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Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 July 2019

Chair: Sabine Straus – Vice-Chair: Martin Huber

08 July 2019, 13:00 – 19:30, room 1/C

09 July 2019, 08:30 – 19:30, room 1/C

10 July 2019, 08:30 – 19:30, room 1/C

11 July 2019, 08:30 – 16:00, room 1/C

Organisational, regulatory and methodological matters (ORGAM)

25 July 2019, 09:00-12:00, room 6/D, 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).

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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 08-11 July 2019 12

1.3. Minutes of the previous meeting on 11-14 June 2019 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

2.4. Planned public hearings 12

3. EU referral procedures for safety reasons: other EU referral procedures 13

3.1. Newly triggered procedures 13

3.1.1. Cyproterone acetate (NAP) - EMEA/H/A-31/1488 13

3.2. Ongoing procedures 13

3.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/A-20/1483 13

3.2.2. Estradiol (NAP) - EMEA/H/A-31/1482 13

3.2.3. Fluorouracil and related substances: capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); CAPECITABINE TEVA (CAP); ECANSYA (CAP); XELODA (CAP); NAP flucytosine (NAP); 5-fluorouracil (5-FU) (NAP); tegafur (NAP); tegafur, gimeracil, oteracil – TEYSUNO (CAP) - EMEA/H/A-31/1481 13

3.3. Procedures for finalisation 14

3.3.1. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP); NAP - EMEA/H/A-31/1463 14

3.4. Re-examination procedures 14

3.5. Others 14

4. Signals assessment and prioritisation 14

4.1. New signals detected from EU spontaneous reporting systems 14

4.2. New signals detected from other sources 14

4.2.1. Imiquimod – ALDARA (CAP); ZYCLARA (CAP); NAP 14

4.3. Signals follow-up and prioritisation 15

4.3.1. Amino acid, lipid combinations with vitamins or trace elements (NAP) 15

4.3.2. Mesalazine (NAP) 15

4.3.3. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/SDA/068 15

4.3.4. Ondansetron (NAP) 15

4.3.5. Vascular endothelial growth factor (VEGF) inhibitors: aflibercept – ZALTRAP (CAP) – EMEA/H/C/002532/SDA/009; axitinib – INLYTA (CAP) – EMEA/H/C/002406/SDA/014; bevacizumab – AVASTIN (CAP) – EMEA/H/C/000582/SDA/087, MVASI (CAP) – EMEA/H/C/004728/SDA/002, ZIRABEV (CAP) – EMEA/H/C/004697/SDA/002; cabozantinib –

CABOMETYX (CAP) – EMEA/H/C/004163/SDA/004, COMETRIQ (CAP) – EMEA/H/C/002640/SDA/020; lenvatinib - KISPLYX (CAP) – EMEA/H/C/004224/SDA/015, LENVIMA (CAP) – EMEA/H/C/003727/SDA/017; nintedanib – OFEV (CAP) – EMEA/H/C/003727/SDA/005, VARGATEF (CAP) – EMEA/H/C/002569/SDA/007; pazopanib – VOTRIENT (CAP) – EMEA/H/C/001141/SDA/038; ponatinib – ICLUSIG (CAP) – EMEA/H/C/002695/SDA/017; ramucirumab – CYRAMZA (CAP) – EMEA/H/C/002829/SDA/007; regorafenib – STIVARGA (CAP) – EMEA/H/C/002573/SDA/012; sorafenib – NEXAVAR (CAP) – EMEA/H/C/000690/SDA/040, NAP; sunitinib – SUTENT (CAP) – EMEA/H/C/000687/SDA/054; NAP; tivozanib – FOTIVDA (CAP) – EMEA/H/C/004131/SDA/004; vandetanib – CAPRELSA (CAP) – EMEA/H/C/002315/SDA/021 16

5. Risk management plans (RMPs) 16

5.1. Medicines in the pre-authorisation phase 16

5.1.1. Arsenic trioxide - EMEA/H/C/005175 16

5.1.2. Clofarabine - EMEA/H/C/005039 16

5.1.3. Esketamine - EMEA/H/C/004535 17

5.1.4. Lidocaine, prilocaine - EMEA/H/C/005298 17

5.1.5. Osilodrostat - EMEA/H/C/004821, Orphan 17

5.1.6. Plazomicin - EMEA/H/C/004457 17

5.1.7. Solriamfetol - EMEA/H/C/004893 17

5.2. Medicines in the post-authorisation phase – PRAC-led procedures 17

5.2.1. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/II/0016 17

5.2.2. Exenatide - BYETTA (CAP) - EMEA/H/C/000698/II/0069 18

5.2.3. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/WS1608/0049; Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/WS1608/0050 18

5.2.4. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0039 18

5.2.5. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0114 18

5.2.6. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0068 19

5.2.7. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/II/0057 19

5.2.8. Pregabalin - PREGABALIN MYLAN (CAP) - EMEA/H/C/004078/WS1603/0013; PREGABALIN MYLAN PHARMA (CAP) - EMEA/H/C/003962/WS1603/0011 19

