcome of the article 20 referral regarding lower limb amputations in the RMP. The variation is submitted in order to give the rapporteur the possibility to review and assess the way the requested information has been included in the RMPs."

Opinion adopted on 20.07.2017.

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMA/H/C/003854/II/0006, Orphan, ATMP

MAH: GlaxoSmithKline Trading Services Limited, Rapporteur: Christiane Niederlaender, PRAC Rapporteur: Sabine Straus

Opinion adopted on 20.07.2017, 14.07.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.7. PRAC assessed ATMP procedures

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

WS1081

Hexacima-EMA/H/C/002702/WS1081/0055

Hexaxim-EMA/H/W/002495/WS1081/0062

Hexyon-EMA/H/C/002796/WS1081/0059

MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus

Opinion adopted on 20.07.2017.

Request for Supplementary Information adopted on 21.04.2017, 16.02.2017.

Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1122/G

Hexacima-EMA/H/C/002702/WS1122/0060/G

Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Hexaxim-EMA/H/W/002495/WS1122/0066/G Hexyon-EMA/H/C/002796/WS1122/0064/G MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.07.2017. Request for Supplementary Information adopted on 11.05.2017.	recommendation.
WS1153 Hexacima-EMA/H/C/002702/WS1153/0063 Hexaxim-EMA/H/W/002495/WS1153/0069 Hexyon-EMA/H/C/002796/WS1153/0067 MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.07.2017.	Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1165 Aflunov-EMA/H/C/002094/WS1165/0035 Foclivia-EMA/H/C/001208/WS1165/0030 MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 20.07.2017. Request for Supplementary Information adopted on 22.06.2017, 18.05.2017.	Positive Opinion adopted by consensus on 20.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1170 Aflunov-EMA/H/C/002094/WS1170/0036 Foclivia-EMA/H/C/001208/WS1170/0031 MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 06.07.2017. Request for Supplementary Information adopted on 01.06.2017.	Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1173 Glyxambi-EMA/H/C/003833/WS1173/0006 Jardiance-EMA/H/C/002677/WS1173/0032 Synjardy-EMA/H/C/003770/WS1173/0028 MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege	Positive Opinion adopted by consensus on 13.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 13.07.2017.

WS1192

Hexacima-EMA/H/C/002702/WS1192/0066

Hexaxim-EMA/H/W/002495/WS1192/0072

Hexyon-EMA/H/C/002796/WS1192/0070

MAH: Sanofi Pasteur SA, Lead Rapporteur:
Kristina Dunder

Request for Supplementary Information adopted with a specific timetable.

Request for Supplementary Information adopted on 20.07.2017.

WS1200

Lyrica-EMA/H/C/000546/WS1200/0089 Pregabalin

Pfizer-EMA/H/C/003880/WS1200/0019

MAH: Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege

Opinion adopted on 06.07.2017.

Positive Opinion adopted by consensus on 06.07.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Blincyto - blinatumomab - EMA/H/C/003731/II/0014, Orphan

MAH: Amgen Europe B.V., Rapporteur:
Alexandre Moreau, PRAC Rapporteur: Eva Jirsová
Withdrawal request submitted on 13.07.2017.

The MAH withdrew the procedure on 13.07.2017.

Strensiq - asfotase alfa - EMA/H/C/003794/II/0020, Orphan

MAH: Alexion Europe SAS, Rapporteur: Greg Markey
Withdrawal request submitted on 10.07.2017.

The MAH withdrew the procedure on 10.07.2017.

Xeljanz - tofacitinib - EMA/H/C/004214/II/0002

MAH: Pfizer Limited, Rapporteur: Robert James Hemmings
Withdrawal request submitted on 06.07.2017.

The MAH withdrew the procedure on 06.07.2017.

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

- glycopyrronium / formoterol fumarate dihydrate - EMA/H/C/004245

, indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD)

- bictegrovir / emtricitabine / tenofovir

alafenamide - EMEA/H/C/004449

, treatment of adults infected with human immunodeficiency virus-1 (HIV-1)

- dapivirine - EMEA/H/W/002168, Article 58

See 3.4. of the main agenda

, Reducing the risk of HIV-1 infection via vaginal intercourse in sexually active HIV-uninfected women

- darunavir - EMEA/H/C/004891

, treatment of HIV-1 infection

- deferiprone - EMEA/H/C/004710

, treatment of iron overload in thalassemia major

- lesinurad / allopurinol -

EMEA/H/C/004412, gout

- pacritinib - EMEA/H/C/004793, Orphan

Applicant: CTI Life Sciences Limited, treatment of disease-related splenomegaly and control of symptoms in patients with primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (PPV-MF), or post-essential thrombocythemia myelofibrosis (PET-MF) who have thrombocytopenia (platelet counts $\leq 100,000$ / μ L).

- emicizumab - EMEA/H/C/004406

Accelerated review

, routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors.

- botulinum toxin type a -

EMEA/H/C/004587

, temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

- trastuzumab - EMEA/H/C/004463

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

- meropenem / vaborbactam -

EMEA/H/C/004669

, treatment of infections

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

Dasatinib Monohydrate -
EMA/H/C/000709/X/0556/G)

- everolimus -
EMA/H/C/002311/X/0045, Orphan
MAH: Novartis Europharm Ltd

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

- anagrelide - EMA/H/C/004585
, reduction of elevated platelet counts in at risk
essential thrombocythaemia patients,
List of Questions adopted on 21.04.2017.

- plitidepsin - EMA/H/C/004354, Orphan
Applicant: Pharma Mar, S.A., treatment of
multiple myeloma
List of Questions adopted on 23.02.2017.

- benralizumab - EMA/H/C/004433
, treatment of severe asthma with an eosinophilic
phenotype
List of Questions adopted on 21.04.2017.

- darunavir - EMA/H/C/004273
, treatment of HIV-1 infection,
List of Questions adopted on 23.03.2017.

- ulipristal acetate -
EMA/H/C/001027/X/0045
List of Questions adopted on 22.06.2017.

- fulvestrant - EMA/H/C/004649
, treatment of breast cancer,
List of Questions adopted on 21.04.2017.

- imatinib - EMA/H/C/004748
, treatment of newly diagnosed and chronic
Philadelphia chromosome (bcr-abl) positive
(Ph+) chronic myeloid leukaemia (CML),
gastrointestinal stromal tumours (GIST),
unresectable dermatofibrosarcoma protuberans
(DFSP) and recurrent and/or metastatic DFSP,
Request for Supplementary Information adopted
on 22.06.2017.

