



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 November 2018
EMA/PRAC/829194/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 26-29 November 2018

Chair: Sabine Straus – Vice-Chair: Martin Huber

26 November 2018, 13:00 – 19:30, room 3/A

27 November 2018, 08:30 – 19:30, room 3/A

28 November 2018, 08:30 – 19:30, room 3/A

29 November 2018, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

13 December 2018, 09:00-12:00, room 9/B, via teleconference

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 change during the course of the review. Additional details on some of these procedures will be published in the PRAC meeting highlights once the procedures are finalised.

Of note, this agenda is a working document primarily designed for PRAC 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, Rev. 1](#)).



Table of contents

1.	Introduction	12
1.1.	Welcome and declarations of interest of members, alternates and experts.....	12
1.2.	Agenda of the meeting on 26-29 November 2018.....	12
1.3.	Minutes of the previous meeting on 29-31 October 2018	12
2.	EU referral procedures for safety reasons: urgent EU procedures	12
2.1.	Newly triggered procedures	12
2.2.	Ongoing procedures	12
2.3.	Procedures for finalisation.....	12
3.	EU referral procedures for safety reasons: other EU referral procedures	12
3.1.	Newly triggered procedures	12
3.2.	Ongoing procedures	12
3.3.	Procedures for finalisation.....	12
3.4.	Re-examination procedures.....	13
3.5.	Others	13
4.	Signals assessment and prioritisation	13
4.1.	New signals detected from EU spontaneous reporting systems	13
4.1.1.	Alectinib – ALECENSA (CAP).....	13
4.1.2.	Benralizumab – FASENRA (CAP)	13
4.1.3.	Idelalisib – ZYDELIG (CAP)	13
4.1.4.	Ivacaftor – KALYDECO (CAP); ivafactor, tezacaftor – SYMKEVI (CAP).....	14
4.1.5.	Trastuzumab emtansine – KADCYLA (CAP)	14
4.2.	New signals detected from other sources	14
4.2.1.	Clopidogrel – CLOPIDOGREL APOTEX (CAP), CLOPIDOGREL BGR (CAP), CLOPIDOGREL HCS (CAP), CLOPIDOGREL KRKA (CAP), CLOPIDOGREL KRKA D.D. (CAP), CLOPIDOGREL MYLAN (CAP), CLOPIDOGREL RATIOPHARM (CAP), CLOPIDOGREL RATIOPHARM GMBH (CAP), CLOPIDOGREL TAD (CAP), CLOPIDOGREL TEVA (CAP), CLOPIDOGREL ZENTIVA (CAP), GREPID (CAP), ISCOVER (CAP), PLAVIX (CAP), ZYLLT (CAP); NAP; clopidogrel/acetylsalicylic acid – CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA (CAP), DUOPLAVIN (CAP); NAP Lopinavir, ritonavir – KALETRA (CAP), LOPINAVIR/RITONAVIR MYLAN (CAP), NAP; ritonavir – NORVIR (CAP), RITONAVIR (CAP), NAP	14
4.2.2.	Selective serotonin reuptake inhibitors (SSRI): citalopram (NAP); escitalopram (NAP)	15
4.2.3.	Sorafenib – NEXAVAR (CAP).....	15
4.2.4.	Inactivated poliomyelitis vaccine (NAP)	15
4.2.5.	Natalizumab – TYSABRI (CAP).....	15
4.2.6.	Vascular endothelial growth factor (VEGF) inhibitors: aflibercept – EYLEA (CAP), ZALTRAP (CAP); axitinib – INLYTA (CAP); bevacizumab – AVASTIN (CAP), MVASI (CAP); cabozantinib – CABOMETYX (CAP), COMETRIQ (CAP); lenvatinib - KISPLYX (CAP), LENVIMA (CAP); nintedanib – OFEV (CAP), VARGATEF (CAP); pazopanib – VOTRIENT (CAP); pegaptanib – MACUGEN (CAP); ponatinib – ICLUSIG (CAP); ramucirumab – CYRAMZA (CAP); ranibizumab – LUCENTIS (CAP);	

regorafenib – STIVARGA (CAP); sorafenib – NEXAVAR(CAP); sunitinib – SUTENT (CAP); tivozanib – FOTIVDA (CAP); vandetanib – CAPRELSA (CAP)..... 15

4.3. Signals follow-up and prioritisation 16

4.3.1. Canagliflozin – INVOKANA (CAP) – EMEA/H/C/002649/SDA/017; dapagliflozin - FORXIGA (CAP) – EMEA/H/C/002322/SDA/026; empagliflozin - JARDIANCE (CAP) – EMEA/H/C/002677/SDA/016; ertugliflozin – STEGLATRO (CAP) – EMEA/H/C/004315/SDA/005 16

4.3.2. Carbimazole (NAP); thiamazole (NAP) 16

4.3.3. Carbimazole (NAP); thiamazole (NAP) 16

4.3.4. Certolizumab pegol – CIMZIA (CAP) - EMEA/H/C/001037/SDA/031; etanercept – ENBREL (CAP) - EMEA/H/C/000262/SDA/169, LIFMIOR (CAP) - EMEA/H/C/004167/SDA/003; golimumab – SIMPONI (CAP) - EMEA/H/C/000992/SDA/034; infliximab – REMICADE (CAP) - EMEA/H/C/000240/SDA/157 17

4.3.5. Dasabuvir – EXVIERA (CAP) - EMEA/H/C/003837/SDA/012; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/SDA/014 17

4.3.6. Dulaglutide – TRULICITY (CAP); exenatide – BYDUREON (CAP), BYETTA (CAP); liraglutide – VICTOZA (CAP) 17

4.3.7. Olmesartan (NAP)..... 17

4.3.8. Perindopril (NAP) 18

4.3.9. Propranolol (NAP) 18

4.3.10. Ranibizumab – LUCENTIS (CAP) - EMEA/H/C/000715/SDA/074 18

4.3.11. Vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/SDA/038..... 18

5. Risk management plans (RMPs) 18

5.1. Medicines in the pre-authorisation phase 18

5.1.1. Avacopan - EMEA/H/C/004487, Orphan..... 18

5.1.2. Febuxostat - EMEA/H/C/004773 19

5.1.3. Ibalizumab - EMEA/H/C/004961 19

5.1.4. Larotrectinib - EMEA/H/C/004919, Orphan..... 19

5.1.5. Pegfilgrastim - EMEA/H/C/004556 19

5.1.6. Pegvaliase - EMEA/H/C/004744, Orphan..... 19

5.2. Medicines in the post-authorisation phase – PRAC-led procedures..... 19

5.2.1. Acridinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/WS1402/0038; EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/WS1402/0038 19

5.2.2. Acridinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/WS1403/0023; DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/WS1403/0023 20

5.2.3. Ambrisentan - VOLIBRIS (CAP) - EMEA/H/C/000839/II/0055 20

5.2.4. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/II/0148 20

5.2.5. Emtricitabine - EMTRIVA (CAP) - EMEA/H/C/000533/II/0127 20

5.2.6. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/II/0028..... 21

5.2.7. Human fibrinogen, human thrombin - EVICEL (CAP) - EMEA/H/C/000898/II/0063 21

5.2.8. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0099 21

5.2.9.	Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS1364/0092; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS1364/0021	21
5.2.10.	Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/II/0048	22
5.2.11.	Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/WS1357/0063; RISTABEN (CAP) - EMEA/H/C/001234/WS1357/0055; TESAVEL (CAP) - EMEA/H/C/000910/WS1357/0063; XELEVIA (CAP) - EMEA/H/C/000762/WS1357/0067; sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/WS1357/0089; JANUMET (CAP) - EMEA/H/C/000861/WS1357/0089; RISTFOR (CAP) - EMEA/H/C/001235/WS1357/0076; VELMETIA (CAP) - EMEA/H/C/000862/WS1357/0092	22
5.2.12.	Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0028.....	22
5.2.13.	Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0042/G	23
5.3.	Medicines in the post-authorisation phase – CHMP-led procedures	23
5.3.1.	Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/X/0117/G	23
5.3.2.	Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0047, Orphan	23
5.3.3.	Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0055, Orphan.....	24
5.3.4.	Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0026	24
5.3.5.	Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/II/0062/G.....	24
5.3.6.	Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1344/0025; FORXIGA (CAP) - EMEA/H/C/002322/WS1344/0044	25
5.3.7.	Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0020, Orphan	25
5.3.8.	Dasatinib - SPRYCEL (CAP) - EMEA/H/C/000709/II/0059	25
5.3.9.	Decitabine - DACOGEN (CAP) - EMEA/H/C/002221/II/0033, Orphan	25
5.3.10.	Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/II/0128	26
5.3.11.	Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0065	26
5.3.12.	Eftrenonacog alfa - ALPROLIX (CAP) - EMEA/H/C/004142/II/0021, Orphan.....	26
5.3.13.	Elotuzumab - EMPLICITI (CAP) - EMEA/H/C/003967/II/0012.....	27
5.3.14.	Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0002	27
5.3.15.	Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS1461/0017; Linagliptin, metformin - JENTADUETO (CAP) - EMEA/H/C/002279/WS1461/0047; Linagliptin - TRAJENTA (CAP) - EMEA/H/C/002110/WS1461/0035	27
5.3.16.	Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/X/0001.....	28
5.3.17.	Etelcalcetide - PARSABIV (CAP) - EMEA/H/C/003995/II/0010.....	28
5.3.18.	Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/X/0083/G	28
5.3.19.	Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0005	29
5.3.20.	Insulin glargine - TOUJEO (CAP) - EMEA/H/C/000309/II/0105/G	29
5.3.21.	Irinotecan hydrochloride trihydrate - ONIVYDE (CAP) - EMEA/H/C/004125/II/0008.....	29
5.3.22.	Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS1372/0053; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS1372/0057	29
5.3.23.	Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/II/0029, Orphan.....	30
5.3.24.	Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/II/0006, Orphan	30
5.3.25.	Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0020	31
5.3.26.	Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0023	31

5.3.27.	Omalizumab - XOLAIR (CAP) - EMEA/H/C/000606/II/0093	31
5.3.28.	Plerixafor - MOZOBIL (CAP) - EMEA/H/C/001030/II/0034, Orphan.....	32
5.3.29.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0152.....	32
5.3.30.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0157.....	32
5.3.31.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0158.....	33
5.3.32.	Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0001, Orphan.....	33
5.3.33.	Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0191	33
5.3.34.	Thalidomide - THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/II/0056, Orphan	34
5.3.35.	Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0034	34

6. Periodic safety update reports (PSURs) 34

6.1.	PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only	34
6.1.1.	Abiraterone - ZYTIGA (CAP) - PSUSA/00000015/201804	34
6.1.2.	Apixaban - ELIQUIS (CAP) - PSUSA/00000226/201805	34
6.1.3.	Arteminol, piperaquine tetraphosphate - EURARTESIM (CAP) - PSUSA/00001069/201804	35
6.1.4.	Atezolizumab - TECENTRIQ (CAP) - PSUSA/00010644/201805 (with RMP).....	35
6.1.5.	Basiliximab - SIMULECT (CAP) - PSUSA/00000301/201804.....	35
6.1.6.	Benralizumab - FASENRA (CAP) - PSUSA/00010661/201805.....	35
6.1.7.	Cerliponase alfa - BRINEURA (CAP) - PSUSA/00010596/201804.....	35
6.1.8.	Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/201805	35
6.1.9.	Daratumumab - DARZALEX (CAP) - PSUSA/00010498/201805.....	36
6.1.10.	Darunavir, cobicistat - REZOLSTA (CAP) - PSUSA/00010315/201805	36
6.1.11.	Decitabine - DACOGEN (CAP) - PSUSA/00009118/201805	36
6.1.12.	Delamanid - DELTYBA (CAP) - PSUSA/00010213/201804	36
6.1.13.	Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/201805	36
6.1.14.	Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/201805	36
6.1.15.	Empagliflozin, linagliptin - GLYXAMBI (CAP) - PSUSA/00010539/201805	37
6.1.16.	Epoetin theta - BIOPOIN (CAP); EPORATIO (CAP) - PSUSA/00001240/201804	37
6.1.17.	Etelcalcetide - PARSABIV (CAP) - PSUSA/00010533/201805	37
6.1.18.	Fentanyl - IONSYS - PSUSA/00010453/201805	37
6.1.19.	Fluticasone furoate - AVAMYS (CAP) - PSUSA/00009154/201804.....	37
6.1.20.	Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) - PSUSA/00010099/201805	37
6.1.21.	Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/201805.....	38
6.1.22.	Interferon beta-1a - AVONEX (CAP); REBIF (CAP) - PSUSA/00009198/201805.....	38
6.1.23.	Ixazomib - NINLARO (CAP) - PSUSA/00010535/201805	38
6.1.24.	Ketoconazole - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/201805	38
6.1.25.	Laronidase - ALDURAZYME (CAP) - PSUSA/00001830/201804.....	38
6.1.26.	Letermovir - PREVYMIS (CAP) - PSUSA/00010660/201805	38