5.2.9. Ribavirin - REBETOL (CAP) - EMEA/H/C/000246/II/0086 19

5.2.10. Saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/II/0046 20

5.2.11. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0034 20

5.3. Medicines in the post-authorisation phase – CHMP-led procedures 20

5.3.1. Afatinib - GIOTRIF (CAP) - EMEA/H/C/002280/II/0031 20

5.3.2. Buprenorphine, naloxone - SUBOXONE (CAP) - EMEA/H/C/000697/X/0042 21

5.3.3. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/II/0010 21

5.3.4. Ceftazidime, avibactam - ZAVICEFTA (CAP) - EMEA/H/C/004027/II/0015 21

5.3.5. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0029, Orphan 22

5.3.6. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0030, Orphan 22

5.3.7. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/II/0150 22

5.3.8. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/II/0128 23

5.3.9. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0058 23
5.3.10. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0040 23
5.3.11. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0105, Orphan 24
5.3.12. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS1601/0022; Linagliptin, metformin - JENTADUETO (CAP) - EMEA/H/C/002279/WS1601/0051; Linagliptin - TRAJENTA (CAP) - EMEA/H/C/002110/WS1601/0038 24
5.3.13. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/II/0053 24
5.3.14. Fluciclovine (^{18}F) - AXUMIN (CAP) - EMEA/H/C/004197/II/0011 25
5.3.15. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/X/0062 25
5.3.16. Insulin human - ACTRAPHANE (CAP) - EMEA/H/C/000427/WS1582/0076; ACTRAPID (CAP) - EMEA/H/C/000424/WS1582/0070; INSULATARD (CAP) - EMEA/H/C/000441/WS1582/0073; MIXTARD (CAP) - EMEA/H/C/000428/WS1582/0077; PROTAPHANE (CAP) - EMEA/H/C/000442/WS1582/0072 25
5.3.17. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/II/0130 26
5.3.18. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/X/0075/G, Orphan 26
5.3.19. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0014/G, Orphan 26
5.3.20. Lapatinib - TYVERB (CAP) - EMEA/H/C/000795/II/0062 27
5.3.21. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0013 27
5.3.22. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0029/G 27
5.3.23. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/II/0046/G 28
5.3.24. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0034, Orphan 28
5.3.25. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/II/0093 28
5.3.26. Pegfilgrastim - PELGRAZ (CAP) - EMEA/H/C/003961/II/0005 29
5.3.27. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0017, Orphan 29
5.3.28. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0074/G 30
5.3.29. Telotristat ethyl - XERMELO (CAP) - EMEA/H/C/003937/II/0015, Orphan 30
5.3.30. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/II/0020 30
5.3.31. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/X/0040 30

6. Periodic safety update reports (PSURs) 31

6.1. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only 31

6.1.1. Adalimumab - AMGEVITA (CAP); HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HYRIMOZ (CAP); IMRALDI (CAP) - PSUSA/00010589/201812 31
6.1.2. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201812 31
6.1.3. Alectinib - ALECENSA (CAP) - PSUSA/00010581/201901 31
6.1.4. Allopurinol, lesinurad - DUZALLO (CAP) - PSUSA/00010704/201812 31
6.1.5. Amifampridine - FIRDAPSE (CAP) - PSUSA/00000141/201812 32
6.1.6. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201901 32
6.1.7. Asparaginase - SPECTRILA (CAP) - PSUSA/00010445/201901 32

6.1.8. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/201901 32
6.1.9. Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/201812 32
6.1.10. Birch bark extract - EPISALVAN (CAP) - PSUSA/00010446/201901 32
6.1.11. Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/201901 33
6.1.12. Budesonide - JORVEZA (CAP) - PSUSA/00010664/201901 33
6.1.13. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/201901 33
6.1.14. Cholic acid - ORPHACOL (CAP) - PSUSA/00010208/201809 33
6.1.15. Cladribine - MAVENCLAD (CAP) - PSUSA/00010634/201901 33
6.1.16. Clofarabine - EVOLTRA (CAP) - PSUSA/00000805/201812 34
6.1.17. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - PSUSA/00010028/201812 34
6.1.18. Dasabuvir - EXVIERA (CAP) - PSUSA/00010363/201901 34
6.1.19. Dimethyl fumarate - SKILARENCE (CAP) - PSUSA/00010647/201812 34
6.1.20. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/201812 34
6.1.21. Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/201812 35
6.1.22. Ertugliflozin, metformin - SEGLUROMET (CAP) - PSUSA/00010680/201812 35
6.1.23. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010681/201812 35
6.1.24. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/201901 35
6.1.25. Human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/201812 35
6.1.26. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201901 35
6.1.27. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/201901 36
6.1.28. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/201812 36
6.1.29. Lamivudine - EPIVIR (CAP); lamivudine, zidovudine - COMBIVIR (CAP) - PSUSA/00009207/201811 36
6.1.30. Lesinurad - ZURAMPIC (CAP) - PSUSA/00010470/201812 36
6.1.31. Liraglutide - SAXENDA (CAP); VICTOZA (CAP) - PSUSA/00001892/201812 36
6.1.32. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/201901 37
6.1.33. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/201812 37
6.1.34. Neratinib - NERLYNX (CAP) - PSUSA/00010712/201901 37
6.1.35. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/201901 37
6.1.36. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/201812 37
6.1.37. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - PSUSA/00010367/201901 37
6.1.38. Peramivir - ALPIVAB (CAP) - PSUSA/00010687/201812 38
6.1.39. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/201812 38
6.1.40. Sarilumab - KEVZARA (CAP) - PSUSA/00010609/201901 38
6.1.41. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/201901 38
6.1.42. Secukinumab - COSENTYX (CAP) - PSUSA/00010341/201812 38
6.1.43. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201812 38