- bevacizumab - EMA/H/C/004360
, treatment of breast cancer, non-small cell lung
cancer, renal cell cancer, advanced epithelial
ovarian, fallopian tube, or primary peritoneal
cancer, platinum-sensitive epithelial ovarian,

fallopian tube or primary peritoneal cancer
List of Questions adopted on 21.04.2017.

- velmanase alfa - EMEA/H/C/003922, Orphan

Applicant: Chiesi Farmaceutici S.p.A., indicated for long-term enzyme replacement therapy in patients with alpha-mannosidosis
List of Questions adopted on 26.01.2017.

- bevacizumab - EMEA/H/C/004728

, treatment of metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, unresectable advanced metastatic or recurrent non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer, platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer,
List of Questions adopted on 21.04.2017.

- semaglutide - EMEA/H/C/004174

, to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events
List of Questions adopted on 21.04.2017.

- d-biotin - EMEA/H/C/004153

, treatment of progressive multiple sclerosis (primary or secondary)
List of Questions adopted on 15.12.2016.

- ciclosporin - EMEA/H/C/004229

, for the treatment of moderate dry eye disease in adults
List of Questions adopted on 23.03.2017.

- rucaparib - EMEA/H/C/004272, Orphan

Applicant: Clovis Oncology UK Ltd, treatment of ovarian cancer
List of Questions adopted on 23.03.2017.

- human herpesvirus 3 - EMEA/H/C/004336

, prevention of herpes zoster (HZ) and HZ-related complications
List of Questions adopted on 21.04.2017.

- human fibrinogen / human thrombin - EMEA/H/C/004446

, treatment of haemostasis
List of Questions adopted on 21.04.2017.

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

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

Actelsar HCT - telmisartan /

hydrochlorothiazide -

EMA/H/C/002676/R/0015

MAH: Actavis Group PTC ehf, Generic, Generic of
MicardisPlus, Rapporteur: Alar Irs, PRAC
Rapporteur: Carmela Macchiarulo

Hexacima - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) -

EMA/H/C/002702/R/0068

MAH: Sanofi Pasteur SA, Rapporteur: Jan
Mueller-Berghaus, Co-Rapporteur: Bart Van der
Schueren, PRAC Rapporteur: Brigitte
Keller-Stanislawski

Hexyon - diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) - EMA/H/C/002796/R/0072

MAH: Sanofi Pasteur Europe, Duplicate, Duplicate
of Hexacima, Rapporteur: Jan Mueller-Berghaus,
Co-Rapporteur: Bart Van der Schueren, PRAC
Rapporteur: Brigitte Keller-Stanislawski

matinib Actavis - imatinib -

EMA/H/C/002594/R/0015

MAH: Actavis Group PTC ehf, Generic, Generic of
Glivec, Rapporteur: Hrefna Gudmundsdottir,
PRAC Rapporteur: Eva A. Segovia

Marixino - memantine -

EMA/H/C/002658/R/0012

MAH: Consilient Health Ltd., Generic, Generic of
Ebixa, Rapporteur: Milena Stain, PRAC
Rapporteur: Dolores Montero Corominas

Mycamine - micafungin -

EMA/H/C/000734/R/0034

MAH: Astellas Pharma Europe B.V., Rapporteur:
Harald Enzmann, Co-Rapporteur: Koenraad
Norga, PRAC Rapporteur: Martin Huber

Ocaliva - obeticholic acid -

EMA/H/C/004093/R/0002, Orphan

MAH: Intercept Pharma Ltd, Rapporteur: Jorge

Camarero Jiménez, Co-Rapporteur: Daniela
Melchiorri, PRAC Rapporteur: Sabine Straus

Perjeta - pertuzumab -

EMA/H/C/002547/R/0031

MAH: Roche Registration Limited, Rapporteur:

Sinan B. Sarac, Co-Rapporteur: Daniela

Melchiorri, PRAC Rapporteur: Doris Stenver

Prepandrix - A/Indonesia/05/2005 (H5N1)

like strain used (PR8-IBCDC-RG2) -

EMA/H/C/000822/R/0071

MAH: GlaxoSmithkline Biologicals SA,

Rapporteur: Greg Markey, Co-Rapporteur:

Johann Lodewijk Hillege, PRAC Rapporteur: Julie

Williams

Privigen - human normal immunoglobulin -

EMA/H/C/000831/R/0122

MAH: CSL Behring GmbH, Rapporteur: Jan

Mueller-Berghaus, Co-Rapporteur: Luca Pani,

PRAC Rapporteur: Brigitte Keller-Stanislowski,

Thalidomide Celgene - thalidomide -

EMA/H/C/000823/R/0054, Orphan

MAH: Celgene Europe Limited, Rapporteur:

Alexandre Moreau, Co-Rapporteur: Filip

Josephson, PRAC Rapporteur: Ghania Chamouni

Tolucombi - telmisartan /

hydrochlorothiazide -

EMA/H/C/002549/R/0020

MAH: KRKA, d.d., Novo mesto, Generic, Generic

of MicardisPlus, Rapporteur: Alar Irs, PRAC

Rapporteur: Carmela Macchiarul

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

Blincyto - blinatumomab -

EMA/H/C/003731/II/0018, Orphan

MAH: Amgen Europe B.V., Rapporteur:

Alexandre Moreau, PRAC Rapporteur: Eva

Jirsová“Extension of Indication to include the

children 1 month and older to the authorised

population for the treatment of adults with

Philadelphia chromosome-negative relapsed or

refractory B-precursor acute lymphoblastic

leukaemia (ALL) for BLINCYTO;

as a consequence, sections 4.1, 4.2, 4.4, 4.8,

5.1, 5.2 and 6.6 of the SmPC are updated in order to include the new population, updated the posology and update the safety information. The Package Leaflet is updated in accordance. RMP version 6.0 has been submitted"

Briviact - brivaracetam -

EMA/H/C/003898/II/0010/G

MAH: UCB Pharma S.A., Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Adam Przybylkowski"Extension of Indication to include adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy 4 years of age and older for Briviact. As a consequence, sections 4.1, 4.2, 4.7, 5.1 and 5.2 of the SmPC are updated.

In addition, the Marketing authorisation holder (MAH) submitted a 5ml oral syringe and adaptor for the paediatric population.

The Package Leaflet and Labelling are updated in accordance.