6.1.27.	Lidocaine, prilocaine - FORTACIN (CAP) - PSUSA/00010110/201805.....	39
6.1.28.	Linagliptin - TRAJENTA (CAP); linagliptin, metformin - JENTADUETO (CAP); - PSUSA/00010427/201805	39
6.1.29.	Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/201805.....	39
6.1.30.	Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - PSUSA/00010607/201805	39
6.1.31.	Necitumumab - PORTRAZZA (CAP) - PSUSA/00010471/201805	39
6.1.32.	Padeliporfin - TOOKAD (CAP) - PSUSA/00010654/201805	39
6.1.33.	Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/201805.....	40
6.1.34.	Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP); prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - PREPANDRIX (CAP) - PSUSA/00002281/201805	40
6.1.35.	Pixantrone - PIXUVRI (CAP) - PSUSA/00009261/201805	40
6.1.36.	Prasterone - INTRAROSA (CAP) - PSUSA/00010672/201805	40
6.1.37.	Radium (²²³ Ra) dichloride - XOFIGO (CAP) - PSUSA/00010132/201805	40
6.1.38.	Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/201805.....	41
6.1.39.	Shingles (herpes zoster) vaccine (live) - ZOSTAVAX (CAP) - PSUSA/00009289/201805....	41
6.1.40.	Sunitinib - SUTENT (CAP) - PSUSA/00002833/201804	41
6.1.41.	Susoctocog alpha - OBIZUR (CAP) - PSUSA/00010458/201805	41
6.1.42.	Tafamidis - VYNDAQEL (CAP) - PSUSA/00002842/201805	41
6.1.43.	Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201804	41
6.1.44.	Tenofovir alafenamide - VEMLIDY (CAP) - PSUSA/00010575/201805	42
6.1.45.	Tilmanocept - LYMPHOSEEK (CAP) - PSUSA/00010313/201805	42
6.1.46.	Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/201805	42
6.1.47.	Tolvaptan - JINARC (CAP) - PSUSA/00010395/201805.....	42
6.1.48.	Tolvaptan - SAMSCA (CAP) - PSUSA/00002994/201805	42
6.1.49.	Ulipristal - ELLAONE (CAP) - PSUSA/00003074/201805.....	42
6.1.50.	Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/201805.....	43
6.2.	PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)	43
6.2.1.	Bortezomib - BORTEZOMIB ACCORD (CAP); BORTEZOMIB HOSPIRA (CAP); BORTEZOMIB SUN (CAP); VELCADE (CAP); NAP - PSUSA/00000424/201804.....	43
6.2.2.	Capecitabine - XELODA (CAP); NAP - PSUSA/00000531/201804.....	43
6.2.3.	Efavirenz - STOCRIN (CAP); SUSTIVA (CAP); NAP - PSUSA/00001200/201804	43
6.2.4.	Enoxaparin - INHIXA (CAP); THORINANE (CAP); NAP - PSUSA/00010553/201804.....	43
6.2.5.	Hydrochlorothiazide, telmisartan - KINZALKOMB (CAP); MICARDISPLUS (CAP); PRITORPLUS (CAP); telmisartan - KINZALMONO (CAP); MICARDIS (CAP); PRITOR (CAP); NAP - PSUSA/00002882/201804	44
6.2.6.	Ivabradine - CORLENTOR (CAP); IVABRADINE ANPHARM (CAP); PROCORALAN (CAP); NAP - PSUSA/00001799/201804	44

6.2.7.	Mycophenolate mofetil - CELLCEPT (CAP); MYCLAUSEN (CAP); MYCOPHENOLATE MOFETIL TEVA (CAP); MYFENAX (CAP); NAP mycophenolic acid (NAP) - PSUSA/00010550/201805.....	44
6.2.8.	Tacrolimus - ADVAGRAF (CAP); ENVARSUS (CAP); MODIGRAF (CAP); NAP - PSUSA/00002839/201803 (with RMP)	44
6.3.	PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only	45
6.3.1.	Acarbose (NAP) - PSUSA/00000017/201803	45
6.3.2.	Amlodipine besilate, ramipril (NAP) - PSUSA/00000181/201803	45
6.3.3.	Benzyl nicotinate, camphor, dimethyl sulfoxide, nonivamide, turpentine oil (NAP) - PSUSA/00010584/201803	45
6.3.4.	Calcium chloride, glutamic acid, glutathione, histidine, lactobionic acid, magnesium chloride, mannitol, potassium chloride, sodium hydroxide (NAP) - PSUSA/00009162/201803.....	45
6.3.5.	Chlorprothixene (NAP) - PSUSA/00000717/201803.....	45
6.3.6.	Deoxycholic acid (NAP) - PSUSA/00010525/201804.....	45
6.3.7.	Dihydroergotamine (NAP) - PSUSA/00001075/201804	46
6.3.8.	Dihydroergotoxine (NAP) - PSUSA/00001079/201804	46
6.3.9.	Enalapril (NAP) - PSUSA/00001211/201803.....	46
6.3.10.	Felodipine, ramipril (NAP) - PSUSA/00001358/201803	46
6.3.11.	Foscarnet (NAP) - PSUSA/00001472/201803	46
6.3.12.	Human anti-D immunoglobulin (NAP) - PSUSA/00001614/201803	46
6.3.13.	Isotretinoin (NAP) - PSUSA/00010488/201805.....	47
6.3.14.	Ivabradine, metoprolol (NAP) - PSUSA/00010381/201804	47
6.3.15.	Ivermectin (NAP) - PSUSA/00010376/201804	47
6.3.16.	Mepivacaine (NAP); mepivacaine hydrochloride, epinephrine (NAP); mepivacaine, norepinephrine (NAP) - PSUSA/00001979/201803.....	47
6.3.17.	Metamizole (NAP) - PSUSA/00001997/201804	47
6.3.18.	Metformin (NAP) - PSUSA/00002001/201804.....	48
6.3.19.	Methylphenobarbital (NAP) - PSUSA/00002025/201803	48
6.3.20.	Nadroparin (NAP) - PSUSA/00002104/201803	48
6.3.21.	Nebivolol (NAP) - PSUSA/00002129/201803	48
6.3.22.	Nitrendipine (NAP) - PSUSA/00002171/201803	48
6.3.23.	Nortriptyline (NAP) - PSUSA/00002192/201803.....	48
6.3.24.	Ofloxacin (NAP) - PSUSA/00002203/201804	49
6.3.25.	Ofloxacin (NAP) - PSUSA/00002204/201804	49
6.3.26.	Oxaliplatin (NAP) - PSUSA/00002229/201804	49
6.3.27.	Oxycodone (NAP) - PSUSA/00002254/201804	49
6.3.28.	Paracetamol (NAP) - PSUSA/00002311/201805.....	49
6.4.	Follow-up to PSUR/PSUSA procedures	49
7.	Post-authorisation safety studies (PASS)	50
7.1.	Protocols of PASS imposed in the marketing authorisation(s).....	50
7.1.1.	Eliglustat – CERDELGA (CAP) - EMEA/H/C/PSA/S/0035	50

7.1.2.	Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0034	50
7.1.3.	Tisagenlecleucel – KYMRIAHA (CAP) - EMEA/H/C/PSP/S/0066	50
7.2.	Protocols of PASS non-imposed in the marketing authorisation(s)	50
7.2.1.	Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 009	50
7.2.2.	Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 003.1	51
7.2.3.	Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002.2.....	51
7.2.4.	Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/MEA 004.1	51
7.2.5.	Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 013.3	51
7.2.6.	Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 012.3	52
7.2.7.	Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/LEG 010	52
7.2.8.	Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 001.1.....	52
7.2.9.	Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/MEA 045.6	52
7.2.10.	Florbetaben (¹⁸ F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 001.7	53
7.2.11.	Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 026.6.....	53
7.2.12.	Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.6	53
7.2.13.	Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/MEA 003.1	54
7.2.14.	Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/MEA 059.1	54
7.2.15.	Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.2	54
7.3.	Results of PASS imposed in the marketing authorisation(s)	54
7.4.	Results of PASS non-imposed in the marketing authorisation(s).....	54
7.4.1.	Atazanavir, atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/II/0117	54
7.4.2.	Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0039.....	55
7.4.3.	Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0040.....	55
7.4.4.	Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/II/0042/G	55
7.4.5.	Orlistat - ALLI (CAP) - EMEA/H/C/000854/II/0058	56
7.4.6.	Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS1476/0028; Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS1476/0070; Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS1476/0052; Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/WS1476/0016	56
7.5.	Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation.....	56
7.5.1.	Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 075.7	56
7.5.2.	Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 080.6	57
7.5.3.	Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 002.4	57
7.5.4.	Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.9....	57
7.5.5.	Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 003.5....	57
7.5.6.	Follitropin alfa - OVALEAP (CAP) - EMEA/H/C/002608/MEA 002.3	57
7.5.7.	Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.4	58
7.5.8.	Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.4	58
7.5.9.	Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 003.1	58

7.5.10.	Somatropin - OMNITROPE (CAP) - EMEA/H/C/000607/MEA 012.2.....	58
7.6.	Others	59
7.6.1.	Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 014	59
7.6.2.	Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 013	59
7.6.3.	Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/MEA 001.5.....	59
7.6.4.	Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 005.1	60
7.6.5.	Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/MEA 001.5	60
7.7.	New Scientific Advice	60
7.8.	Ongoing Scientific Advice	61
7.9.	Final Scientific Advice (Reports and Scientific Advice letters)	61
8.	Renewals of the marketing authorisation, conditional renewal and annual reassessments	61
8.1.	Annual reassessments of the marketing authorisation	61
8.1.1.	Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/S/0035 (without RMP)	61
8.1.2.	Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/S/0032 (without RMP)	61
8.2.	Conditional renewals of the marketing authorisation	61
8.2.1.	Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/R/0035 (without RMP).....	61
8.2.2.	Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0033 (without RMP)	61
8.3.	Renewals of the marketing authorisation	62
8.3.1.	Brinzolamide, brimonidine - SIMBRINZA (CAP) - EMEA/H/C/003698/R/0014 (without RMP).....	62
8.3.2.	Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/R/0040 (with RMP)	62
8.3.3.	Mifamurtide - MEPACT (CAP) - EMEA/H/C/000802/R/0047 (without RMP)	62
8.3.4.	Oseltamivir - EBILFUMIN (CAP) - EMEA/H/C/003717/R/0012 (without RMP)	62
8.3.5.	Sevelamer carbonate - RENVELA (CAP) - EMEA/H/C/000993/R/0046 (without RMP)	62
8.3.6.	Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/R/0029 (without RMP)	62
8.3.7.	Trametinib - MEKINIST (CAP) - EMEA/H/C/002643/R/0029 (without RMP).....	63
9.	Product related pharmacovigilance inspections	63
9.1.	List of planned pharmacovigilance inspections.....	63
9.1.1.	Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products	63
9.2.	Ongoing or concluded pharmacovigilance inspections.....	63
9.3.	Others	63
10.	Other safety issues for discussion requested by the CHMP or the EMA	63
10.1.	Safety related variations of the marketing authorisation.....	63
10.1.1.	Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0051	63
10.2.	Timing and message content in relation to Member States' safety announcements.....	64
10.3.	Other requests.....	64
10.4.	Scientific Advice	64