6.1.44. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/201812 39
6.1.45. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/201901 39
6.1.46. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201812 39
6.1.47. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/201901 (with RMP) 39
6.1.48. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/201901 39
6.1.49. Thyrotropin alfa - THYROGEN (CAP) - PSUSA/00002940/201811 40
6.1.50. Umeclidinium bromide - INCRUSE ELLIPTA (CAP); ROLUFTA ELLIPTA (CAP) - PSUSA/00010263/201812 40
6.1.51. Umeclidinium bromide, vilanterol - ANORO ELLIPTA (CAP); LAVENTAIR ELLIPTA (CAP) - PSUSA/00010264/201812 40
6.1.52. Ustekinumab - STELARA (CAP) - PSUSA/00003085/201812 40
6.1.53. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/201812 40
6.1.54. Ziconotide - PRIALT (CAP) - PSUSA/00003142/201812 40
6.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs) 41
6.2.1. Bimatoprost, timolol - GANFORT (CAP); NAP - PSUSA/00002961/201811 41
6.2.2. Caspofungin - CANCIDAS (CAP); CASPOFUNGIN ACCORD (CAP); NAP - PSUSA/00000576/201812 41
6.2.3. Doxorubicin - CAELYX (CAP); MYOCET (CAP), NAP - PSUSA/00001172/201811 41
6.2.4. Edotreotide - SOMAKIT TOC (CAP); NAP - PSUSA/00010552/201812 41
6.2.5. Levetiracetam - KEPPRA (CAP); NAP - PSUSA/00001846/201811 41
6.2.6. Lutetium (^{177}Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/201812 42
6.2.7. Nitric oxide - INOMAX (CAP); NAP - PSUSA/00002172/201812 42
6.2.8. Paclitaxel – APEALEA (CAP); NAP - PSUSA/00002264/201812 42
6.2.9. Raloxifene - EVISTA (CAP); OPTRUMA (CAP); RALOXIFENE TEVA (CAP), NAP - PSUSA/00002603/201812 42
6.2.10. Sufentanil - DZUVEO (CAP); ZALVISO (CAP); NAP - PSUSA/00002798/201811 42
6.3. PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only 43
6.3.1. Acetylsalicylic acid, bisoprolol (NAP) - PSUSA/00010287/201811 43
6.3.2. Amino acid combinations, glucose, triglyceride combinations, with or without electrolytes, mineral compounds (NAP) - PSUSA/00010190/201812 43
6.3.3. Anti-T lymphocyte immunoglobulin (horse) (NAP) - PSUSA/00010433/201811 43
6.3.4. Atomoxetine (NAP) - PSUSA/00000262/201811 43
6.3.5. Azathioprine (NAP) - PSUSA/00000275/201812 43
6.3.6. Cefotaxime (NAP) - PSUSA/00000599/201812 44
6.3.7. Clevidipine (NAP) - PSUSA/00010288/201811 44
6.3.8. Danaparoid (NAP) - PSUSA/00000923/201812 44
6.3.9. Hydromorphone (NAP) - PSUSA/00001686/201811 44
6.3.10. Hydroxycarbamide (NAP) - PSUSA/00009182/201812 44

6.3.11. Iron (NAP) - PSUSA/00010236/201901 45
6.3.12. Iron dextran (NAP) - PSUSA/00010696/201901 45
6.3.13. Ketamine (NAP) - PSUSA/00001804/201812 45
6.3.14. Levonorgestrel, ethinylestradiol; ethinylestradiol (NAP) - PSUSA/00010442/201901 45
6.3.15. Metoclopramide (NAP) - PSUSA/00002036/201811 45
6.3.16. Naltrexone (NAP) - PSUSA/00002117/201811 45
6.3.17. Sertindole (NAP) - PSUSA/00002695/201901 46
6.3.18. Tapentadol (NAP) - PSUSA/00002849/201811 46
6.3.19. Terazosin (NAP) - PSUSA/00002895/201811 46
6.3.20. Valaciclovir (NAP) - PSUSA/00003086/201812 46
6.3.21. Yellow fever vaccine (live) (NAP) - PSUSA/00003135/201812 46
6.4. Follow-up to PSUR/PSUSA procedures 47
6.4.1. Capecitabine - XELODA (CAP) - EMEA/H/C/000316/LEG 034 47
6.4.2. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/LEG 005 47
6.4.3. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/LEG 013 47
6.4.4. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 069 47

7. Post-authorisation safety studies (PASS) 48

7.1. Protocols of PASS imposed in the marketing authorisation(s) 48
7.1.1. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/PSP/S/0070.1 48
7.1.2. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/PSA/S/0039 48
7.1.3. Radium (Ra^{223}) dichloride - XOFIGO (CAP) - EMEA/H/C/PSP/S/0076.1 48
7.1.4. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/PSP/S/0077.1 49
7.1.5. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/PSA/S/0040 49
7.1.6. Umeclidinium bromide – INCRUSE ELLIPTA (CAP), ROLUFTA ELLIPTA (CAP); umeclidinium bromide, vilanterol – ANORO ELLIPTA (CAP), LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/PSA/S/0032.2 49
7.1.7. Valproate (NAP) - EMEA/H/N/PSP/J/0072.1 49
7.1.8. Valproate (NAP) - EMEA/H/N/PSP/J/0073.1 50
7.1.9. Valproate (NAP) - EMEA/H/N/PSP/J/0075.1 50
7.1.10. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/PSP/S/0078.1 50
7.2. Protocols of PASS non-imposed in the marketing authorisation(s) 51
7.2.1. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.2 51
7.2.2. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/MEA 002 51
7.2.3. Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/MEA 001.1 51
7.2.4. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/MEA 001 51
7.2.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.12 .. 52
7.2.6. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.1 52
7.2.7. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/MEA 001 52
7.2.8. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 002 52