Submission of the final Environmental Risk Assessment for the inclusion of the paediatric population in accordance with the new indication sought."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

BeneFIX - nonacog alfa -

EMA/H/C/000139/II/0146

MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus,

Benepali - etanercept -

EMA/H/C/004007/II/0026

MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Andrea Laslop

Cosentyx - secukinumab -

EMA/H/C/003729/II/0026

MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen,

Cystadane - betaine anhydrous -

EMA/H/C/000678/II/0029

MAH: Orphan Europe SARL, Rapporteur: Harald Enzmann

Deltyba - delamanid -

EMA/H/C/002552/II/0020/G, Orphan

MAH: Otsuka Novel Products GmbH, Rapporteur:
Greg Markey

Elocta - efmoroctocog alfa -
EMA/H/C/003964/II/0016/G

MAH: Swedish Orphan Biovitrum AB (publ),
Rapporteur: Jan Mueller-Berghaus,

Foscan - temoporfin -
EMA/H/C/000318/II/0042

MAH: biolitec Pharma Ltd, Rapporteur: Paula
Boudewina van Hennik

Hizentra - human normal immunoglobulin -
EMA/H/C/002127/II/0086

MAH: CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus,

**Intanza - influenza vaccine (split virion,
inactivated) - EMA/H/C/000957/II/0054**

MAH: Sanofi Pasteur Europe, Rapporteur: Jorge
Camarero Jiménez

Opdivo - nivolumab -
EMA/H/C/003985/II/0037/G

MAH: Bristol-Myers Squibb Pharma EEIG,
Rapporteur: Jorge Camarero Jiménez

ergoveris - follitropin alfa / lutropin alfa -
EMA/H/C/000714/II/0052/G

MAH: Merck Serono Europe Limited, Rapporteur:
Nithyanandan Nagercoil,

Soliris - eculizumab -
EMA/H/C/000791/II/0100, Orphan

MAH: Alexion Europe SAS, Rapporteur: Jorge
Camarero Jiménez

Suliqua - insulin glargine / lixisenatide -
EMA/H/C/004243/II/0003/G

MAH: sanofi-aventis groupe, Rapporteur: Kristina
Dunder,

Uptravi - selexipag -
EMA/H/C/003774/II/0010

MAH: Actelion Registration Limited, Rapporteur:
Martina Weise

Voncento - human coagulation factor VIII /
human von willebrand factor -
EMA/H/C/002493/II/0030/G

MAH: CSL Behring GmbH, Rapporteur: Paula
Boudewina van Hennik

WS1084/G
Ganfort-EMA/H/C/000668/WS1084/002

8/G

Lumigan-EMA/H/C/000391/WS1084/005

3/G

MAH: Allergan Pharmaceuticals Ireland, Lead

Rapporteur: Hanne Lomholt Larsen,

WS1177/G

Neulasta-EMA/H/C/000420/WS1177/00

97/G

Ristempa-EMA/H/C/003910/WS1177/00

12/G

MAH: Amgen Europe B.V., Lead Rapporteur:

Robert James Hemmings

WS1226

Humalog-EMA/H/C/000088/WS1226/01

58

Liprolog-EMA/H/C/000393/WS1226/012

1

MAH: Eli Lilly Nederland B.V., Lead Rapporteur:

Robert James Hemmings

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

Ameluz - 5-aminolevulinic acid -

EMA/H/C/002204/II/0027/G

MAH: Biofrontera Bioscience GmbH, Rapporteur:

Harald Enzmann, "C.I.4

Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the posology and method of administration of Ameluz for the treatment of actinic keratosis (AK) and field cancerization in combination with daylight and to update the safety information, based on the clinical study results from ALA-AK-CT009; this is a phase III, randomised, interventional, observer-blinded study aimed to compare the efficacy and safety of Ameluz in the treatment of mild to moderate AK with Metvix in combination with daylight photodynamic therapy. Section 5.2 of the SmPC has included a minor editorial change. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

C.I.5.b

Change in the legal status of Ameluz from "medicinal product subject to restricted medical prescription" to "medicinal product subject to

medical prescription".

**Aranesp - darbepoetin alfa -
EMA/H/C/000332/II/0143**

MAH: Amgen Europe B.V., Rapporteur: Martina Weise "Update of section of section 4.8 the SmPC in order to add a warning on injection site bruise and haemorrhage with frequency unknown and to provide additional instructions on the use of the device in the PL following signal procedure EMA/H/C000332/SDA/090 on cases of incorrect device use / device malfunction"

**Deltyba - delamanid -
EMA/H/C/002552/II/0021, Orphan**

MAH: Otsuka Novel Products GmbH, Rapporteur: Greg Markey, "Update of sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC to reflect the results of the final study report of 242-09-213 (A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Trial to Evaluate the Safety and Efficacy of Delamanid (OPC-67683) Administered Orally as 200 mg Total Daily Dose for Six Months in Patients With Pulmonary Sputum Culture-positive, Multidrug-resistant Tuberculosis), submitted to fulfill SOB-01. The Package leaflet is updated accordingly."

**Epclusa - sofosbuvir / velpatasvir -
EMA/H/C/004210/II/0012**

MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson "Update of section 5.3 of the SmPC in order to add non-clinical safety findings based on a 6-month carcinogenicity study conducted with velpatasvir in transgenic mice"

**ReFacto AF - moroctocog alfa -
EMA/H/C/000232/II/0140**

MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen, "Submission of the report 'The Immunogenicity of ReFacto AF in UK PUPs Who Started Treatment from 2010' prepared by the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO). This report is being submitted in the context of a post-approval commitment, MEA 115.1 ('The MAH commits to submit the CSR for "A Postauthorization Safety Surveillance Registry or ReFacto AF in Previously Untreated Patients (PUPs) in Usual Care Settings – study number 4435" and to initiate the registry'), as supporting

evidence of the ongoing safety evaluation of ReFacto AF in PUPs with haemophilia A and with a specific focus on the development of inhibitors.”

Revatio - sildenafil -

EMA/H/C/000638/II/0077

MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.6 of the SmPC in order to revise the statement concerning the detection of sildenafil and its active metabolite in human milk and the potential for impact on the breastfed infant.

The Package Leaflet and Labelling are updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0.”