11.	Other safety issues for discussion requested by the Member States	64
11.1.	Safety related variations of the marketing authorisation	64
11.1.1.	Esomeprazole, naproxen (NAP) - NL/H/1848/001/II/026	64
11.2.	Other requests	64
11.2.1.	Atorvastatin (NAP) - DE/H/PSUFU/00010347/201710/A	64
11.2.2.	Cabergoline (NAP)	64
11.2.3.	Paroxetine (NAP) - NL/H/PSUFU/00002319/201712	65
12.	Organisational, regulatory and methodological matters	65
12.1.	Mandate and organisation of the PRAC	65
12.2.	Coordination with EMA Scientific Committees or CMDh-v	65
12.3.	Coordination with EMA Working Parties/Working Groups/Drafting Groups	65
12.4.	Cooperation within the EU regulatory network	65
12.4.1.	Brexit – EMA knowledge sharing package to support UK portfolio transfer	65
12.4.2.	PRAC strategic review and learning meeting (SRLM), Vienna, Austria, 25-26 September 2018 - report	65
12.5.	Cooperation with International Regulators	65
12.6.	Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee	65
12.7.	PRAC work plan	66
12.7.1.	PRAC work plan 2019 – preparation	66
12.8.	Planning and reporting	66
12.9.	Pharmacovigilance audits and inspections	66
12.9.1.	Pharmacovigilance systems and their quality systems	66
12.9.2.	Pharmacovigilance inspections	66
12.9.3.	Pharmacovigilance audits	66
12.10.	Periodic safety update reports (PSURs) & Union reference date (EURD) list	66
12.10.1.	Periodic safety update reports	66
12.10.2.	Granularity and Periodicity Advisory Group (GPAG)	66
12.10.3.	PSURs repository	66
12.10.4.	Union reference date list – consultation on the draft list	66
12.10.5.	Good Pharmacovigilance Practice (GVP) module V on ‘Risk management systems’ and module VII on ‘Periodic safety update report’ – clarifications on safety specification	66
12.11.	Signal management	67
12.11.1.	Signal management – feedback from Signal Management Review Technical (SMART) Working Group	67
12.11.2.	Signal Management Review Technical (SMART) methods activities - update	67
12.12.	Adverse drug reactions reporting and additional monitoring	67
12.12.1.	Management and reporting of adverse reactions to medicinal products	67
12.12.2.	Additional monitoring	67
12.12.3.	List of products under additional monitoring – consultation on the draft list	67

12.13.	EudraVigilance database	67
12.13.1.	Activities related to the confirmation of full functionality	67
12.14.	Risk management plans and effectiveness of risk minimisations	67
12.14.1.	Risk management systems	67
12.14.2.	Good Pharmacovigilance Practice (GVP) module V on 'Risk management systems' and module VII on 'Periodic safety update report' – clarifications on safety specification	67
12.14.3.	Tools, educational materials and effectiveness measurement of risk minimisations	67
12.15.	Post-authorisation safety studies (PASS)	68
12.15.1.	Post-authorisation Safety Studies – imposed PASS	68
12.15.2.	Post-authorisation Safety Studies – non-imposed PASS	68
12.16.	Community procedures.....	68
12.16.1.	Referral procedures for safety reasons	68
12.17.	Renewals, conditional renewals, annual reassessments.....	68
12.18.	Risk communication and transparency	68
12.18.1.	Public participation in pharmacovigilance	68
12.18.2.	Safety communication	68
12.19.	Continuous pharmacovigilance	68
12.19.1.	Incident management	68
12.20.	Others	68
12.20.1.	EMA relocation to Amsterdam, the Netherlands – meeting premises.....	68
12.20.2.	EMA relocation to Amsterdam, the Netherlands – adjustment to March 2019 meeting start time	68
12.20.3.	Patient registry initiative and cross-committee task force on registries – update.....	68
13.	Any other business	69
14.	Explanatory notes	70

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 26-29 November 2018. See December 2018 PRAC minutes (to be published post January 2019 PRAC meeting).

1.2. Agenda of the meeting on 26-29 November 2018

Action: For adoption

1.3. Minutes of the previous meeting on 29-31 October 2018

Action: For adoption

2. EU referral procedures for safety reasons: urgent EU procedures

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

3. EU referral procedures for safety reasons: other EU referral procedures

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation²

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Alectinib – ALECENSA (CAP)

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Patrick Batty

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

EPITT 19321 – New signal

Lead Member State(s): UK

4.1.2. Benralizumab – FASENRA (CAP)

Applicant(s): AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19319 – New signal

Lead Member State(s): NO

4.1.3. Idelalisib – ZYDELIG (CAP)

Applicant(s): Gilead Sciences Ireland UC

PRAC Rapporteur: Patrick Batty

Scope: Signal of arthritis and arthralgia

Action: For adoption of PRAC recommendation

EPITT 19312 – New signal

Lead Member State(s): UK

¹ Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

² Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

4.1.4. Ivacaftor – KALYDECO (CAP); ivafactor, tezacaftor – SYMKEVI (CAP)

Applicant(s): Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: To be appointed

Scope: Signal of increased blood creatine phosphokinase (CPK)

Action: For adoption of PRAC recommendation

EPITT 19316 – New signal

Lead Member State(s): ES, IE

4.1.5. Trastuzumab emtansine – KADCYLA (CAP)

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Signal of sepsis

Action: For adoption of PRAC recommendation

EPITT 19326 – New signal

Lead Member State(s): DK

4.2. New signals detected from other sources

4.2.1. Clopidogrel – CLOPIDOGREL APOTEX (CAP), CLOPIDOGREL BGR (CAP), CLOPIDOGREL HCS (CAP), CLOPIDOGREL KRKA (CAP), CLOPIDOGREL KRKA D.D. (CAP), CLOPIDOGREL MYLAN (CAP), CLOPIDOGREL RATIOPHARM (CAP), CLOPIDOGREL RATIOPHARM GMBH (CAP), CLOPIDOGREL TAD (CAP), CLOPIDOGREL TEVA (CAP), CLOPIDOGREL ZENTIVA (CAP), GREPID (CAP), ISCOVER (CAP), PLAVIX (CAP), ZYLLT (CAP); NAP; clopidogrel/acetylsalicylic acid – CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA (CAP), DUOPLAVIN (CAP); NAP Lopinavir, ritonavir – KALETRA (CAP), LOPINAVIR/RITONAVIR MYLAN (CAP), NAP; ritonavir – NORVIR (CAP), RITONAVIR (CAP), NAP

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Kaletra, Norvir), Apotex Europe BV (Clopidogrel Apotex), Archie Samuel s.r.o. (Clopidogrel Ratiopharm GmbH), HCS bvba (Clopidogrel HCS), Krka, d.d., Novo mesto (Clopidogrel Krka, Clopidogrel Krka d.d., Zyllt), Laboratoires Biogaran (Clopidogrel BGR), Mylan S.A.S (Clopidogrel Mylan, Lopinavir/Ritonavir Mylan, Ritonavir Mylan), Pharmathen S.A. (Grepid), Sanofi-aventis groupe (Clopidogrel/Acetylsalicylic acid Zentiva, Iscover), Sanofi Clir SNC (Duoplavin, Plavix), TAD Pharma GmbH (Clopidogrel TAD), Teva B.V. (Clopidogrel Ratiopharm, Clopidogrel Teva), Zentiva k.s. (Clopidogrel Zentiva), various

PRAC Rapporteur: To be appointed

Scope: Signal of interaction with ritonavir boosted antiviral human immunodeficiency virus (HIV) therapy leading to insufficient inhibition of platelet aggregation

Action: For adoption of PRAC recommendation

EPITT 19325 – New signal

Lead Member State(s): FR, NL, PT

4.2.2. Selective serotonin reuptake inhibitors (SSRI): citalopram (NAP); escitalopram (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of drug interaction with fluconazole

Action: For adoption of PRAC recommendation

EPITT 19327 – New signal

Lead Member State(s): SE

4.2.3. Sorafenib – NEXAVAR (CAP)

Applicant(s): Bayer AG

PRAC Rapporteur: Annika Folin

Scope: Signal of acute generalised exanthous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18109 – New signal

Lead Member State(s): SE

4.2.4. Inactivated poliomyelitis vaccine³ (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of case reports from outside the EU of immune thrombocytopenic purpura

Action: For adoption of PRAC recommendation

EPITT 19336 – New signal

Lead Member State(s): DK

4.2.5. Natalizumab – TYSABRI (CAP)

Applicant(s): Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of human papillomavirus (HPV) infection and complications

Action: For adoption of PRAC recommendation

EPITT 19329 – New signal

Lead Member State(s): DE

4.2.6. Vascular endothelial growth factor (VEGF) inhibitors: afibercept – EYLEA (CAP), ZALTRAP (CAP); axitinib – INLYTA (CAP); bevacizumab – AVASTIN (CAP), MVASI (CAP); cabozantinib – CABOMETYX (CAP), COMETRIQ (CAP); lenvatinib – KISPLYX (CAP), LENVIMA (CAP); nintedanib – OFEV (CAP), VARGATEF

³ Including combination vaccines

(CAP); pazopanib – VOTRIENT (CAP); pegaptanib – MACUGEN (CAP); ponatinib – ICLUSIG (CAP); ramucirumab – CYRAMZA (CAP); ranibizumab – LUCENTIS (CAP); regorafenib – STIVARGA (CAP); sorafenib – NEXAVAR(CAP); sunitinib – SUTENT (CAP); tivozanib – FOTIVDA (CAP); vandetanib – CAPRELSA (CAP)

Applicant(s): Amgen Europe B.V. (Mvasi), Bayer AG (Eylea, Nexavar, Stivarga), Boehringer Ingelheim (Ofev, Vargatef), Eisai Europe Ltd. (Kispilyx, Lenvima), Eli Lilly Nederland B.V. (Cyramza), EUSA Pharma (UK) Limited (Fotivda), Genzyme Europe BV (Caprelsa), Incyte Biosciences Distribution (Iclusig), Ipsen Pharma (Cabometyx, Cometriq), Novartis Europharm Limited (Lucentis, Votrient), Pfizer Europe MA EEIG (Inlyta, Sutent), PharmaSwiss Ceska Republika (Macugen), Roche Registration GmbH (Avastin), Sanofi-aventis groupe (Zaltrap)

PRAC Rapporteur: To be appointed

Scope: Signal of artery dissections and aneurysms

Action: For adoption of PRAC recommendation

EPITT 19330 – New signal

Lead Member State(s): BE, DE, DK, FR, GR, HR, IT, LT, NL, NO, SE, UK

4.3. Signals follow-up and prioritisation

4.3.1. Canagliflozin – INVOKANA (CAP) – EMEA/H/C/002649/SDA/017; dapagliflozin - FORXIGA (CAP) – EMEA/H/C/002322/SDA/026; empagliflozin - JARDIANCE (CAP) – EMEA/H/C/002677/SDA/016; ertugliflozin – STEGLATRO (CAP) – EMEA/H/C/004315/SDA/005

Applicant(s): AstraZeneca AB (Forxiga), Boehringer Ingelheim International GmbH (Jardiance), Janssen-Cilag International NV (Invokana), Merck Sharp & Dohme B.V. (Steglatro)

PRAC Rapporteur: Martin Huber

Scope: Signal of Fournier’s gangrene

Action: For adoption of PRAC recommendation

EPITT 19308 – Follow-up to October 2018

4.3.2. Carbimazole (NAP); thiamazole (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: New information on the known risk of birth defects and neonatal disorders in case of exposure during pregnancy

Action: For adoption of PRAC recommendation

EPITT 19238 – Follow-up to June 2018

4.3.3. Carbimazole (NAP); thiamazole (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of pancreatitis

Action: For adoption of PRAC recommendation

EPITT 19274 – Follow-up to July 2018

4.3.4. Certolizumab pegol – CIMZIA (CAP) - EMEA/H/C/001037/SDA/031; etanercept – ENBREL (CAP) - EMEA/H/C/000262/SDA/169, LIFMIOR (CAP) - EMEA/H/C/004167/SDA/003; golimumab – SIMPONI (CAP) - EMEA/H/C/000992/SDA/034; infliximab – REMICADE (CAP) - EMEA/H/C/000240/SDA/157