7.2.9. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 003 53
7.2.10. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 004 53
7.2.11. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 002.1 53
7.2.12. Ropeginterferon alfa-2b - BESREMI (CAP) - EMEA/H/C/004128/MEA 001 53
7.2.13. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.3 54
7.2.14. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.2 54
7.2.15. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.2 54
7.2.16. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.2 55
7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.2 55
7.3. Results of PASS imposed in the marketing authorisation(s) 55
7.4. Results of PASS non-imposed in the marketing authorisation(s) 55
7.4.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0124/G 55
7.4.2. Bosentan - STAYVEER (CAP) - EMEA/H/C/002644/II/0027 56
7.4.3. Bosentan - TRACLEER (CAP) - EMEA/H/C/000401/II/0091 56
7.4.4. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0059 56
7.4.5. Pegvisomant - SOMAVERT (CAP) - EMEA/H/C/000409/II/0089 57
7.4.6. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/WS1557/0120; PROMETAX (CAP) - EMEA/H/C/000255/WS1557/0121 57
7.5. Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation 57
7.5.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017.4 57
7.5.2. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 005.5 58
7.5.3. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.5 58
7.5.4. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.4 58
7.5.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 003.6 58
7.5.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 002.1 59
7.5.7. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 005.1 59
7.5.8. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 006.1 59
7.5.9. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.3 59
7.5.10. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 023.11 60
7.5.11. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.12 60
7.6. Others 60
7.6.1. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.1 60
7.6.2. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 006 60
7.7. New Scientific Advice 61
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. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/S/0010 (without RMP) 61

8.1.2. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0080 (without RMP) 61

8.2. Conditional renewals of the marketing authorisation 62

8.2.1. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0067 (without RMP) 62

8.2.2. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/R/0017 (without RMP) 62

8.3. Renewals of the marketing authorisation 62

8.3.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/R/0026 (without RMP) 62

8.3.2. Dalbavancin - XYDALBA (CAP) - EMEA/H/C/002840/R/0028 (without RMP) 62

8.3.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/R/0045 (without RMP) 62

8.3.4. Dronedarone - MULTAQ (CAP) - EMEA/H/C/001043/R/0042 (with RMP) 63

8.3.5. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/R/0022 (without RMP) 63

8.3.6. Lapatinib - TYVERB (CAP) - EMEA/H/C/000795/R/0060 (without RMP) 63

8.3.7. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/R/0028 (without RMP) 63

8.3.8. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/R/0025 (without RMP) 63

8.3.9. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/R/0029 (without RMP) 63

8.3.10. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/R/0054 (without RMP) 64

8.3.11. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/R/0028 (without RMP) 64

8.3.12. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/R/0094 (without RMP) 64

8.3.13. Ramucirumab - CYRAMZA (CAP) - EMEA/H/C/002829/R/0031 (without RMP) 64

8.3.14. Rasagiline - RASAGILINE RATIOPHARM (CAP) - EMEA/H/C/003957/R/0014 (without RMP) 64

8.3.15. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/R/0032 (without RMP) 64

8.3.16. Sevelamer carbonate - SEVELAMER CARBONATE WINTHROP (CAP) - EMEA/H/C/003971/R/0022 (without RMP) 65

8.3.17. Tilmanocept - LYMPHOSEEK (CAP) - EMEA/H/C/002085/R/0016 (with RMP) 65

9. Product related pharmacovigilance inspections 65

9.1. List of planned pharmacovigilance inspections 65

9.2. Ongoing or concluded pharmacovigilance inspections 65

9.3. Others 65

10. Other safety issues for discussion requested by the CHMP or the EMA 65

10.1. Safety related variations of the marketing authorisation 65

10.2. Timing and message content in relation to Member States' safety announcements 66

10.3. Other requests 66

10.4. Scientific Advice 66

11. Other safety issues for discussion requested by the Member States 66

11.1. Safety related variations of the marketing authorisation 66

11.2. Other requests 66

12. Organisational, regulatory and methodological matters 66

12.1. Mandate and organisation of the PRAC 66

12.2. Coordination with EMA Scientific Committees or CMDh-v 66

12.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups 66

12.3.1. Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products on requirements for previously untreated patients (PUPs) - PRAC and PDCO flow for paediatric investigation plans (PIPs) of authorised medicinal products with studies on PUPs 66

12.4. Cooperation within the EU regulatory network 67

12.5. Cooperation with International Regulators 67

12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee 67

12.6.1. International Conference on Harmonisation (ICH) E2B(R3) on electronic transmission of individual case safety reports - data elements and message specification - stakeholder readiness for mandatory use 67