Stelara - ustekinumab -

EMA/H/C/000958/II/0058

MAH: Janssen-Cilag International NV, Rapporteur: Greg Markey, “Update of section 4.8 of the SmPC in order to include Lower Respiratory Tract Infection as an Adverse Drug Reaction based on a comprehensive evaluation of safety information from the STELARA clinical studies database and post-marketing database, as well as available literature.

The Package Leaflet is updated accordingly.”

trensiq - asfotase alfa -

EMA/H/C/003794/II/0019/G, Orphan

MAH: Alexion Europe SAS, Rapporteur: Greg Markey, “Update of section 5.1 of the SmPC in order to update information following final results from studies ENB-006-09 [A Randomized, Open-Label, Multicenter, Multinational, Dose-Ranging, Historical Control Study of the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of Asfotase Alfa (Human Recombinant Tissue-Nonspecific Alkaline Phosphatase Fusion Protein) in Children with Hypophosphatasia (HPP)] (and its extension ENB-008-10 [Extension Study of Protocol ENB-006-09 Evaluating the Long-Term Safety and Efficacy of Asfotase Alfa (Human Recombinant Tissue-Nonspecific Alkaline Phosphatase Fusion Protein) in Children with Hypophosphatasia (HPP)]) and ENB-009-10 [A Randomized, Open-Label, Multicenter, Multinational, Dose-Ranging, Concurrent Control

Study of the Safety, Efficacy, and Pharmacokinetics of ENB-0040 (Human Recombinant Tissue-Nonspecific Alkaline Phosphatase Fusion Protein) in Adolescents and Adults with Hypophosphatasia (HPP)] listed as an obligation in the Annex II (ANX002). In addition, the Marketing authorisation holder (MAH) took the opportunity to propose editorial changes for section 4.5 to better clarify the information provided."

Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0083

MAH: Gilead Sciences International Ltd, Rapporteur: Robert James Hemmings, "Update of sections 4.5 of the SmPC in order to add drug-drug interaction data from Study GS-US-292-1316; this is a Phase 1, Open-Label, Fixed Sequence Study Evaluating the Pharmacokinetics and Drug Interaction Potential Between Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Single-Table Regimen and Sertraline in Healthy Subjects.

In addition, the Marketing authorisation holder (MAH) took the opportunity make administrative amendments to section 4.8 of the SmPC."

ecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0041

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "Update of sections 4.4 and 4.8 of the SmPC in order to add anaphylactic reaction as a warning and as an adverse reaction with unknown frequency, based on post-marketing experience. The Package Leaflet is updated accordingly.

In addition, the Biogen Idec Ltd took the opportunity to bring the PI in line with the latest QRD template version 10."

Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0042

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information in the paediatric population based on the clinical study results from study 109MS202, listed as a category 3 study in the RMP; this is an open-label, multicentre,

multidose study designed to assess the effect of Tecfidera on magnetic resonance imaging lesions and pharmacokinetics, safety and tolerability in paediatric population with relapsing-remitting multiple sclerosis.

There are no updates proposed in the package leaflet or RMP."

**Tecfidera - dimethyl fumarate -
EMA/H/C/002601/II/0043/G**

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "C.I.13

Submission of non-clinical study report for study PD-15-73: a haemotoxicity study of two test compounds (BIO 0022819 and BIO 0022817) on T-CFC progenitor stem cells and T-cells derived from both human and non-human primate bone marrow and peripheral blood mononuclear cells (MNCs). This submission is linked to a category 3 study in the RMP.

C.I.13

Submission of non-clinical study report for study P00012-15-05: a preclinical study to evaluate the toxicity potential and toxicokinetic profile of dimethyl fumarate and hydroxyurea, when co-administered once daily via nasogastric intubation to cynomolgus monkeys for a minimum of 91 days. This submission is linked to a category 3 study in the RMP."

**Tecfidera - dimethyl fumarate -
EMA/H/C/002601/II/0044**

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "Submission of the final study report of an interventional PASS listed as a category 4 study in the RMP: A Multicentre, Open-Label, Single-Arm Study to Evaluate Gastrointestinal Tolerability in Subjects with Relapsing-Remitting Multiple Sclerosis Receiving Dimethyl Fumarate (TOLERATE), study number 109MS407."

**Toviaz - fesoterodine -
EMA/H/C/000723/II/0049**

MAH: Pfizer Limited, Rapporteur: Concepcion Prieto Yerro "Update of the SmPC sections 4.6 and 5.3 with revised information from reproductive toxicity studies in mice. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.0."

**Translarna - ataluren -
EMA/H/C/002720/II/0036, Orphan**

MAH: PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in order to include information regarding the effects of ataluren on the pharmacokinetics of sensitive probe substrate of organic anion transporter 3 (OAT3)) following results from study PTC124-GD-037-HV (MEA015). In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI."

Trevicta - paliperidone -

EMA/H/C/004066/II/0011

MAH: Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder "Update of section 4.8 of the SmPC in order to update the safety information after assessment of study R092670-SCA-3004 (A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Paliperidone Palmitate Evaluating Time to Relapse in Subjects With Schizoaffective Disorder). The Package Leaflet has been updated accordingly"

Vargatef - nintedanib -

EMA/H/C/002569/II/0017

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add 'weight decreased' as a new adverse drug reaction based on a safety review of clinical trials and post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement a minor correction in the English product information, minor corrections to the Croatian, Danish, Dutch and Finnish translations and to bring section 4 of the Package Leaflet in line with QRD template version 10."

Vargatef - nintedanib -

EMA/H/C/002569/II/0018

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC to amend the current warning on hepatic function to include that drug liver induced injury was associated with nintedanib administration, to include female sex as a factor of increased risk of liver enzyme elevations, update of section 4.8 of the SmPC to add 'drug-induced liver injury' (DILI) as new ADR and update of section 5.2 of the SmPC to amend the

current information related to the mean exposure to nintedanib by race, based on a review of clinical trials and post-marketing data on DILI and on the exposure safety relationship between nintedanib plasma exposure and liver enzyme elevations, as requested by the PRAC as part of PSUSA/00010318/201611. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make some minor changes to section 4.4 and 4.8 of the SmPC."

**Xeljanz - tofacitinib -
EMA/H/C/004214/II/0003**

MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, "Submission of 2 transported inhibition studies evaluating tofacitinib for its potential to inhibit organic anion transporter (OAT) 1, OAT3 and to interact with Human MRP2 Efflux (ABC) Transporter in fulfilment of the Recommendation dated 26 January 2017."