Applicant(s): Janssen Biologics B.V. (Remicade, Simponi), Pfizer Europe MA EEIG (Enbrel, Lifmior), UCB Pharma S.A. (Cimzia)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of lichenoid skin reactions for tumour necrosis factor alfa (TNF α) inhibitors

EPITT 19128 – Follow-up to July 2018

Action: For adoption of PRAC recommendation

4.3.5. Dasabuvir – EXVIERA (CAP) - EMEA/H/C/003837/SDA/012; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/SDA/014

Applicant(s): AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Signal of interstitial lung disease

EPITT 19257 – Follow-up to July 2018

Action: For adoption of PRAC recommendation

4.3.6. Dulaglutide – TRULICITY (CAP); exenatide – BYDUREON (CAP), BYETTA (CAP); liraglutide – VICTOZA (CAP)

Applicant(s): AstraZeneca AB (Bydureon, Byetta), Eli Lilly Nederland B.V. (Trulicity), Novo Nordisk A/S (Victoza)

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of diabetic ketoacidosis (DKA)

EPITT 19237 – Follow-up to June 2018

Action: For adoption of PRAC recommendation

4.3.7. Olmesartan (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of risk of autoimmune hepatitis

EPITT 19258 - Follow-up to July 2018

Action: For adoption of PRAC recommendation

4.3.8. Perindopril (NAP)

Applicant(s): various

PRAC Rapporteur: Doris Stenver

Scope: Signal of Raynaud's phenomenon

EPITT 19248 – Follow-up to July 2018

Action: For adoption of PRAC recommendation

4.3.9. Propranolol (NAP)

Applicant(s): various

PRAC Rapporteur: Karen Pernille Harg

Scope: Signal of increased risk of Parkinson's disease

EPITT 19223 – Follow-up to July 2018

Action: For adoption of PRAC recommendation

4.3.10. Ranibizumab – LUCENTIS (CAP) - EMEA/H/C/000715/SDA/074

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of angioedema

EPITT 19245 – Follow-up to July 2018

Action: For adoption of PRAC recommendation

4.3.11. Vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/SDA/038

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Signal of cardiac failure

EPITT 19268 – Follow-up to July 2018

Action: For adoption of PRAC recommendation

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Avacopan - EMEA/H/C/004487, Orphan

Applicant: ChemoCentryx Ltd

Scope: Induction of response in adult patients with granulomatosis with polyangiitis (Wegener's) (GPA) or microscopic polyangiitis (MPA)

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.2. Febuxostat - EMEA/H/C/004773

Scope: Treatment of hyperuricaemia

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.3. Ibalizumab - EMEA/H/C/004961

Scope (accelerated assessment): Treatment of adults infected with human immunodeficiency virus 1 (HIV-1) resistant to at least 1 agent in 3 different classes

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Larotrectinib - EMEA/H/C/004919, Orphan

Applicant: Bayer AG

Scope (accelerated assessment): Treatment of adult and paediatric patients with locally advanced or metastatic solid tumours

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. Pegfilgrastim - EMEA/H/C/004556

Scope: Reduction in the duration of neutropenia and the incidence of febrile neutropenia

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.6. Pegvaliase - EMEA/H/C/004744, Orphan

Applicant: BioMarin International Limited

Scope: Treatment of adults with phenylketonuria (PKU) with inadequate blood phenylalanine control

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

5.2.1. Aclidinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/WS1402/0038; EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/WS1402/0038

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 7.0) in order to reflect changes in the categorisation of safety concerns and missing information in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.2. [Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR \(CAP\) - EMEA/H/C/003969/WS1403/0023; DUAKLIR GENUAIR \(CAP\) - EMEA/H/C/003745/WS1403/0023](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 4.0) in order to reflect changes in the categorisation of safety concerns and missing information in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.3. [Ambrisentan - VOLIBRIS \(CAP\) - EMEA/H/C/000839/II/0055](#)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Eva Segovia

Scope: Update of the RMP (version 7.6) in order to remove the educational materials for healthcare professionals given the information provide in the product information and the experience gained in using ambrisentan, as requested by PRAC in the PSUR single assessment procedure (PSUSA/00000129/201706) concluded in January 2018. Annex II of the product information is updated accordingly. In addition, the MAH took the opportunity to update Annex II to include minor changes including the correction of typographical errors

Action: For adoption of PRAC Assessment Report

5.2.4. [Darbeoetin alfa - ARANESP \(CAP\) - EMEA/H/C/000332/II/0148](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' to implement information on education material proposal to address the incorrect self-administration of Aranesp (darbeoetin alfa) via the SureClick pre-filled pen and associated dosing errors. The RMP (version 9.1) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.5. [Emtricitabine - EMTRIVA \(CAP\) - EMEA/H/C/000533/II/0127](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 9.1) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template). In addition, updates have been made to the Antiretroviral Pregnancy Registry (APR) and the Mitochondrial Collaborative Committee (MITOC) study: a cross-sectional study of human immunodeficiency virus (HIV) negative children aged 18-24 months born to HIV-1 infected mothers in Europe. Finally, the RMP is also updated to reflect the approved transfer of

the marketing authorisation from Gilead Sciences International Ltd, Cambridge (GSIL) to Gilead Sciences Ireland UC, Cork (GSIUC)

Action: For adoption of PRAC Assessment Report

5.2.6. [Evolocumab - REPATHA \(CAP\) - EMEA/H/C/003766/II/0028](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of the RMP (version 5.0) in order to provide the final results of study 20120332 (GAUSS-3, part C) (listed as a category 3 study in the RMP): a 3-part, phase 3, multicentre, randomized, double-blind, ezetimibe-controlled, parallel-group study. Part C was a 2-year, open-label extension that evaluated the long-term safety and efficacy of evolocumab in hypercholesterolemic subjects unable to tolerate an effective dose of a statin. As a consequence, the MAH proposes to remove missing information of use in patients with severe hepatic impairment (Child-Pugh class C) and use in patients with hepatitis C

Action: For adoption of PRAC Assessment Report

5.2.7. [Human fibrinogen, human thrombin - EVICEL \(CAP\) - EMEA/H/C/000898/II/0063](#)

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of the RMP (version 14.2) in order to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template) to update exposure data, and to remove 'lack of efficacy' as an identified risk as requested by PRAC in the outcome of the PSUR single assessment procedure (PSUSA/00010297/201706) concluded in January 2018

Action: For adoption of PRAC Assessment Report

5.2.8. [Pegfilgrastim - NEULASTA \(CAP\) - EMEA/H/C/000420/II/0099](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Update of the RMP (version 5.1) in order to add study 20160176 (listed as category 3 in the RMP): a retrospective cohort study of female breast cancer patients aged 66 years and over selected from the US Surveillance, Epidemiology and End Results (SEER)-Medicare database to investigate the association between granulocyte colony stimulating factor (G-CSF) use and myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML), as a new pharmacovigilance activity. In addition, the MAH submitted a draft protocol for study 20160176

Action: For adoption of PRAC Assessment Report

5.2.9. [Pregabalin - LYRICA \(CAP\) - EMEA/H/C/000546/WS1364/0092; PREGABALIN PFIZER \(CAP\) - EMEA/H/C/003880/WS1364/0021](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of the RMP (version 12.0) in order to update the safety specifications and risk minimisation measures as requested in the outcome of the PSUR single assessment procedure (PSUSA/00002511/201701) finalised in September 2017. The pharmacovigilance plan is also updated. The draft protocol for a non-interventional non-imposed PASS (study A0081359) entitled 'a population-based cohort study of pregabalin to characterize pregnancy outcomes' is submitted. The MAH took the opportunity to include minor updates and to align the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.10. [Saxagliptin - ONGLYZA \(CAP\) - EMEA/H/C/001039/II/0048](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 14) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.11. [Sitagliptin - JANUVIA \(CAP\) - EMEA/H/C/000722/WS1357/0063; RISTABEN \(CAP\) - EMEA/H/C/001234/WS1357/0055; TESAVEL \(CAP\) - EMEA/H/C/000910/WS1357/0063; XELEVIA \(CAP\) - EMEA/H/C/000762/WS1357/0067; sitagliptin, metformin hydrochloride - EFFICIB \(CAP\) - EMEA/H/C/000896/WS1357/0089; JANUMET \(CAP\) - EMEA/H/C/000861/WS1357/0089; RISTFOR \(CAP\) - EMEA/H/C/001235/WS1357/0076; VELMETIA \(CAP\) - EMEA/H/C/000862/WS1357/0092](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 9.1) in order to remove 'theoretic carcinogenic potential' currently classified as missing information from the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.12. [Talimogene laherparepvec - IMLYGIC \(CAP\) - EMEA/H/C/002771/II/0028](#)

Applicant: Amgen Europe B.V., ATMP⁴

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of the RMP (version 4.0) in order to reflect changes in the categorisation of safety concerns and missing information in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

⁴ Advanced therapy medicinal product

5.2.13. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0042/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of an update of the RMP (version 8) in order to: 1) remove MoTHER pharmacovigilance activities (MEA 011): 'an observational study of pregnancy and pregnancy outcomes in women with breast cancer treated with trastuzumab, pertuzumab in combination with trastuzumab or pertuzumab during pregnancy or within 7 months prior to conception'; and use the global enhanced pharmacovigilance pregnancy programme to fulfil the commitment; 2) change the due date of final results for the provision of the final study report for BO27938 (KATHERINE) (a category 3 study in the RMP): a randomized, multicentre, open label phase 3 study to evaluate the efficacy and safety of trastuzumab emtansine versus trastuzumab as adjuvant therapy for patients with human epidermal growth factor receptor 2 (HER2)-positive primary breast cancer who have residual tumour present pathologically in the breast or axillary lymph nodes following preoperative therapy to address the following safety concerns: left ventricular dysfunction, safety in elderly patients, immunogenicity (anti-therapeutic antibodies [ATAs]). In addition, the MAH took the opportunity to update the RMP in line with revision 2 of GVP module V on 'Risk management systems' and include an update of Kadcyla (trastuzumab emtansine) educational material to reflect changes in the prescribing information following the completion of the renewal procedure of the marketing authorisation in July 2018

Action: For adoption of PRAC Assessment Report

5.3. Medicines in the post-authorisation phase – CHMP-led procedures

5.3.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/X/0117/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped applications consisting of: 1) extension application to add two new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard for subcutaneous (SC) administration; 2) variation to include paediatric use of polyarticular juvenile idiopathic arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg). The RMP (version 25.0) is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the product information

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0047, Orphan

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include non-ambulatory patients with Duchenne muscular dystrophy. As supportive data, the variation includes the final results of the long term clinical study PTC-124-GD-019-DMD: an open-label study for previously treated ataluren (PTC124) patients with nonsense mutation dystrophinopathy. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. [Brentuximab vedotin - ADCETRIS \(CAP\) - EMEA/H/C/002455/II/0055, Orphan](#)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the frontline treatment of adult patients with CD30+ advanced Hodgkin lymphoma (HL) in combination with chemotherapy, based on data from ECHELON-1 (C25003): a phase 3 multicentre, randomised, open-label study comparing the modified progression-free survival (mPFS) obtained with brentuximab vedotin, doxorubicin, vinblastine and dacarbazine versus the mPFS obtained with doxorubicin, bleomycin, vinblastine and dacarbazine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13) are updated accordingly. Furthermore, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.4. [Ceritinib - ZYKADIA \(CAP\) - EMEA/H/C/003819/II/0026](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.5 of the SmPC in order to update the safety information based on the final results from study CLDK378A2103 (listed as a category 3 study in the RMP, MEA 002): a phase I, multicentre, open label, drug-drug interaction study to assess the effect of ceritinib on the pharmacokinetics of warfarin and midazolam administered as a two-drug cocktail in patients with anaplastic lymphoma kinase (ALK)-positive advanced tumours including non-small cell lung cancer (NSCLC). The package leaflet and the RMP (version 14) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.5. [Cinacalcet - MIMPARA \(CAP\) - EMEA/H/C/000570/II/0062/G](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of section 4.4 of the SmPC to provide additional information on switching from etelcalcetide to Mimpara (cinacalcet) as requested by PRAC in the PSUR single assessment procedure for etelcalcetide (PSUSA/00010533/201711) concluded in May 2018; 2) update of section 6.1 of the SmPC to replace the term 'silica, dental type' by 'amorphous silicon dioxide'. The RMP is updated (version 9.0) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1344/0025; FORXIGA \(CAP\) - EMEA/H/C/002322/WS1344/0044](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include the treatment of insufficiently controlled type 1 diabetes mellitus (T1DM) as an adjunct to insulin, when insulin does not provide adequate glycaemic control, for Forxiga and Edistride (dapagliflozin). 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 RMP (version 16) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the SmPC and package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. [Daratumumab - DARZALEX \(CAP\) - EMEA/H/C/004077/II/0020, Orphan](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of study report of study SMM2001: a randomised phase 2 trial to evaluate 3 daratumumab dose schedules in smouldering multiple myeloma. As a consequence, the RMP is updated (version 4.1) in order to remove QTc prolongation as an important potential risk