12.7. PRAC work plan 67

12.8. Planning and reporting 67

12.8.1. Marketing authorisation applications (MAA) forecast for 2019 – planning update dated Q2 2019 67

12.9. Pharmacovigilance audits and inspections 67

12.9.1. Pharmacovigilance systems and their quality systems 67

12.9.2. Pharmacovigilance inspections 67

12.9.3. Pharmacovigilance audits 67

12.10. Periodic safety update reports (PSURs) & Union reference date (EURD) list 68

12.10.1. Periodic safety update reports 68

12.10.2. Granularity and Periodicity Advisory Group (GPAG) 68

12.10.3. PSURs repository 68

12.10.4. Union reference date list – consultation on the draft list 68

12.11. Signal management 68

12.11.1. Signal management – feedback from Signal Management Review Technical (SMART) Working Group 68

12.11.2. Signal management - monitoring EudraVigilance data by MAHs – experience from the pilot period 68

12.12. Adverse drug reactions reporting and additional monitoring 68

12.12.1. Management and reporting of adverse reactions to medicinal products 68

12.12.2. Additional monitoring 68

12.12.3. List of products under additional monitoring – consultation on the draft list 69

12.13. EudraVigilance database 69

12.13.1. Activities related to the confirmation of full functionality 69

12.13.2. EudraVigilance – EMA data management and quality activities 69
12.14. Risk management plans and effectiveness of risk minimisations..... 69
12.14.1. Risk management systems 69
12.14.2. Tools, educational materials and effectiveness measurement of risk minimisations 69
12.15. Post-authorisation safety studies (PASS) 69
12.15.1. Post-authorisation Safety Studies – imposed PASS 69
12.15.2. Post-authorisation Safety Studies – non-imposed PASS 69
12.16. Community procedures 69
12.16.1. Referral procedures for safety reasons 69
12.17. Renewals, conditional renewals, annual reassessments 69
12.18. Risk communication and transparency 70
12.18.1. Public participation in pharmacovigilance 70
12.18.2. Safety communication 70
12.19. Continuous pharmacovigilance 70
12.19.1. Incident management 70
12.20. Others 70
12.20.1. EMA policy on handling of competing interests for scientific committees' members and experts – reminder training 70
12.20.2. EMA reimbursement rules for delegates - update 70
12.20.3. Rapid data analytical process - pilot 70

13. Any other business 70
14. Explanatory notes 71

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 on 08-11 July 2019. See July 2019 PRAC minutes (to be published post September 2019 PRAC meeting).

1.2. Agenda of the meeting on 08-11 July 2019

Action: For adoption

1.3. Minutes of the previous meeting on 11-14 June 2019

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

2.4. Planned public hearings

None

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

3.1. Newly triggered procedures

3.1.1. Cyproterone acetate (NAP) - EMEA/H/A-31/1488

Applicant(s): various

PRAC Rapporteur: To be appointed; PRAC Co-rapporteur: To be appointed

Scope: Review of the benefit-risk balance following notification by France of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of questions (LoQ)

3.2. Ongoing procedures

3.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/A-20/1483

Applicant: Sanofi Belgium

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Ulla Wändel Liminga

Scope: Review of the benefit-risk balance following notification by European Commission of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data

Action: For adoption of a list of outstanding issues (LoOI)

3.2.2. Estradiol[1] (NAP) - EMEA/H/A-31/1482

Applicant(s): various

PRAC Rapporteur: Eva Jirsova; PRAC Co-rapporteur: Menno van der Elst

Scope: Review of the benefit-risk balance following notification by European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of outstanding issues (LoOI)

3.2.3. Fluorouracil and related substances: capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); CAPECITABINE TEVA (CAP); ECANSYA (CAP); XELODA (CAP); NAP flucytosine (NAP); 5-fluorouracil (5-FU) (NAP); tegafur (NAP); tegafur, gimeracil, oteracil – TEYSUNO (CAP) - EMEA/H/A-31/1481

Applicants: Accord Healthcare Limited (Capecitabine Accord), Krka, d.d., Novo mesto (Ecansya), Medac Gesellschaft fur klinische Spezialpraparate mbH (Capecitabine medac), Nordic Group B.V. (Teysuno), Roche Registration GmbH (Xeloda), Teva B.V. (Capecitabine

[1] 0.01%, topical use only

Teva), various

PRAC Rapporteur: Jean-Michel Dogné; PRAC Co-rapporteur: Martin Huber

Scope: Review of the benefit-risk balance following notification by France of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of outstanding issues (LoOI)

3.3. Procedures for finalisation

3.3.1. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP); NAP - EMEA/H/A-31/1463

Applicants: Nordic Group B.V. (Nordimet), Therakind Limited (Jylamvo), various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Željana Margan Koletić

Scope: Review of the benefit-risk balance following notification by Spain of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For a recommendation to CHMP

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

None

4.2. New signals detected from other sources

4.2.1. Imiquimod – ALDARA (CAP); ZYCLARA (CAP); NAP

Applicant(s): Meda AB, various

PRAC Rapporteur: To be appointed

Scope: Signal of pemphigus, new onset and relapse

Action: For adoption of PRAC recommendation

[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[3] 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

EPITT 19441 – New signal

Lead Member State(s): PL

4.3. Signals follow-up and prioritisation

4.3.1. Amino acid, lipid combinations with vitamins or trace elements[4] [5] (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of adverse outcomes in neonates treated with solutions not protected from light

Action: For adoption of PRAC recommendation

EPITT 19423 – Follow-up to May 2019

4.3.2. Mesalazine (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of nephrolithiasis

Action: For adoption of PRAC recommendation

EPITT 19405 – Follow-up to May 2019

4.3.3. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/SDA/068

Applicant(s): Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of psoriasis

Action: For adoption of PRAC recommendation

EPITT 19365 – Follow-up to March 2019

4.3.4. Ondansetron (NAP)

Applicant(s): various

PRAC Rapporteur: Gabriela Jazbec

Scope: Signal of birth defects following in-utero exposure during the first trimester of pregnancy arising from recent publications

Action: For adoption of PRAC recommendation

EPITT 19353 – Follow-up to March 2019

[4] For parenteral nutrition of neonates only
[5] Including amino acid combinations, glucose, triglyceride combinations (e.g. olive oil, soya bean oil, fish oil), with or without electrolytes, mineral compounds (intravenous (I.V) application)