**Xultophy - insulin degludec / liraglutide -
EMA/H/C/002647/II/0021**

MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to reflect data for transfer from insulin glargine U100 to Xultophy as compared to a basal-bolus regimen. The update is based on data from the clinical trial NN9068-4185: "A clinical trial comparing efficacy and safety of insulin degludec/liraglutide (IDegLira) versus basal-bolus therapy in subjects with type 2 diabetes mellitus".

The MAH has taken the opportunity to make minor editorial and formatting changes throughout the Annexes."

**Xyrem - sodium oxybate -
EMA/H/C/000593/II/0067/G**

MAH: UCB Pharma Limited, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to add the adverse reactions "increased libido" and "seborrhea" with an unknown frequency. Update of section 4.6 of the SmPC in order to amend the information about breast-feeding. The Package Leaflet is updated accordingly."

**Zykadia - ceritinib -
EMA/H/C/003819/II/0016**

MAH: Novartis Europharm Ltd, Rapporteur: Jorge Camarero Jiménez "Update of sections 4.2, 4.4,

4.8 and 5.2 of the SmPC in order to include amendments to the posology in hepatically impaired patients and update the safety information, respectively. The updates are based on the results from the hepatic function Study CLDK378A2110 which evaluated the PK, safety and tolerability of a single oral dose of ceritinib in subjects with varying degrees of impaired hepatic function and results from physiology-based pharmacokinetic (PBPK) modeling at steady-state.

Submission of the Report for Study A2110 fulfils MEA 001 for Zykadia."

WS1203/G

Docetaxel

Winthrop-EMEA/H/C/000808/WS1203/0053/G

Taxotere-EMEA/H/C/000073/WS1203/0128/G

MAH: Aventis Pharma S.A., Lead Rapporteur:

Alexandre Moreau"1) C.I.4 (type II)

Update of sections 4.4 and 4.8 of the SmPC to add information about ventricular arrhythmia including ventricular tachycardia based on review of the MAH's global pharmacovigilance database and scientific literature. The Package Leaflet is updated accordingly.

2) C.I.4 (type II)

Update of section 4.8 of the SmPC on the 10-year follow-up data for studies TAX316 and GEICAM 9805 studies in order to clarify the persisting events in the follow-up periods."

WS1205

Descovy-EMEA/H/C/004094/WS1205/0020

Genvoya-EMEA/H/C/004042/WS1205/0034

Odefsey-EMEA/H/C/004156/WS1205/0018

MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings"Update of section 4.5 of the SmPC in order to provide the final study report for the in vitro study AD-120-2045; this is a non-clinical study on the Effect of Xanthine Oxidase Inhibitors on Metabolism of Tenofovir alafenamide fumarate in Primary Human Hepatocytes.

This study is listed in their respective Risk

Management Plans (RMPs) as an additional pharmacovigilance activity (Category 3) (Genvoya: MEA 006; Descovy: MEA 004; Odefsey: MEA 007).

The requested worksharing procedure proposed amendments to the Summary of Product Characteristics."

WS1218

Brimica

Genuair-EMEA/H/C/003969/WS1218/001

5

Duaklir

Genuair-EMEA/H/C/003745/WS1218/001

5

MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil "Update of section 5.1 of the SmPC in order to update information following results from study M-40464-33 (A Multiple Dose, Randomised, Double-Blind, Placebo Controlled, Parallel Clinical Trial to Assess the Effect of Acclidinium Bromide/Formoterol Fumarate Fixed-Dose Combination on Lung Hyperinflation, Exercise Capacity and Physical Activity in Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD))"

WS1219

Brimica

Genuair-EMEA/H/C/003969/WS1219/001

4

Duaklir

Genuair-EMEA/H/C/003745/WS1219/001

4

MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil "Update of section 5.2 of the SmPC in order to update information based on results from study KRP-AB1102F-302 [KRP-AB1102F Phase II Clinical Pharmacology Study - An Investigation into the Pharmacokinetics upon Repeated Administration of KRP-AB1102F to COPD Patients as Subjects]. In addition, the Worksharing applicant (WSA) took the opportunity to update footnotes of the table in section 4.8 as requested during PSUR procedure EMEA/H/C/PSUSA/00010307/201511 and to amend annex II following request from procedure EMEA/H/C/PSA/S/0017."

WS1225/G

Exviera-EMEA/H/C/003837/WS1225/0031

/G

Viekirax-EMA/H/C/003839/WS1225/0035/G

MAH: AbbVie Limited, Lead Rapporteur: Filip Josephson"Submission of the final reports for two phase IIIb studies (studies M14-226 and M15-461) listed as category 3 studies in the RMP. These are open-label studies evaluating the safety and efficacy of ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin in hepatitis C virus infected patients with severe renal impairment or end-stage renal disease with or without compensated cirrhosis."

WS1234/G

Genvoya-EMA/H/C/004042/WS1234/0036/G

Stribild-EMA/H/C/002574/WS1234/0084/G

Tybost-EMA/H/C/002572/WS1234/0038/G

MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings"Update of sections 4.4 and 4.5 of the SmPC based on data from the following Pharmacology Studies (GS-US-216-1008 and GS-US-216-4032).

- Study GS-US-216-1008 is a Phase 1, randomized, fixed-sequence, open -label, single_and multiple -dose, multiple-cohort, single-center study that evaluated the drug interaction potential between darunavir (DRV)+COBI, atazanavir (ATV)+COBI, or Genvoya and the 3 hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors rosuvastatin and/or atorvastatin.
- Study GS-US-216-4032 is an open-label, single -center, multiple-cohort, fixed_sequence, Phase 1 study that evaluated the effect of DRV+COBI or ATV+COBI on the pharmacokinetic (PK) of a representative hormonal contraceptive medication, drospirenone/ethinyl estradiol.

The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to make administrative changes to the PI of all three products and update the list of local representatives for Estonia, Latvia and Lithuania for Tybost and

Stribild.

Minor linguistic amendments were made to the Product Information."

B.6.10. CHMP-PRAC assessed procedures

Adcetris - brentuximab vedotin - EMA/H/C/002455/II/0049, Orphan

MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data from study C25002; a phase 1/2 study of brentuximab vedotin (SGN-35) in paediatric patients with relapsed or refractory systemic anaplastic large cell lymphoma or hodgkin lymphoma (listed in the agreed PIP covering the conditions of Hodgkin lymphoma and anaplastic large cell lymphoma for ADCETRIS (EMA-000980-PIP01-10-M04)). An updated RMP version 11.0 was provided as part of the application."