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.8. [Dasatinib - SPRYCEL \(CAP\) - EMEA/H/C/000709/II/0059](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia for the treatment of paediatric patients. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 16.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the product information

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. [Decitabine - DACOGEN \(CAP\) - EMEA/H/C/002221/II/0033, Orphan](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from the paediatric study DACOGENAML2004: 'a phase 1-2 safety and efficacy study of Dacogen (decitabine) in sequential administration with cytarabine in children with relapsed or refractory acute myeloid leukaemia' as per the requirement of Article 46 of Regulation (EC) No1901/2006. The RMP (version 3.1) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised European Commission guideline on 'Excipients in the labelling and package

leaflet of medicinal products for human use'. The package leaflet is updated accordingly. Moreover, the contact details of the local representative in Slovenia are updated in the package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/II/0128

Applicant: Apotex Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Update of section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of absolute neutrophil count (ANC) monitoring throughout Ferriprox (deferiprone) treatment from a weekly basis to every week for the first six months of therapy, once every two weeks after six months and to monthly after one year of therapy. The package leaflet and the RMP (version 13.2) are updated accordingly. In addition, the MAH took the opportunity to update minor linguistic amendments in the Hungarian and Maltese product information

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0065

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC to modify the frequency category of atypical femoral fracture (AFF) as an adverse drug reaction (ADR) from 'rare' to 'uncommon' and to add descriptive language regarding latency observed in clinical studies. The package leaflet and the RMP (version 33) are updated accordingly. In addition, the MAH took the opportunity to remove the black triangle and corresponding text from the Annexes as Xgeva (denosumab) is no longer under additional monitoring. The MAH also took the opportunity to implement editorial changes in the annexes and to update the contact details of the local representative in Ireland in the package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.12. Eftrenonacog alfa - ALPROLIX (CAP) - EMEA/H/C/004142/II/0021, Orphan

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to include new clinical efficacy and safety data on long-term treatment with Alprolix (eftrenonacog alfa) based on the data from extension study 9HB01EXT (BYOND): an open-label, multicentre evaluation of the long-term safety and efficacy of recombinant, human coagulation factor IX fusion protein (rFIXFc) in the prevention and treatment of bleeding episodes in previously treated subjects with haemophilia B as well data from the pivotal parent studies. The package leaflet and the RMP (version 1.4) are updated accordingly. In addition, the MAH took the opportunity to update the product information to comply with the latest version of the European Commission (EC) guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. In addition, the MAH took the opportunity to update the list of local representatives and to

introduce minor editorial changes in the package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. [Elotuzumab - EMLICITI \(CAP\) - EMEA/H/C/003967/II/0012](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment in combination with pomalidomide and dexamethasone of adult patients with multiple myeloma. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.14. [Emicizumab - HEMLIBRA \(CAP\) - EMEA/H/C/004406/II/0002](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include routine prophylaxis of bleeding episodes in patients with haemophilia A without factor VIII (FVIII) inhibitors. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the following pivotal trials: 1) study BH30071 (HAVEN 3): an ongoing, multicentre, open-label, randomized phase 3 clinical study evaluating the efficacy, safety and pharmacokinetic (PK) of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against FVIII; 2) study BO39182 (HAVEN 4): an ongoing multicentre, open-label, non-randomized phase 3 study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6 mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with haemophilia A with or without FVIII inhibitors; 3) study BH29992 (HAVEN 2): a multicentre, open-label, non-randomized phase 3 study evaluating the efficacy, safety and PK of emicizumab at the QW dose in paediatric patients (<12 years old or 12-17 years old and <40kg) with haemophilia A with FVIII inhibitors. The package leaflet and the RMP (version.2.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.15. [Empagliflozin, linagliptin - GLYXAMBI \(CAP\) - EMEA/H/C/003833/WS1461/0017;](#) [Linagliptin, metformin - JENTADUETO \(CAP\) - EMEA/H/C/002279/WS1461/0047;](#) [Linagliptin - TRAJENTA \(CAP\) - EMEA/H/C/002110/WS1461/0035](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC to update the warnings related to acute pancreatitis and bullous pemphigoid as well as the efficacy and safety information based on the final results from study CARMELINA (listed as a category 3 study in the RMP): a multicentre, international, randomised, parallel group, double blind, placebo-controlled

Cardiovascular Safety & Renal Microvascular outcome study with LINAgliptin, 5 mg once daily in patients with type 2 diabetes mellitus (T2DM) at high vascular risk. The RMP is updated accordingly (Trajenta and Jentaduetto version 12, Glyxambi version 4.0) and in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/X/0001

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Extension application to add a new strength of 140 mg. The RMP (version 2.0) is updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.17. Etelcalcetide - PARSABIV (CAP) - EMEA/H/C/003995/II/0010

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 4.8 to add 'convulsions secondary to hypocalcaemia' as an adverse drug reaction with a frequency uncommon and to reflect further information on reports related to hypersensitivity reactions. The package leaflet is updated accordingly. The RMP (version 2) is also updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template) introducing some changes in the categorisation of safety concerns. In addition, the MAH took the opportunity to introduce minor editorial changes in SmPC

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/X/0083/G

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 100 mg/ml solution for injection for paediatric use; 2) extension of indication to include paediatric patients from the age of 2 years and older for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) with Simponi (golimumab) 100 mg/mL solution for injection. As a consequence, sections 4.1, 4.2, 5.1 and section 4.1 of the 50mg strength are updated; 3) update of the RMP (version 18.0) to delete the following safety concerns: vasculitis, psoriasis (new onset or worsening of pre-existing), and sarcoidosis/sarcoid like reaction as requested in the outcome of variation II/068/G concluded in May 2016; 4) update of the RMP (version 18.0) to change the due date of study MK-8259-050 (listed as a category 3 study in the RMP) as requested by CHMP in the conclusion of MEA 033 dated April 2017. Finally, the MAH took the opportunity to update the product information in line with the latest QRD template (version 10) to implement the recommendations stated in the revised Annex to the European Commission (EC) guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regard to the excipient sorbitol (E420); to add a statement in section 4.4 of the SmPC to record the name and the batch number of the administered product in line with GVP Module P.II on 'Biological medicinal products' (EMA/168402/2014 Corr*)

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0005

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add hypersensitivity and rash as adverse drug reactions with the frequency uncommon, together with a statement describing the characteristics of the serious hypersensitivity events. The package leaflet and the RMP (version 3.0) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.20. Insulin glargine - TOUJEO (CAP) - EMEA/H/C/000309/II/0105/G

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations to introduce a new 3 mL pre-filled pen. Introduction of four new pack sizes: packs of 1, 3, 6 (multipack) and 9 pens (multipack). As a consequence, Annex A, I, IIA and IIIB are amended. In addition, the RMP (version 5.0) in line with revision 2 of the guidance on the format of RMP in the EU (template) is updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.21. Irinotecan hydrochloride trihydrate - ONIVYDE (CAP) - EMEA/H/C/004125/II/0008

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: David Olsen

Scope: Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The labelling, package leaflet and the RMP (version 2.1) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes throughout the product information

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS1372/0053; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS1372/0057

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include first-line treatment of adult patients with metastatic non-small cell lung carcinoma (NSCLC). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information from pivotal study CA209227: an open-label, randomised phase 3 trial of nivolumab, or nivolumab plus ipilimumab, or nivolumab plus platinum doublet chemotherapy versus platinum doublet chemotherapy in subjects with chemotherapy-naïve stage IV or recurrent NSCLC. The package leaflet and RMP (version 14.0 for Opdivo and version 21.0 for Yervoy) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial and formatting revisions in the product

information

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. [Macitentan - OPSUMIT \(CAP\) - EMEA/H/C/002697/II/0029, Orphan](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), based on: 1) pivotal study MERIT-1 (AC-055E201): a prospective, randomized, placebo-controlled, double-blind, multicentre, parallel-group, 24-week study to assess the efficacy, safety and tolerability of macitentan in subjects with inoperable CTEPH; 2) 6 months of efficacy and safety data (cut-off date 17 October 2017) from its ongoing open-label extension study MERIT-2 (AC-055E202): a long term, multicentre, single-arm, open-label extension study of the merit-1 study, to assess the safety, tolerability and efficacy of macitentan in subjects with inoperable CTEPH; 3) drug-drug interaction (DDI) study AC-055-122: a single-centre, open-label, one-sequence, two-treatment study to investigate the effect of macitentan at steady state on the pharmacokinetics (PK) of rosuvastatin in healthy male subjects; 4) DDI study AC-055-123: a single-center, open-label, one-sequence, two-treatment study to investigate the effect of macitentan at steady state on the PK of riociguat in healthy male subjects; 5) observational data from the OPUS registry (OPsumit USers Registry; cut-off date of 17 April 2018): safety and tolerability of macitentan in a real-world setting. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 are updated. The package leaflet and the RMP (version 9.2) are updated accordingly. In addition, the MAH took the opportunity to implement editorial changes, to align the annexes with the latest QRD template and to update the contact details of the local representatives in the package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.24. [Niraparib - ZEJULA \(CAP\) - EMEA/H/C/004249/II/0006, Orphan](#)

Applicant: Tesaro UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to optimise the starting dose of niraparib and clarify dose modification information, modify the existing warning on haematologic adverse reactions, amend the description of thrombocytopenia and amend existing efficacy and pharmacokinetics information, respectively. The changes are based on the integrated population clinical report that contains information from: 1) completed phase 3 study NOVA (submitted as part of the initial application): a phase 3 randomized double-blind trial of maintenance with niraparib versus placebo in patients with platinum-sensitive ovarian cancer; 2) supportive information from ongoing study PR-30-5020-C (QUADRA): a phase 2, open-label, single-arm study to evaluate the safety and efficacy of niraparib in patients with advanced, relapsed, high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received three or four previous chemotherapy regimens; 3) study 300-PN-162-01-001 (TOPACIO): a phase 1/2 clinical study of niraparib in combination with pembrolizumab (MK-3475) in patients with advanced or metastatic triple-negative breast cancer and in patients with recurrent ovarian cancer. The package leaflet and the RMP (version 1.1) are updated accordingly. The RMP is also updated in

line with revision 2 of the guidance on the format of RMP in the EU (template) and the outcome of the PSUR single assessment procedure (PSUSA/00010655/201803) finalised in October 2018