4.3.5. Vascular endothelial growth factor (VEGF) inhibitors[6]: aflibercept – ZALTRAP (CAP) – EMEA/H/C/002532/SDA/009; axitinib – INLYTA (CAP) – EMEA/H/C/002406/SDA/014; bevacizumab – AVASTIN (CAP) – EMEA/H/C/000582/SDA/087, MVASI (CAP) – EMEA/H/C/004728/SDA/002, ZIRABEV (CAP) – EMEA/H/C/004697/SDA/002; cabozantinib – CABOMETYX (CAP) – EMEA/H/C/004163/SDA/004, COMETRIQ (CAP) – EMEA/H/C/002640/SDA/020; lenvatinib - KISPLYX (CAP) – EMEA/H/C/004224/SDA/015, LENVIMA (CAP) – EMEA/H/C/003727/SDA/017; nintedanib – OFEV (CAP) – EMEA/H/C/003727/SDA/005, VARGATEF (CAP) – EMEA/H/C/002569/SDA/007; pazopanib – VOTRIENT (CAP) – EMEA/H/C/001141/SDA/038; ponatinib – ICLUSIG (CAP) – EMEA/H/C/002695/SDA/017; ramucirumab – CYRAMZA (CAP) – EMEA/H/C/002829/SDA/007; regorafenib – STIVARGA (CAP) – EMEA/H/C/002573/SDA/012; sorafenib – NEXAVAR (CAP) – EMEA/H/C/000690/SDA/040, NAP; sunitinib – SUTENT (CAP) – EMEA/H/C/000687/SDA/054; NAP; tivozanib – FOTIVDA (CAP) – EMEA/H/C/004131/SDA/004; vandetanib – CAPRELSA (CAP) – EMEA/H/C/002315/SDA/021

Applicant(s): Amgen Europe B.V. (Mvasi), Bayer AG (Nexavar, Stivarga), Boehringer Ingelheim (Ofev, Vargatef), Eisai Europe Ltd. (Kisplyx, 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 (Votrient), Pfizer Europe MA EEIG (Inlyta, Sutent, Zirabev), PharmaSwiss Ceska Republika (Macugen), Roche Registration GmbH (Avastin), Sanofi-aventis groupe (Zaltrap), various

PRAC Rapporteur: Annika Folin

Scope: Signal of artery dissections and aneurysms

EPITT 19330 – Follow-up to May 2019

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Arsenic trioxide - EMEA/H/C/005175

Scope: Treatment of relapsed acute promyelocytic leukaemia (APL)

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

5.1.2. Clofarabine - EMEA/H/C/005039

Scope: Treatment of acute lymphoblastic leukaemia

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

[6] For systemic use only

5.1.3. Esketamine - EMEA/H/C/004535

Scope: Major depressive disorder in adults who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode (treatment-resistant depression)

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

5.1.4. Lidocaine, prilocaine - EMEA/H/C/005298

Scope: Treatment of primary premature ejaculation

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

5.1.5. Osilodrostat - EMEA/H/C/004821, Orphan

Applicant: Novartis Europharm Limited

Scope: Treatment of Cushing's syndrome

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

5.1.6. Plazomicin - EMEA/H/C/004457

Scope: Treatment of complicated urinary tract infection (cUTI), including treatment of pyelonephritis, treatment of bloodstream infection (BSI) and treatment of infections due to *Enterobacteriaceae*

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

5.1.7. Solriamfetol - EMEA/H/C/004893

Scope: Improvement of wakefulness in patients with narcolepsy or obstructive sleep apnoea

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. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/II/0016

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 4) in order to revise safety concerns in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the outcome of procedure MEA 003.3 adopted at the November 2018 PRAC meeting (held on 29-31 October 2018) is implemented as requested

Action: For adoption of PRAC Assessment Report

5.2.2. Exenatide - BYETTA (CAP) - EMEA/H/C/000698/II/0069

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Submission of a justification for extrapolating exenatide once weekly clinical data (previously assessed for Bydureon) to exenatide twice daily (Byetta) in order to include the latest agreed RMP versions for Bydureon (v30, v31s2 and v32s2) also in the dossier for Byetta. As a consequence, the removal of the important potential risk 'Cardiac Events' is proposed also for Byetta

Action: For adoption of PRAC Assessment Report

5.2.3. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/WS1608/0049; Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/WS1608/0050

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 12.0) in order to align the due dates and deliverables for post-authorisation measure MEA 007 relating to study EP06-501: a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell mobilisation. The due date is extended from December 2019 to March 2020, to combine the annual safety report (ASR) with the 5-year interim clinical study report (CSR) in 2020 and the final CSR in 2024 and for the MEA to cover the entire duration of study EP06-501

Action: For adoption of PRAC Assessment Report

5.2.4. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0039

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 9.0) to replace the current registries with one company-sponsored initiated registry, PERFUSE: one-year persistence to treatment of patients receiving Flixabi (infliximab): a French cohort study; together with three inflammatory bowel disease (IBD) registries, namely: long-term observation registry in German IBD patients (CEDUR), Czech registry of IBD patients on biological therapy (CREDIT) and Dutch network of hospitals IBD registry (DREAM)

Action: For adoption of PRAC Assessment Report

5.2.5. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0114

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an update of the RMP (version 25.0) with information related to extended interval dosing that will be added to the educational materials. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'

of the product information is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.6. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0068

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 23.1) in order to discuss the effectiveness of the educational materials put in place for Keytruda (pembrolizumab) at the time of the initial marketing authorisation, to provide a proposal to update these materials and to revise the safety specification as requested in the outcome of the PSUR single assessment procedure (PSUSA/00010403/201803) finalised in October 2018

Action: For adoption of PRAC Assessment Report

5.2.7. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/II/0057

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 15.1) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' with the consequent applicable re-evaluation of some safety concerns. In addition, the MAH took the opportunity to include data from the completed clinical trial in paediatric subjects PN097: a phase 1B study of the safety, tolerability, and pharmacokinetics of intravenous (IV) and powder for oral suspension formulations of posaconazole (POS) in immunocompromised paediatric subjects, and update the due date for submission changed from December 2019 to Q4 2020 for the final report of the ongoing post-marketing efficacy trial PN069: a phase 3 randomized study on the efficacy and safety of posaconazole versus voriconazole for the treatment of invasive aspergillosis in adults and adolescents