Adenuric - febuxostat - EMA/H/C/000777/II/0047

MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.4 and 4.5 of the SmPC in order to reflect the results of preclinical study MRPO-2015-PKM-005 "Pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol" and clinical study REP-POPPK-MRP-2015-PKM-005 "Population Pharmacokinetic analysis from study titled Pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol", investigating the drug-drug interaction with azathioprine when co-administered with febuxostat.

The RMP version 6.0 has also been submitted.

In addition, the MAH took the opportunity to correct the typing errors and to bring the PI in line with the latest QRD template version 10."

Cabometyx - cabozantinib - EMA/H/C/004163/II/0002/G

MAH: Ipsen Pharma, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus, "1)
C.I.4 (type II)

Update of section 5.1 of the SmPC to reflect the final study results from clinical study XL184-308: A Phase 3, Randomized, Controlled Study of Cabozantinib (XL184) vs Everolimus in Subjects with Metastatic Renal Cell Carcinoma that has Progressed after Prior VEGFR Tyrosine Kinase Inhibitor Therapy, to fulfil the condition to the marketing authorisation listed as a PAES in the Annex II. The RMP version 2.0 has also been submitted.

2) C.I.4 (type II)

Update of section 5.3 of the SmPC to reflect the final study results from non-clinical study XL184-NC-036: 104-Week Oral Gavage Carcinogenicity and Toxicokinetic Study with Cabozantinib (XL184) in Rats. The RMP version 2.0 has also been submitted.

3) C.I.3.z (type IB)

Update of section 4.5 of the SmPC to implement the wording agreed by the PRAC following the outcome of the PSUR procedure
EMA/H/C/PSUSA/10180/201603."

Cerdelga - eliglustat -

EMA/H/C/003724/II/0013, Orphan

MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, "Update of section 4.8. of the SmPC in order to amend the safety information based on the analysis of Adverse Events from the following clinical trials: GZGD00304 (Phase 2), GZGD02507 (ENGAGE), GZGD02607 (ENCORE) and GZGD03109 (EDGE) to address post-authorisation MEA011.1 which is included in the current approved Risk Management Plan.

Update of the labelling in order to reflect the instructions on use for the sleeve of the intermediate packaging of the single blister.

The RMP version 4.0 has also been submitted."

Eperzan - albiglutide -

EMA/H/C/002735/II/0033

MAH: GlaxoSmithKline Trading Services Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams "Update of the Package Leaflet in order to amend the layout and content of the Instructions for Use (IFU). In addition, the RMP

version 8 has also been submitted to implement additional pharmacovigilance and risk minimisation activities addressing the safety concern of “medication errors/device issue potentially leading to lack of efficacy or inadequate diabetes control” and to add a PASS study to investigate the effectiveness of the new IFU.”

Ibrance - palbociclib -

EMA/H/C/003853/II/0007

MAH: Pfizer Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Torbjorn Callreus, “Update of sections 4.2, 4.4 and 5.2 of the SmPC to reflect the results of studies A5481013 and A5481014. The mentioned studies provide information of the impact of hepatic impairment (Study A5481013) on the PK of a single oral dose of 75 mg palbociclib and the impact of renal impairment (Study A5481014) on the PK of a single oral dose of 125 mg palbociclib both administered under fed conditions to subjects with varying degrees of hepatic function or renal function. The RMP (version 1.4) is proposed to be amended to reflect the completion of these studies.”

Nulojix - belatacept -

EMA/H/C/002098/II/0045

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on the risk of venous thrombosis of the renal allograft when anti-thymocyte globulin (ATG) and belatacept are coadministered (at the same or nearly the same time) in patients with other predisposing risk factors for thrombosis.

The update is based on a review of the potential increased risk for allograft thrombosis with belatacept given in close temporal relation to Thymoglobulin, as requested during assessment of PSUR 8 (EMA/H/C/PSUSA/00000311/201606).

In addition, the MAH took the opportunity update section 6.6 “Special precautions for disposal and other handling” of the SmPC and the “Information for healthcare professionals (HCPs)” in the Package Leaflet (PL) with additional safety instructions for the

co-administration of Belatacept.

Submission of this variation application fulfils LEG 021 for Nulojix.

Consistently with the above, RMP version 14 has also been submitted, including addition of the potential risk of venous thrombosis of the allograft when ATG and belatacept are coadministered in patients with other predisposing risk factors for thrombosis and a number of administrative changes.”

Olumiant - baricitinib -

EMA/H/C/004085/II/0002

MAH: Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, “Update of sections 4.5 and 5.2 of the SmPC, based on the final study report of in vitro study to investigate the inhibitory effect of baricitinib on the organic anion transporter 2 (OAT2) in fulfilment of PAM (MEA 001). The updated RMP version 3.0 has been submitted as part of this application.”

Opdivo - nivolumab -

EMA/H/C/003985/II/0038

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of section 4.8 of the SmPC with longer follow-up for subjects proceeding to allogeneic transplant following nivolumab treatment, of section 5.1 of the SmPC with efficacy data from longer follow-up based on final results from study CA209205 listed as a PAES in the Annex II; this is a Phase 2, non-comparative, multi-cohort, single-arm, open-label study of nivolumab (BMS-936558) in cHL subjects after failure of ASCT

Annex II is updated to remove the commitment. Version 7.5 of the RMP has been submitted.”

Soliris - eculizumab -

EMA/H/C/000791/II/0098, Orphan

MAH: Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, “Update of sections 4.6 and 5.3 of the SmPC in order to update the safety information related to pregnancy, lactation and fertility following the review of data in PSUR 13 and 14. Annex II and the Package Leaflet are updated accordingly.

The RMP version 17 has also been submitted with updated information on pregnancy and lactation and fertility.”

Spedra - avanafil -

EMA/H/C/002581/II/0027/G

MAH: Menarini International Operations
Luxembourg S.A., Rapporteur: Concepcion Prieto
Yerro, PRAC Rapporteur: Dolores Montero
Corominas“Update of section 4.4. to reflect the results of clinical study TA-402 “A Double-Blind, Randomized, Placebo-Controlled, Single-Dose, Parallel Study to Assess the Effects of Avanafil on Multiple Parameters of Vision, including, but Not Limited to Visual Acuity, Intraocular Pressure, Pupillometry, and Color Vision Discrimination, in Healthy Male Subjects).