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0020](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) tablets as monotherapy for the treatment of adult patients with BRCA-1/2-mutated human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant or metastatic setting. 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 and the RMP (version 16) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.26. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0023](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) as a monotherapy for the maintenance treatment of adult patients with newly diagnosed advanced BRCA-mutated high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to first-line platinum-based chemotherapy. As a consequence, sections 4.1 and 4.8 of the SmPC are updated in order to include information from single pivotal study D0818C00001 (SOLO 1): a phase 3, randomised, double blind, placebo controlled, multicentre study of olaparib maintenance monotherapy in patients with BRCA mutated advanced (FIGO⁵ stage III-IV) ovarian cancer following first line platinum based chemotherapy. The package leaflet and the RMP (version 17) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. [Omalizumab - XOLAIR \(CAP\) - EMEA/H/C/000606/II/0093](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.6 of the SmPC based on the data from the Xolair Pregnancy Registry (EXPECT): an observational study of the use and safety of Xolair (omalizumab) during pregnancy; and the final study report for study Q2952g (listed as a category 3 study in the RMP): an observational study to evaluate pregnancy outcomes and estimate the incidence of spontaneous foetal loss in pregnant women exposed to omalizumab prenatally and to explore the potential risk to newborn infants exposed via breast milk. The package leaflet and the RMP (version 14.0) are updated accordingly

⁵ International Federation of Gynaecology and Obstetrics

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.28. [Plerixafor - MOZOBIL \(CAP\) - EMEA/H/C/001030/II/0034, Orphan](#)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include paediatric patients aged 1 to 18 years for Mozobil (plerixafor). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 10) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.29. [Rituximab - MABTHERA \(CAP\) - EMEA/H/C/000165/II/0152](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.2 and 4.4 of the SmPC following the submission of the final study report for the non-interventional drug utilisation study (DUS) BA28478: MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach. Annex II-E is updated to remove the patient alert card as an additional risk minimisation measure for the risks of progressive multifocal leukoencephalopathy (PML) and infections for the non-oncology indications. The package leaflet and the RMP (version 18) are updated accordingly. This submission fulfils FUM-68.1 and FUM-71

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.30. [Rituximab - MABTHERA \(CAP\) - EMEA/H/C/000165/II/0157](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' resulting from the obligation fulfilment for the rituximab subcutaneous (SC) formulation at a dose of 1,400 mg by the submission of the final clinical study report for study BO22334 (SABRINA, listed as a category 1 study) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SABRINA is a two-stage phase 3, international, multicentre, randomized, controlled, open-label study investigating the pharmacokinetics (PK), efficacy and safety of rituximab SC in combination with cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) chemotherapy or cyclophosphamide, vincristine, prednisolone (CVP) chemotherapy versus rituximab intravenous (IV) in combination with CHOP or CVP chemotherapy followed by maintenance treatment with either rituximab SC or rituximab IV. The RMP (version 19.0) is updated accordingly. In addition, the MAH took the opportunity to include other changes to the RMP including the fulfilment of the previous information on concluded commitments such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.31. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0158

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product', resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1,400 mg by the submission of the final clinical study report for study BO25341 (SAWYER, listed as a category 1 study) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SAWYER is a phase Ib adaptive, comparative, randomized, parallel-group, multicentre study of subcutaneous (SC) rituximab versus intravenous (IV) rituximab both in combination with chemotherapy (fludarabine and cyclophosphamide), in patients with previously untreated chronic lymphocytic leukaemia (CLL). The RMP (version 19.0) is updated accordingly. In addition, the MAH took the opportunity to include the changes on the concluded commitment such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.32. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0001, Orphan

Applicant: Clovis Oncology UK Limited

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include a new indication for Rubraca (rucaparib) 'as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy'. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated with the expanded clinical efficacy and safety data. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the applicant took the opportunity to propose to move one paragraph from section 4.4 to 5.1 in the SmPC for consistency with other SmPC for agents in the class with this indication

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.33. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0191

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication to include as a new indication treatment of chronic hepatitis B (CHB) in paediatric patients aged 6 to < 12 years (film coated tablets 123 mg; 163 mg; 204 mg) and to extend the existing CHB indication to include treatment of CHB in paediatric patients aged 2 to < 12 years (granules 33 mg/g), based on results from interim week 48 clinical study report (CSR) for study GS-US-174-0144: a randomized, double-blind evaluation of the antiviral efficacy, safety and tolerability of tenofovir disoproxil fumarate versus placebo in paediatric patients with CHB infection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated for Viread (tenofovir disoproxil) 123 mg, 163 mg and 204 mg; sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Viread (tenofovir disoproxil) 245 mg; and sections 4.1, 4.2, 4.4, 5.1 and 5.2 for Viread (tenofovir disoproxil) granules 33 mg/g. The

package leaflet and the RMP (version 22.1) are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.34. Thalidomide - THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/II/0056, Orphan

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Update of the RMP (version 19) in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template) to propose the reclassification and/or renaming of known safety concerns associated with the use of Thalidomide Celgene (thalidomide). Consequently, Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product', section 4.4 and 4.6 of the SmPC as well as the package leaflet are updated accordingly

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.35. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0034

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 5.1 of the SmPC in order to provide the final efficacy results up to week 348 regarding clinical study c13008 (listed as a category 3 study in the RMP): a phase 3, open-label study to determine the long-term safety and efficacy of vedolizumab in subjects with ulcerative colitis and Crohn's disease. The RMP is updated accordingly (version 4.0)

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

6. Periodic safety update reports (PSURs)

6.1. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only

6.1.1. Abiraterone - ZYTIGA (CAP) - PSUSA/00000015/201804

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/201805

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. [Artemimol, piperazine tetraphosphate - EURARTESIM \(CAP\) - PSUSA/00001069/201804](#)

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. [Atezolizumab - TECENTRIQ \(CAP\) - PSUSA/00010644/201805 \(with RMP\)](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. [Basiliximab - SIMULECT \(CAP\) - PSUSA/00000301/201804](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. [Benralizumab - FASENRA \(CAP\) - PSUSA/00010661/201805](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. [Cerliponase alfa - BRINEURA \(CAP\) - PSUSA/00010596/201804](#)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. [Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA \(CAP\) - PSUSA/00010449/201805](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Daratumumab - DARZALEX (CAP) - PSUSA/00010498/201805

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Darunavir, cobicistat - REZOLSTA (CAP) - PSUSA/00010315/201805

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Decitabine - DACOGEN (CAP) - PSUSA/00009118/201805

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201804

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/201805

Applicant: EUSA Pharma (UK) Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/201805

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Empagliflozin, linagliptin - GLYXAMBI (CAP) - PSUSA/00010539/201805

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Epoetin theta - BIOPOIN (CAP); EPORATIO (CAP) - PSUSA/00001240/201804

Applicant(s): Teva GmbH (Biopoin), Ratiopharm GmbH (Eporatio)

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Etelcalcetide - PARSABIV (CAP) - PSUSA/00010533/201805

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Fentanyl⁶ - IONSYS⁷ - PSUSA/00010453/201805

Applicant: Incline Therapeutics Europe Ltd

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For information

6.1.19. Fluticasone furoate - AVAMYS (CAP) - PSUSA/00009154/201804

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) - PSUSA/00010099/201805

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

⁶ Transdermal system - centrally authorised product(s) only

⁷ European Commission (EC) decision on the MA withdrawal of Ionsys dated 27 September 2018

Action: For adoption of recommendation to CHMP

6.1.21. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/201805

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Interferon beta-1a - AVONEX (CAP); REBIF (CAP) - PSUSA/00009198/201805

Applicant(s): Biogen Netherlands B.V. (Avonex), Merck Europe B.V. (Rebif)

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ixazomib - NINLARO (CAP) - PSUSA/00010535/201805

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ketoconazole⁸ - KETOCONAZOLE HRA (CAP) - PSUSA/00010316/201805

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Laronidase - ALDURAZYME (CAP) - PSUSA/00001830/201804

Applicant: Genzyme Europe BV

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Letemovir - PREVYMIS (CAP) - PSUSA/00010660/201805

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

⁸ Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.27. Lidocaine, prilocaine⁹ - FORTACIN (CAP) - PSUSA/00010110/201805

Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Linagliptin - TRAJENTA (CAP); linagliptin, metformin - JENTADUETO (CAP); - PSUSA/00010427/201805

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/201805

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - PSUSA/00010607/201805

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Necitumumab - PORTRAZZA (CAP) - PSUSA/00010471/201805

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Padeliporfin - TOOKAD (CAP) - PSUSA/00010654/201805

Applicant: Steba Biotech S.A

⁹ Centrally authorised product(s) only

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. [Pandemic influenza vaccine \(H5N1\) \(live attenuated, nasal\) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA \(CAP\) - PSUSA/00010501/201805](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Daniela Philadelphly

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. [Pandemic influenza vaccine \(H5N1\) \(split virion, inactivated, adjuvanted\) - ADJUPANRIX \(CAP\); prepandemic influenza vaccine \(H5N1\) \(split virion, inactivated, adjuvanted\) - PREPANDRIX \(CAP\) - PSUSA/00002281/201805](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. [Pixantrone - PIXUVRI \(CAP\) - PSUSA/00009261/201805](#)

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. [Prasterone¹⁰ - INTRAROSA \(CAP\) - PSUSA/00010672/201805](#)

Applicant: Endoceutics Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. [Radium \(²²³Ra\) dichloride - XOFIGO \(CAP\) - PSUSA/00010132/201805](#)

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁰ Pessary, vaginal use only

6.1.38. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/201805

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Shingles (herpes zoster) vaccine (live) - ZOSTAVAX (CAP) - PSUSA/00009289/201805

Applicant: MSD Vaccins

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Sunitinib - SUTENT (CAP) - PSUSA/00002833/201804

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Susoctocog alpha - OBIZUR (CAP) - PSUSA/00010458/201805

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Tafamidis - VYNDAQEL (CAP) - PSUSA/00002842/201805

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201804

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Tenofovir alafenamide - VEMLIDY (CAP) - PSUSA/00010575/201805

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Tilmanocept - LYMPHOSEEK (CAP) - PSUSA/00010313/201805

Applicant: Norgine B.V.

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/201805

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Tolvaptan¹¹ - JINARC (CAP) - PSUSA/00010395/201805

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Tolvaptan¹² - SAMSCA (CAP) - PSUSA/00002994/201805

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Ulipristal¹³ - ELLAONE (CAP) - PSUSA/00003074/201805

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

¹¹ Indicated for adults with autosomal dominant polycystic kidney disease (ADPKD) only

¹² Indicated for adults with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH) only

¹³ indicated in female emergency contraception only

Action: For adoption of recommendation to CHMP

6.1.50. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/201805

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

6.2.1. Bortezomib - BORTEZOMIB ACCORD (CAP); BORTEZOMIB HOSPIRA (CAP); BORTEZOMIB SUN (CAP); VELCADE (CAP); NAP - PSUSA/00000424/201804

Applicants: Accord Healthcare Limited (Bortezomib Accord), Janssen-Cilag International NV (Velcade), Pfizer Europe MA EEIG (Bortezomib Hospira), Sun Pharmaceutical Industries Europe B.V. (Bortezomib SUN), various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Capecitabine - XELODA (CAP); NAP - PSUSA/00000531/201804

Applicants: Roche Registration GmbH, various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For preliminary discussion

6.2.3. Efavirenz - STOCRIN (CAP); SUSTIVA (CAP); NAP - PSUSA/00001200/201804

Applicant(s): Merck Sharp & Dohme B.V. (Stocrin), Bristol-Myers Squibb Pharma EEIG (Sustiva)

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Enoxaparin¹⁴ - INHIXA (CAP); THORINANE (CAP); NAP - PSUSA/00010553/201804

Applicants: Techdow Europe AB (Inhixa), Techdow Pharma Netherlands B.V. (Thorinane), various

PRAC Rapporteur: Menno van der Elst

¹⁴ Biosimilar products only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Hydrochlorothiazide, telmisartan - KINZALKOMB (CAP); MICARDISPLUS (CAP); PRITORPLUS (CAP); telmisartan - KINZALMONO (CAP); MICARDIS (CAP); PRITOR (CAP); NAP - PSUSA/00002882/201804

Applicants: Bayer AG (Kinzalkomb, Kinzalmono, Pritor, PritorPlus), Boehringer Ingelheim International GmbH (Micardis, MicardisPlus), various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Ivabradine - CORLENTOR (CAP); IVABRADINE ANPHARM (CAP); PROCORALAN (CAP); NAP - PSUSA/00001799/201804