Action: For adoption of PRAC Assessment Report

5.2.8. Pregabalin - PREGABALIN MYLAN (CAP) - EMEA/H/C/004078/WS1603/0013; PREGABALIN MYLAN PHARMA (CAP) - EMEA/H/C/003962/WS1603/0011

Applicant: Mylan S.A.S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 6) to get adjusted to the RMP of the originator medicinal product containing pregabalin. In addition, the RMP is updated in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.9. Ribavirin - REBETOL (CAP) - EMEA/H/C/000246/II/0086

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 5.1) in order to revise safety concerns for ribavirin in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the MAH took the opportunity to revise the safety concerns of ribavirin in light of the current era of interferon (IFN) free regimen, as requested in a previous PSUSA procedure (EMEA/H/C/PSUSA/00010007/201707) concluded in March 2018

Action: For adoption of PRAC Assessment Report

5.2.10. Saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/II/0046

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 15) in order to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template). As a result, the list of safety concerns has been revised and a number of important identified risks, important potential risks and missing information have been reclassified or removed from the RMP

Action: For adoption of PRAC Assessment Report

5.2.11. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0034

Applicant: Amgen Europe B.V., ATMP[7]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 7.0) in order to add 2 category 3 studies, namely: 1) study 20180062: a cross-sectional survey to evaluate patient knowledge of safety messages included in the patient safety brochure and patient alert card and; 2) study 20180099: a cross-sectional survey to evaluate physician knowledge of safety messages included in the physician education booklet; as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimisation measures (aRMM)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Afatinib - GIOTRIF (CAP) - EMEA/H/C/002280/II/0031

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add gastrointestinal (GI) perforation as an additional side effect based on summaries of clinical trial and post-marketing safety data. The package leaflet is updated accordingly. In addition, the RMP (version 8.0) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template), taking also into consideration recommendations part of the conclusions of renewal procedure R/0026 adopted in March 2018. Furthermore, the MAH

[7] Advanced therapy medicinal product

took the opportunity to correct some typographical errors in the German, Austrian and Spanish product information and to update the list of the local representatives for Austria in the package leaflet

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

5.3.2. Buprenorphine, naloxone - SUBOXONE (CAP) - EMEA/H/C/000697/X/0042

Applicant: Indivior Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5 mg, 4/1 mg, 8/2 mg and 16/4 mg) and a new route of administration (either sublingual or buccal administration). The RMP (version 14.0) is updated accordingly

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

5.3.3. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/II/0010

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of in vitro metabolism study report for study R188-A15. The RMP (version 1.6) is updated accordingly

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

5.3.4. Ceftazidime, avibactam - ZAVICEFTA (CAP) - EMEA/H/C/004027/II/0015

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (ceftazidime/avibactam) based on data from three paediatric studies namely, study D4280C00014: a phase 1 study to assess the pharmacokinetics, safety and tolerability of a single dose of ceftazidime-avibactam (CAZ-AVI) in children from 3 months of age to <18 years who are receiving systemic antibiotic therapy for suspected or confirmed infection; study C3591004: a single blind, randomised, multicentre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics (PK) and efficacy of ceftazidime and avibactam when given in combination with metronidazole, compared with meropenem, in children from 3 months to less than 18 years of age with complicated intra-abdominal infections (cIAIs); and study C3591005: a single blind, randomised, multicentre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics and efficacy of ceftazidime and avibactam compared with cefepime in children from 3 months to less than 18 years of age with complicated urinary tract infections (CUTIs); as well as population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to correct sections 2 and 4.4 of the SmPC and the package leaflet with information on sodium content, as well as section 5.2 of the SmPC with information on

volumes of distribution of ceftazidime and avibactam. Furthermore, the MAH also introduced minor correction in the Czech product information

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

5.3.5. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0029, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with lenalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 6.0 s1) are updated accordingly

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

5.3.6. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0030, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (ASCT). As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and RMP (version 6.0 s1) are updated accordingly

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

5.3.7. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/II/0150

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on data from: 1) study 20070782: a phase 3, randomised, double-blind, placebo-controlled, non-inferiority study in subjects with chemotherapy-induced anaemia receiving multi-cycle chemotherapy for the treatment of advanced stage non-small cell lung cancer (NSCLC); 2) study EPO-ANE-3010: a randomized, open-label, multicentre, phase 3 study of epoetin alfa plus standard supportive care versus standard supportive care in anaemic patients with metastatic breast cancer receiving standard chemotherapy; 3) the company core data sheet (CCDS). In addition, section 4.6 is revised as requested in the outcome of the PSUR single assessment procedure (PSUSA/00000932/201710) finalised in June 2018. The package leaflet and the RMP (version 9.3) are updated accordingly. Furthermore, the MAH took the opportunity to introduce minor editorial changes, update the information on local representatives and align the product information (PI) with the quality review of documents (QRD) template (version 10.0)

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

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

Applicant: Apotex B.V.