Update of section 4.6. of the SmPC in order to reflect the results of clinical study TA-401 “A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter Clinical Trial of the Effect of Avanafil on Spermatogenesis in Healthy Adult Males and Adult Males with Mild Erectile Dysfunction”. The Package Leaflet is updated accordingly.

The RMP version 5.1 has also been submitted.

In addition, the MAH took the opportunity to make an editorial correction on the approved SmPC by adding the missing adverse reaction epistaxis from the tabulated list of adverse reactions reported in section 4.8. Additionally, the MAH took the opportunity of this variation to align the information included in Section 3 “How to take Spedra” in the Package Leaflet to section 4.2 “Posology” in the SmPC.

Some additional minor amendments, due to translation mistakes are proposed for the French Product Information.”

Tresiba - insulin degludec -

EMA/H/C/002498/II/0028

MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue,
“Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE) conducted for Tresiba. DEVOTE was a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of Tresiba versus insulin glargine (100 units/mL) in

patients with type 2 diabetes mellitus at high risk of cardiovascular events.

The RMP version 8 has also been submitted, with updates consequent to the data in support of the application."

WS1168

AZILECT-EMEA/H/C/000574/WS1168/007

7

Rasagiline

ratiopharm-EMEA/H/C/003957/WS1168/0010

MAH: Teva B.V., Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.4, 4.7 and 4.8 to include a new warning on excessive daytime sleepiness and sudden sleep onset episodes and sudden sleep onset episodes, update of section 4.9 to remove 'dysphoria' as a symptom reported following overdose of rasagiline based on a CCDS update. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to make editorial changes throughout the PI, to correct the invented name for Rasagiline Ratiopharm in the Czech annexes and to bring the PI in line with the latest QRD template version 10."

WS1180

Corlontor-EMEA/H/C/000598/WS1180/0047

47

Ivabradine

Anpharm-EMEA/H/C/004187/WS1180/0006

Procoralan-EMEA/H/C/000597/WS1180/0046

MAH: Les Laboratoires Servier, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update to the section 4.8 of the SmPC with new ADRs: Ventricular tachycardia, Ventricular fibrillation and Torsade de pointes. The PL is updated accordingly. The RMP version 6 has also been submitted. In addition the MAH took the opportunity to align the PI with the latest QRD template 10.0."

WS1211

Januvia-EMEA/H/C/000722/WS1211/0059

9

Ristaben-EMEA/H/C/001234/WS1211/0051

1

Xelevia-EMEA/H/C/000762/WS1211/0063

AH: Merck Sharp & Dohme Limited, Lead

Rapporteur: Johann Lodewijk Hillege, Lead PRAC

Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to modify the information on dosing, an existing warning and administration instructions, respectively for use of sitagliptin in patients with type 2 diabetes mellitus and renal impairment. Consequently, the RMP version 8 has also been updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Tesavel and to bring the PI in line with the latest QRD template version 10. Minor editorial changes are also introduced in the Product Information."

WS1212/G**Effcib-EMEA/H/C/000896/WS1212/0085/
G****Janumet-EMEA/H/C/000861/WS1212/008
5/G****Ristfor-EMEA/H/C/001235/WS1212/0072
/G****Velmetia-EMEA/H/C/000862/WS1212/00
88/G**

MAH: Merck Sharp & Dohme Limited, Lead

Rapporteur: Johann Lodewijk Hillege, Lead PRAC

Rapporteur: Menno van der Elst "Update of sections 4.2, and 5.2 of the SmPC in order to modify the information on dosing, and administration instructions respectively for use of sitagliptin/metformin in patients with type 2 diabetes mellitus and moderate renal impairment. Consequently, the RMP version 8 has also been updated accordingly.

Section 4.5 of the SmPC is also updated to include information on the concomitant use of ranolazine, vandetanib, dolutegravir and cimetidine.

In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Effcib and to bring the PI in line with the latest QRD template version 10. Minor editorial changes are also introduced in the Product Information."

B.6.11. PRAC assessed procedures

PRAC Led

Eliquis - apixaban -

EMA/H/C/002148/II/0043

MAH: Bristol-Myers Squibb / Pfizer EEIG,
Rapporteur: Johann Lodewijk Hillege, PRAC
Rapporteur: Menno van der Elst, PRAC-CHMP
liaison: Johann Lodewijk Hillege“Submission of the final report from study (CV185-365) listed as a category 3 study in the RMP. This is a post authorisation safety study which evaluates the effectiveness of Eliquis (apixaban) risk minimisation tools in the European Economic Area countries. A RMP (version 17.0) has also been submitted to reflect the completion of the study CV185-365.”

PRAC Led

Invokana - canagliflozin -

EMA/H/C/002649/II/0030

MAH: Janssen-Cilag International NV,
Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise“Submission of an updated RMP version 7.0 in order to include prior commitments made to PRAC during the PSUR/LEG procedural review of pancreatitis cases and the Article 20 referral procedure reviewing lower limb amputation in relation to the use of SGLT-2 inhibitors. In addition, the updated RMP reflects labelling changes that resulted from a variation to add information regarding fatal DKA cases to the existing DKA warning and the Article 31 procedure reviewing metformin-containing medicines.”

PRAC Led

Viread - tenofovir disoproxil -

EMA/H/C/000419/II/0182

MAH: Gilead Sciences International Ltd,
Rapporteur: Joseph Emmerich, PRAC
Rapporteur: Caroline Laborde, PRAC-CHMP
liaison: Joseph Emmerich“Submission of the final report from Study GX-US-174-0172, listed as a category 3 study in the RMP. This is a 5-year observational (non-interventional) renal safety registry conducted to provide further safety data in HBV-infected patients with decompensated liver disease.”

PRAC Led

**Vokanamet - canagliflozin / metformin -
EMA/H/C/002656/II/0031**

MAH: Janssen-Cilag International NV,
Rapporteur: Martina Weise, PRAC Rapporteur:
Menno van der Elst, PRAC-CHMP liaison: Johann
Lodewijk Hillege"Submission of an updated RMP
version 7.0 in order to include prior commitments
made to PRAC during the PSUR/LEG procedural
review of pancreatitis cases and the Article 20
referral procedure reviewing lower limb
amputation in relation to the use of SGLT-2
inhibitors. In addition, the updated RMP reflects
labelling changes that resulted from a variation to
add information regarding fatal DKA cases to the
existing DKA warning and the Article 31
procedure reviewing metformin-containing
medicines."