Applicants: Anpharm Przedsiębiorstwo Farmaceutyczne S.A. (Ivabradine Anpharm), Les Laboratoires Servier (Corlentor, Procoralan), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. Mycophenolate mofetil - CELLCEPT (CAP); MYCLAUSEN (CAP); MYCOPHENOLATE MOFETIL TEVA (CAP); MYFENAX (CAP); NAP mycophenolic acid (NAP) - PSUSA/00010550/201805

Applicants: Passauer Pharma GmbH (Myclausen), Roche Registration GmbH (CellCept), Teva B.V. (Mycophenolate mofetil Teva, Myfenax), various

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.8. Tacrolimus¹⁵ - ADVAGRAF (CAP); ENVARBUS (CAP); MODIGRAF (CAP); NAP - PSUSA/00002839/201803 (with RMP)

Applicants: Astellas Pharma Europe B.V. (Advagraf, Modigraf), Chiesi Farmaceutici S.p.A. (Envarsus), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁵ Systemic formulations only

6.3. PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only

6.3.1. Acarbose (NAP) - PSUSA/00000017/201803

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amlodipine besilate, ramipril (NAP) - PSUSA/00000181/201803

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Benzyl nicotinate, camphor, dimethyl sulfoxide, nonivamide, turpentine oil (NAP) - PSUSA/00010584/201803

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Calcium chloride, glutamic acid, glutathione, histidine, lactobionic acid, magnesium chloride, mannitol, potassium chloride, sodium hydroxide (NAP) - PSUSA/00009162/201803

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Chlorprothixene (NAP) - PSUSA/00000717/201803

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Deoxycholic acid (NAP) - PSUSA/00010525/201804

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dihydroergotamine (NAP) - PSUSA/00001075/201804

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Dihydroergotoxine (NAP) - PSUSA/00001079/201804

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Enalapril (NAP) - PSUSA/00001211/201803

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Felodipine, ramipril (NAP) - PSUSA/00001358/201803

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Foscarnet (NAP) - PSUSA/00001472/201803

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Human anti-D immunoglobulin (NAP) - PSUSA/00001614/201803

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Isotretinoin¹⁶ (NAP) - PSUSA/00010488/201805

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Ivabradine, metoprolol (NAP) - PSUSA/00010381/201804

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Ivermectin¹⁷ (NAP) - PSUSA/00010376/201804

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Mepivacaine (NAP); mepivacaine hydrochloride, epinephrine (NAP); mepivacaine, norepinephrine (NAP) - PSUSA/00001979/201803

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Metamizole (NAP) - PSUSA/00001997/201804

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁶ Oral formulations only

¹⁷ Topical use only

6.3.18. Metformin (NAP) - PSUSA/00002001/201804

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Methylphenobarbital (NAP) - PSUSA/00002025/201803

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Nadroparin (NAP) - PSUSA/00002104/201803

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Nebivolol (NAP) - PSUSA/00002129/201803

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Nitrendipine (NAP) - PSUSA/00002171/201803

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Nortriptyline (NAP) - PSUSA/00002192/201803

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Ofloxacin¹⁸ (NAP) - PSUSA/00002203/201804

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Ofloxacin¹⁹ (NAP) - PSUSA/00002204/201804

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Oxaliplatin (NAP) - PSUSA/00002229/201804

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Oxycodone (NAP) - PSUSA/00002254/201804

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Paracetamol²⁰ (NAP) - PSUSA/00002311/201805

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

None

¹⁸ Systemic use only

¹⁹ Topical use only

²⁰ Intravenous (IV) formulation only

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²¹

7.1.1. Eliglustat – CERDELGA (CAP) - EMEA/H/C/PSA/S/0035

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Protocol for a prospective multicentre observational post authorisation safety sub-registry to characterize the long-term safety profile of commercial use of Cerdelga (eliglustat) in adult patients with Gaucher disease

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0034

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Amendment to a previously agreed protocol in April 2014 (ANX 041.4) for a prospective non-interventional PASS, designed as a disease registry of patients with transfusion dependent international prognostic scoring system (IPSS) low or intermediate-1-risk myelodysplastic syndromes (MDS) and isolated del(5q)

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Tisagenlecleucel – KYMRIA (CAP) - EMEA/H/C/PSP/S/0066

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for non-interventional study CCTL019B2401 with secondary use of data from two registries conducted by the 'European Society for Blood and Marrow Transplantation' (EBMT) and 'Centre for International Blood and Marrow Transplant Research' (CIBMTR) to evaluate the long term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel (chimeric antigen receptor (CAR)-T cell therapy) in a real-world setting

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²²

7.2.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 009

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: PASS protocol for study I4V-MC-B0166: assessment of off-label use in paediatric patients in the UK in the Clinical Practice Research Datalink (CPRD) database

²¹ In accordance with Article 107n of Directive 2001/83/EC

²² In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

Action: For adoption of advice to CHMP

7.2.2. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 003.1

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: MAH's response to MEA 003.1 [PASS protocol for study D3250R00026 'the benralizumab pregnancy exposure study': a post-marketing surveillance study on vaccines and medications in pregnancy surveillance system (VAMPSS)] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.2.3. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002.2

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.1 [protocol for study NIS-KYNTHEUM-1345: an observational PASS of suicidal behaviour, serious infections, major adverse cardiovascular events (MACE) and malignancy in psoriasis patients treated with brodalumab. The brodalumab assessment of hazards: a multinational safety (BRAHMS) study in electronic healthcare databases [final report expected in Q3 2030]] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.2.4. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/MEA 004.1

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 002.1 [protocol for a non-interventional prospective cohort study in the treatment of children with X-linked hypophosphataemia (XLH) to assess the long term safety of Crysvida (burosumab) during routine clinical care using data collected in a European disease registry for XLH [final report expected in December 2028]] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.2.5. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 013.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 013.2 [PASS protocol for a US epidemiology database study to further characterise the incidence of below-knee lower limb amputation in patients taking canagliflozin (listed as a category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted in July

2018

Action: For adoption of advice to CHMP

7.2.6. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 012.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 012.2 [PASS protocol for a US epidemiology database study to further characterise the incidence of below-knee lower limb amputation in patients taking canagliflozin (listed as a category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.7. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/LEG 010

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Protocol for study DF-VOD2013-03-REG: a multicentre, multinational, prospective, non-interventional registry to record safety and outcome data in patients diagnosed with severe veno-occlusive disease (VOD) following hematopoietic stem cell transplantation (HSCT) treated or not with Defitelio (defibrotide) describing the objectives and methodology for the literature review and analysis of data from the Center for International Blood and Marrow Transplant Research (CIBMTR), as requested in the outcome of variation II/27 concluded in June 2018

Action: For adoption of advice to CHMP

7.2.8. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 001.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 001 [protocol for study GO40162: a PASS based on the European Haemophilia Safety Surveillance (EUHASS) registry to characterise the safety profile of patients with haemophilia A exposed to emicizumab under real-world conditions, including an estimate of event rates of the following important risks: thromboembolic events, thrombotic microangiopathy, systemic hypersensitivity, anaphylaxis and anaphylactoid events [final clinical study report: (CSR) expected in June 2024]] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.9. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/MEA 045.6

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 045.5, including an enrolment progress report [PASS protocol for study GS-EU-276-4027, a drug utilisation study (DUS) to characterize: 1) prescribers' level of knowledge about the key risks of Truvada for a pre-exposure prophylaxis (PrEP) indication and assess the effectiveness of risk minimisation measures; 2) prescribing practices in routine clinical practice of Truvada for PrEP by describing the demographics of human immunodeficiency virus 1 (HIV-1) uninfected individuals who were prescribed Truvada for PrEP, and the prescribed dosing schedule for Truvada for PrEP as reported by the prescriber] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.10. Florbetaben (¹⁸F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 001.7

Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 003 [amended protocol to previously agreed protocol in September 2016 for PASS study FBB-01_03_13 (PASS 2): a non-interventional, prospective observational multicentre, multi-country registry to observe usage pattern, safety and tolerability of the diagnostic agent NeuraCeq (florbetaben (¹⁸F)) in clinical practice [final clinical study report (CSR) expected in Q2/2020]] as per the request for supplementary information adopted in June 2018

Action: For adoption of advice to CHMP

7.2.11. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 026.6

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Amended protocol (version 2) to a previously agreed protocol in April 2015 for study MK-8259-013, the ulcerative colitis (UC) Nordic registry: a non-interventional observational longitudinal PASS of Simponi (golimumab) in the treatment of UC using Nordic national health registries

Action: For adoption of advice to CHMP

7.2.12. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.6

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 006.5 [amendment for study D3820R00009 (previously study D2288R00084) to a protocol previously agreed in June 2016: an observational PASS of Moventig (naloxegol) among patients aged 18 years and older treated with opioids chronically] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.13. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/MEA 003.1

Applicant: Tesaro UK Limited

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 003 [protocol and statistical analysis plan for a non-interventional non-imposed PASS: a pooled analysis of the incidence of acute myelogenous leukaemia, myelodysplastic syndrome, and other secondary primary malignancies in patients treated with niraparib] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.14. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/MEA 059.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 045.1 [protocol for study 20170701: an observational study to assess the effectiveness of the Neulasta (pegfilgrastim) patient alert card (PAC) and to measure medication errors related to the use of the on-body injector (OBI) to assess respondent awareness of key safety messages and behavioural intent to carry out recommended actions as described in the PAC and to estimate the proportion of OBI administrations associated with medication error [final study report expected in March 2022]] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.15. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 045.1 [protocol for study RRA-20745: a PASS to investigate the long-term safety in adult patients with moderately to severely active Crohn's disease] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²³

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)²⁴

7.4.1. Atazanavir, atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/II/0117

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Adrien Inoubli

²³ In accordance with Article 107p-q of Directive 2001/83/EC

²⁴ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

Scope: Submission of the final reports for studies AI424397 (PRINCE I) and AI424451 (PRINCE II) listed as a category 3 studies in the RMP. These studies were phase 3b, prospective, single arm, open-label, international, multicentre studies to evaluate the safety, efficacy and pharmacokinetics of atazanavir powder boosted with ritonavir and administered with an optimised nucleoside reverse transcriptase inhibitor (NRTI) background therapy, in human immunodeficiency virus (HIV) infected paediatric patients. The RMP is updated accordingly (version 15.0). In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

7.4.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0039

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Submission of the final study report for non-interventional study RRA-21430: a retrospective cohort study exploring acute pancreatitis in patients with type 2 diabetes mellitus (T2DM) who are new users of canagliflozin as compared with new users of other antihyperglycemic agents (AHAs) using large claim databases in the US

Action: For adoption of PRAC Assessment Report

7.4.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0040

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report for non-interventional study RRA-21430: a retrospective cohort study exploring acute pancreatitis in patients with type 2 diabetes mellitus (T2DM) who are new users of canagliflozin as compared with new users of other antihyperglycemic agents (AHAs) using large claim databases in the US

Action: For adoption of PRAC Assessment Report

7.4.4. Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/II/0042/G

Applicant: Oxurion NV

PRAC Rapporteur: Julie Williams

Scope: Grouped variations consisting of: 1) submission of the final report from study (TG-MV-018) 'ocriplasmin research to better inform treatment (ORBIT)': a multicentre, prospective, observational study which assesses clinical outcomes and safety of Jetrea (ocriplasmin) administered in a real-world setting for the treatment of symptomatic vitreomacular adhesion (VMA); 2) submission of the final report from a prospective drug utilisation study TG-MV-017 (listed as a category 3 study in the RMP): a European, multicentre, observational study exploring the utilisation patterns of intravitreal Jetrea (ocriplasmin) in real-life clinical practice. The study includes two parts, a drug utilisation study (DUS) and the patient educational material evaluation survey (PEMES); 3) submission of the final report from study INJECT (investigation of Jetrea (ocriplasmin) in patients with confirmed vitreomacular traction): a non-interventional, multicentre, worldwide study in patients treated with Jetrea (ocriplasmin) in order to evaluate safety, clinical effectiveness, and health-related quality of

life (HRQoL) outcomes in a real world setting among a large population of patients exposed to ocriplasmin across different countries according to country's approved indications. The RMP (version 7.2) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

7.4.5. [Orlistat - ALLI \(CAP\) - EMEA/H/C/000854/II/0058](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for non-interventional PASS study 204675 (listed as a category 3 study in the RMP): 'evaluating the effectiveness of the revised alli (orlistat) pack information in helping pharmacy staff within the EU supply alli appropriately'. In addition, the RMP is updated (version 17) in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

7.4.6. [Sofosbuvir, velpatasvir - EPCLUSA \(CAP\) - EMEA/H/C/004210/WS1476/0028;](#) [Ledipasvir, sofosbuvir - HARVONI \(CAP\) - EMEA/H/C/003850/WS1476/0070;](#) [Sofosbuvir - SOVALDI \(CAP\) - EMEA/H/C/002798/WS1476/0052;](#) [Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI \(CAP\) - EMEA/H/C/004350/WS1476/0016](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study GS-US-334-0154 (listed as a category 3 study in the RMP): a phase 2b randomized, open-label study of 200 mg or 400 mg sofosbuvir + ribavirin for 24 weeks in genotype 1 or 3 hepatitis C virus (HCV)-infected subjects with renal insufficiency. The RMPs are updated accordingly (Eplusa version 3.2, Harvoni version 4.1, Sovaldi version 7.1 and Vosevi version 1.1)

Action: For adoption of PRAC Assessment Report

7.5. **Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation**

7.5.1. [Adalimumab - HUMIRA \(CAP\) - EMEA/H/C/000481/MEA 075.7](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Sixth annual interim study report for Humira ulcerative colitis registry P11-282: a long-term non-interventional post-marketing study to assess safety and effectiveness of Humira (adalimumab) in patients with moderately to severely active ulcerative colitis (UC)

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 080.6

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth annual interim report for P11-292 registry: a long-term non-interventional registry to assess safety and effectiveness of Humira (adalimumab) in paediatric patients with moderately to severely active Crohn's disease (CD) – CAPE

Action: For adoption of advice to CHMP

7.5.3. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 002.4

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 002.3 [third progress report and first interim report for study H9X-MC-B009: dulaglutide European modified prescription-event monitoring and network database study: a multi-database collaborative research programme of observational studies to monitor the utilisation and safety of dulaglutide in the EU] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.5.4. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.9

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.9 [third interim study report for a US (listed as a category 3 study in the RMP) non-interventional PASS (B2311060 study): an active surveillance of conjugated oestrogens (CE)/bazedoxifene acetate (BZA) using US healthcare data] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.5.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 003.5

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.4 [first interim report for a drug utilisation study (DUS) on conjugated oestrogens/ bazedoxifene (CE/BZA) in the European Union (EU) to describe baseline characteristics and utilisation patterns of EU patients initiating Duavive (CE/BZA) or oestrogen + progestin (E+P) combination hormone replacement therapy (HRT)]

Action: For adoption of advice to CHMP

7.5.6. Follitropin alfa - OVALEAP (CAP) - EMEA/H/C/002608/MEA 002.3

Applicant: Teva B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study XM17-WH-50005 (SOFIA): a non-interventional multinational prospective observational study to assess the safety of Ovaleap (follitropin alfa) compared to Gonal-F (follitropin alfa) in one treatment cycle with respect to the incidence rates of ovarian hyperstimulation syndrome (OHSS) in infertile women undergoing superovulation for assisted reproductive technologies (ART)

Action: For adoption of advice to CHMP

7.5.7. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.4

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Second annual interim report for study CA209234 (listed as a category 3 study in the RMP): a PASS exploring the pattern of use, safety, and effectiveness of nivolumab in routine oncology practice [final clinical study report (CSR) due date: 31 December 2024] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.5.8. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.4

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 004.3 [first interim report for study CLCZ696B2015 (PASS 3) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) [final report expected in Q2/2020]] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.5.9. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 003.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 003 [First interim report for study CLCZ696B2015 (PASS 3) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) [final report expected in Q2/2020]] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.5.10. Somatropin - OMNITROPE (CAP) - EMEA/H/C/000607/MEA 012.2

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Second interim report for study EP00-501 (PATRO Children): a non-interventional post-marketing surveillance study to collect long-term safety and efficacy of Omnitrope (somatropin) in infants, children and adolescents with growth hormone deficiency and treated within routine clinical practice in Europe

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 014

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Protocol for a meta-analysis of amputation events from clinical trials DIA3008 (CANVAS: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of JNJ-28431754 (canagliflozin) on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM)), DIA4003 (CANVAS-R: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM), and DNE3001 (CREDENCE: a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy), as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 013

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for a meta-analysis of amputation events from clinical trials DIA3008 (CANVAS: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of JNJ-28431754 (canagliflozin) on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM)), DIA4003 (CANVAS-R: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM), and DNE3001 (CREDENCE: a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy), as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.6.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/MEA 001.5

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 001.3 and MEA 001.4 [interim results and proposal for termination of study P15-421: a prospective, observational cohort study utilising the hepatitis C therapeutic registry and research network (HCV-TARGET) data to evaluate the clinical impact and real world frequency of grade 3+ alanine transaminase (ALT) elevations in patients being treated for hepatitis C with paritaprevir with ritonavir (paritaprevir/ritonavir), ombitasvir and dasabuvir (2 direct-acting antiviral (DAA) regimen) or paritaprevir/ritonavir and ombitasvir (3-DAA regimen) with or without ribavirin for hepatitis C infection (HCV) (SHORT – evaluation of the potential for and clinical impact of increased ALT in patients using the AbbVie 2-DAA or 3-DAA regimens in a real world setting] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.6.4. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 005.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 005 [PASS protocol for study WA40404 (listed as category 3 study in the RMP): a phase 3b multicentre, randomised, double-blind, placebo controlled study to evaluate the efficacy and safety of ocrelizumab in adults with primary progressive multiple sclerosis later in their disease course] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.6.5. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/MEA 001.5

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 001.3 and MEA 001.4 [interim results and proposal for termination of study P15-421: a prospective, observational cohort study utilising the hepatitis C therapeutic registry and research network (HCV-TARGET) data to evaluate the clinical impact and real world frequency of grade 3+ alanine transaminase (ALT) elevations in patients being treated for hepatitis C with paritaprevir with ritonavir (paritaprevir/ritonavir), ombitasvir and dasabuvir (2 direct-acting antiviral (DAA) regimen) or paritaprevir/ritonavir and ombitasvir (3-DAA regimen) with or without ribavirin for hepatitis C infection (HCV) (SHORT – evaluation of the potential for and clinical impact of increased ALT in patients using the AbbVie 2-DAA or 3-DAA regimens in a real world setting] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

7.9. Final Scientific Advice (Reports and Scientific Advice letters)

None

8. Renewals of the marketing authorisation, conditional renewal and annual reassessments

8.1. Annual reassessments of the marketing authorisation

8.1.1. Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/S/0035 (without RMP)

Applicant: Laboratoire Francais du Fractionnement et des Biotechnologies

PRAC Rapporteur: Adrien Inoubli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/S/0032 (without RMP)

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/R/0035 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0033 (without RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Brinzolamide, brimonidine - SIMBRINZA (CAP) - EMEA/H/C/003698/R/0014 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/R/0040 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Mifamurtide - MEPACT (CAP) - EMEA/H/C/000802/R/0047 (without RMP)

Applicant: Takeda France SAS

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Oseltamivir - EBILFUMIN (CAP) - EMEA/H/C/003717/R/0012 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Sevelamer carbonate - RENVELA (CAP) - EMEA/H/C/000993/R/0046 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/R/0029 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Trametinib - MEKINIST (CAP) - EMEA/H/C/002643/R/0029 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

Scope: Pharmacovigilance inspection programme 2018-2021 (second revision for 2018)

Action: For adoption

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore such information is not reported in the agenda.

9.3. Others

None

10. Other safety issues for discussion requested by the CHMP or the EMA

10.1. Safety related variations of the marketing authorisation

10.1.1. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0051

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: PRAC consultation in a variation to update section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301) to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities. This is a multicentre, randomized, active-control, phase 3B study. In addition, the MAH took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format

Action: For adoption of advice to CHMP

10.2. Timing and message content in relation to Member States' safety announcements

None

10.3. Other requests

None

10.4. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

11. Other safety issues for discussion requested by the Member States

11.1. Safety related variations of the marketing authorisation

11.1.1. Esomeprazole, naproxen (NAP) - NL/H/1848/001/II/026

Applicant: AstraZeneca B.V. (Vimovo)

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC consultation on a variation procedure proposing to change the current warning related to naproxen on the cardiovascular and cerebrovascular risk profile

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Atorvastatin (NAP) - DE/H/PSUFU/00010347/201710/A

Applicant: Pfizer

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing PSUR follow-up (PSU FU) procedure on the safety concern of 'systemic lupus erythematosus/lupus erythematosus/lupus-like syndrome' and causal association of atorvastatin as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on atorvastatin (PSUSA/00010347/201710) concluded in June 2018

Action: For adoption of advice to Member States

11.2.2. Cabergoline (NAP)

Applicant: Pfizer Limited

PRAC Lead: Amelia Cupelli

Scope: PRAC consultation on the evaluation of the final report for the 'study on the utilisation of cabergoline for compliance with risk minimisation activities (SUCRE)' requested as an outcome of the referral procedure under Article 31 of Directive 2001/83/EC on ergot-derived

dopamine agonists concluded in 2008 (EMA/H/A-31/881)

Action: For adoption of advice to Member States

11.2.3. Paroxetine (NAP) - NL/H/PSUFU/00002319/201712

Applicant: GlaxoSmithKline (Seroxat)

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC consultation on a worksharing PSUR follow-up (PSU FU) procedure on a detailed review of cases of drug reaction with eosinophilia and systemic symptoms (DRESS) as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on paroxetine (PSUSA/00002319/201712) concluded in July 2018

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Brexit – EMA knowledge sharing package to support UK portfolio transfer

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM), Vienna, Austria, 25-26 September 2018 - report

PRAC lead: Jan Neuhauser

Action: For discussion

12.5. Cooperation with International Regulators

None

12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2019 – preparation

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

12.10. Periodic safety update reports (PSURs) & Union reference date (EURD) list

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

12.10.4. Union reference date list – consultation on the draft list

Action: For adoption

12.10.5. Good Pharmacovigilance Practice (GVP) module V on 'Risk management systems' and module VII on 'Periodic safety update report' – clarifications on safety specification

See under 12.14.2.

12.11. Signal management

12.11.1. Signal management – feedback from Signal Management Review Technical (SMART) Working Group

PRAC lead: Menno van der Elst

Action: For discussion

12.11.2. Signal Management Review Technical (SMART) methods activities - update

Action: For discussion

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

12.12.3. List of products under additional monitoring – consultation on the draft list

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

12.14.2. Good Pharmacovigilance Practice (GVP) module V on 'Risk management systems' and module VII on 'Periodic safety update report' – clarifications on safety specification

PRAC lead: Menno van der Elst

Action: For discussion

12.14.3. Tools, educational materials and effectiveness measurement of risk minimisations

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

12.15.2. Post-authorisation Safety Studies – non-imposed PASS

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. EMA relocation to Amsterdam, the Netherlands – meeting premises

Action: For discussion

12.20.2. EMA relocation to Amsterdam, the Netherlands – adjustment to March 2019 meeting start time

Action: For discussion

12.20.3. Patient registry initiative and cross-committee task force on registries – update

Action: For discussion

13. Any other business

14. Explanatory notes

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

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures

(Items 2 and 3 of the PRAC agenda)

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 European Union (EU). For further detailed information on safety related referrals please see:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.

The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.

The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.

RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.

PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

A PASS is a study of an authorised medicinal product carried out to obtain further information on its safety, or to measure the effectiveness of risk management measures. The results of a PASS help regulatory agencies to evaluate the safety and benefit-risk profile of a medicine.

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

Inspections carried out by regulatory agencies to ensure that marketing authorisation holders comply with their pharmacovigilance obligations.

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