PRAC Led

WS1197

**Actraphane-EMA/H/C/000427/WS1197/
0072**

**Actrapid-EMA/H/C/000424/WS1197/006
6**

**Insulatard-EMA/H/C/000441/WS1197/0
069**

**Mixtard-EMA/H/C/000428/WS1197/007
3**

**Protaphane-EMA/H/C/000442/WS1197/
0068**

MAH: Novo Nordisk A/S, Lead Rapporteur: Hanne
Lomholt Larsen, Lead PRAC Rapporteur: Doris
Stenver, PRAC-CHMP liaison: Sinan B.
Sarac"Submission of an updated RMP version 3.0
according to GVP Module V, in order to remove
three important potential risks (immunogenicity,
allergic reactions and lack of efficacy) related to
the new NN729 manufacturing process from the
RMP, remove hypoglycaemia and anaphylactic
reactions, remove peripheral neuropathy,
refraction disorders, lipodystrophy, urticaria,
rash, oedema and diabetic retinopathy and
remove missing information concerning special
populations. No changes are proposed to the
product information."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS0935/G

Filgrastim

Hexal-EMEA/H/C/000918/WS0935/0035/

G

Zarzio-EMEA/H/C/000917/WS0935/0036/

G

MAH: Sandoz GmbH, Lead Rapporteur: Greg

Markey

WS1172

Infanrix

hexa-EMEA/H/C/000296/WS1172/0221

MAH: GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

WS1184

Eucreas-EMEA/H/C/000807/WS1184/006

3

Icandra-EMEA/H/C/001050/WS1184/006

4

Zomarist-EMEA/H/C/001049/WS1184/00

64

MAH: Novartis Europharm Ltd, Lead Rapporteur:

Kristina Dunder

WS1185/G

Hexacima-EMEA/H/C/002702/WS1185/00

65/G

Hexaxim-EMEA/H/W/002495/WS1185/00

71/G

Hexyon-EMEA/H/C/002796/WS1185/006

9/G

MAH: Sanofi Pasteur Europe, Duplicate, Duplicate
of Hexacima, Lead Rapporteur: Jan

Mueller-Berghaus

WS1187/G

Kalydeco-EMEA/H/C/002494/WS1187/00

61/G

Orkambi-EMEA/H/C/003954/WS1187/002

2/G

MAH: Vertex Pharmaceuticals (Europe) Ltd, Lead

Rapporteur: Nithyanandan Nagercoil

WS1194**Infanrix****hexa-EMEA/H/C/000296/WS1194/0222**

MAH: GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

WS1196/G**Ebymect-EMEA/H/C/004162/WS1196/002****3/G****Xigduo-EMEA/H/C/002672/WS1196/0034****/G**

MAH: AstraZeneca AB, Lead Rapporteur: Kristina

Dunder

WS1201/G**Glyxambi-EMEA/H/C/003833/WS1201/00****09/G****Jentaduo-EMEA/H/C/002279/WS1201/0****041/G****Trajenta-EMEA/H/C/002110/WS1201/003****1/G**

MAH: Boehringer Ingelheim International GmbH,

Lead Rapporteur: Johann Lodewijk Hillege

WS1202/G**Efficib-EMEA/H/C/000896/WS1202/0084/****G****Janumet-EMEA/H/C/000861/WS1202/008****4/G****Januvia-EMEA/H/C/000722/WS1202/005****8/G****Ristaben-EMEA/H/C/001234/WS1202/005****0/G****Ristfor-EMEA/H/C/001235/WS1202/0071****/G****TESAVEL-EMEA/H/C/000910/WS1202/00****58/G****Velmetia-EMEA/H/C/000862/WS1202/00****87/G****Xelevia-EMEA/H/C/000762/WS1202/0062****/G**

MAH: Merck Sharp & Dohme Limited, Lead

Rapporteur: Johann Lodewijk Hillege

WS1204/G**Herceptin-EMEA/H/C/000278/WS1204/01****34/G****Kadcyla-EMEA/H/C/002389/WS1204/003****7/G**

MAH: Roche Registration Limited, Lead

Rapporteur: Jan Mueller-Berghaus

WS1213

Lyrica-EMEA/H/C/000546/WS1213/0090
Pregabalin
Pfizer-EMEA/H/C/003880/WS1213/0020
MAH: Pfizer Limited, Lead Rapporteur: Johann
Lodewijk Hillege

WS1214
Aflunov-EMEA/H/C/002094/WS1214/003
9
Foclivia-EMEA/H/C/001208/WS1214/003
3
MAH: Seqirus S.r.l, Lead Rapporteur: Daniela
Melchiorri

WS1216
IntronA-EMEA/H/C/000281/WS1216/011
2
PegIntron-EMEA/H/C/000280/WS1216/0
131
ViraferonPeg-EMEA/H/C/000329/WS1216
/0124
MAH: Merck Sharp & Dohme Limited, Lead
Rapporteur: Koenraad Norga

WS1224
Relvar
Ellipta-EMEA/H/C/002673/WS1224/0031
Revinty
Ellipta-EMEA/H/C/002745/WS1224/0027
MAH: Glaxo Group Ltd, Lead Rapporteur:
Concepcion Prieto Yerro

WS1235/G
Incredync-EMEA/H/C/002178/WS1235/00
20/G
Vipdomet-EMEA/H/C/002654/WS1235/00
22/G
Vipidia-EMEA/H/C/002182/WS1235/0017
/G
MAH: Takeda Pharma A/S, Lead Rapporteur:
Johann Lodewijk Hillege

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations

E.1.3. Initial PMF Certification

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

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 17-20 July 2017 CHMP plenary:

<i>Oncology</i>		
1.	Treatment of fully resectable metastatic melanoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2.	Vocimagene amiretrorepvec, (SME) ATMP, Treatment of high grade glioma	The CHMP granted eligibility to PRIME and adopted the critical summary report.
3.	(SME) Treatment of cholangiocarcinoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Dermatology</i>		
4.	Treatment of Chronic Hand Eczema	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Oto-rhino-laryngology</i>		
5.	ATMP Treatment of Muscular Disorder	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Neurology</i>		
6.	(SME) ATMP, Treatment of ischaemic stroke	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Ophtalmology</i>		
7.	(SME) Treatment of Neurotrophic Keratitis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Other</i>		
8.	Treatment of Light Chain (AL) Amyloidosis	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in July 2017 for August 2017 CHMP adoption of outcomes

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