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 introduce 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

5.3.9. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0058

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) of study 109MS310 (listed as category 3 study in the RMP): an open-label study to assess the effects of Tecfidera (dimethyl fumarate) on lymphocyte subsets in subjects with relapsing remitting multiple sclerosis (RRMS). The RMP (version 10.1) is updated accordingly, includes updates to reflect safety information available until the data lock point (DLP) of 24 January 2019 and in line with revision 2.01 of the guidance on the format of the risk management plan (RMP) accompanying GVP module V on 'Risk management systems'

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

5.3.10. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0040

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include a new indication to reduce the risk of major adverse cardiovascular events (MACE) (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus (T2DM) who have multiple cardiovascular risk factors without established cardiovascular disease, and in adults with T2DM with established cardiovascular disease. The data supporting this new indication is derived from study GBDJ (researching cardiovascular events with a weekly incretin in diabetes (REWIND)): a single pivotal phase 3 long-term cardiovascular outcomes study, which assessed the efficacy and safety of treatment with once-weekly injection of dulaglutide 1.5 mg when added to glucose-lowering regimen of patients with T2DM, compared to the addition of a once weekly placebo injection (in fulfilment of post-authorisation measure (PAM) (MEA 004)). 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 3.1) are updated accordingly. In addition, the MAH took the opportunity to update the wording of the existing

indication in section 4.1 of the SmPC and to implement a minor change in section 5.1 of the SmPC, in the glycaemic control summary subsection based on the results from the dulaglutide study as add-on to sodium-glucose co-transporter 2 (SGLT2) inhibitor therapy which was assessed as part of II/25 concluded in April 2018

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

5.3.11. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0105, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody (Ab) positive. As a consequence the SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, Annex II are updated. The package leaflet and the RMP (version 19) are updated accordingly

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

5.3.12. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS1601/0022; Linagliptin, metformin - JENTADUETO (CAP) - EMEA/H/C/002279/WS1601/0051; Linagliptin - TRAJENTA (CAP) - EMEA/H/C/002110/WS1601/0038

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 5.1 of the SmPC for Trajenta (linagliptin), update of sections 4.2, 4.4 and 5.1 of the SmPC for Jentadueto (linagliptin/metformin) and section 5.1 of the SmPC of Glyxambi (empagliflozin/linagliptin) based on the final results from study 1218.74 (CAROLINA) (listed as a category 3 study in the RMP of Jentadueto (linagliptin/metformin) and Trajenta (linagliptin), in fulfilment of Trajenta MEA 008.1 and Jentadueto MEA 001.1): a phase 3 randomised, parallel group, double blind study to evaluate cardiovascular safety of linagliptin versus glimepiride in patients with type 2 diabetes mellitus (T2DM) at high cardiovascular risk. The package leaflet for Trajenta (linagliptin) is updated accordingly. The RMPs (version 13.0 for Jentadueto (linagliptin/metformin) and Trajenta (linagliptin) and version 5.0 for Glyxambi (empagliflozin/linagliptin)) are updated accordingly. In addition, the MAH took the opportunity to make corrections throughout the product information for Glyxambi (empagliflozin/linagliptin) and Jentadueto (linagliptin/metformin) and to introduce corrections to the Bulgarian, French, Swedish translations for Glyxambi (empagliflozin/linagliptin)

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

5.3.13. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/II/0053

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Update of sections 4.4, 4.6 and 4.8 of the SmPC to add a warning for women stopping treatment for the purpose of becoming pregnant and for pregnant women and to

add information to prescribers on 'severe exacerbation of disease after Gilenya (fingolimod) discontinuation', timing of reported events and further recommendations on monitoring of patients. The package leaflet is updated accordingly

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

5.3.14. Fluciclovine (^{18}F) - AXUMIN (CAP) - EMEA/H/C/004197/II/0011

Applicant: Blue Earth Diagnostics Ireland Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include diagnosis and continuing assessment of glioma in adult patients. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1, 5.2 and 11 of the SmPC and Annex II are updated. 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

5.3.15. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/X/0062

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to introduce a solution for injection as a new pharmaceutical form, 120 mg as a new strength and subcutaneous use as a new route of administration. The RMP (version 9.1) is updated accordingly

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

5.3.16. Insulin human - ACTRAPHANE (CAP) - EMEA/H/C/000427/WS1582/0076; ACTRAPID (CAP) - EMEA/H/C/000424/WS1582/0070; INSULATARD (CAP) - EMEA/H/C/000441/WS1582/0073; MIXTARD (CAP) - EMEA/H/C/000428/WS1582/0077; PROTAPHANE (CAP) - EMEA/H/C/000442/WS1582/0072

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 3.0) for insulin human-containing products to reclassify the risk of 'medication errors' from an important potential risk to an important identified risk as requested in the outcome of the PSUR single assessment procedure PSUSA/00001753/201710 finalised in June 2018 and in line with the 'Good practice guide on risk minimisation and prevention of medication errors' dated 2015. However, the RMP is also brought 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). As a consequence, the MAH proposes to remove this risk as it is fully characterised and managed through routine pharmacovigilance and routine risk minimisation measures. In addition, section 4.4 of the SmPC is updated in order to add a warning on accidental mix-ups/medication. The package leaflet is updated accordingly. Furthermore, the MAH took the opportunity to include minor updates to Annex III-A on 'labelling' and to bring the package leaflet in line with the latest quality review document (QRD) template (version 10.0)

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

5.3.17. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/II/0130

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final clinical study report (CSR) from study HUBIN_L_05335 (listed as a category 3 study in the RMP): a c phase 3 study covering the evaluation of Insuman Implantable 400 IU/mL (insulin human) in patients with type 1 diabetes treated with the Medtronic MiniMed Implantable Pump System using Insuplant 400 IU/mL (in fulfilment of post-authorisation measure (PAM) MEA040). The RMP (version 4.0) is updated accordingly and includes the amended protocol (version 2) of the ongoing study HUBIN_C_06380: an European observational cohort of patients with type 1 diabetes treated via intraperitoneal route with Insuman Implantable 400 IU/mL (insulin human) in Medtronic MiniMed implantable pump as endorsed by PRAC in procedure MEA 047.5 in May 2018

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

5.3.18. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/X/0075/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 25 mg granules in sachet in the treatment of cystic fibrosis in children aged 6 to less than 12 months old; 2) update of sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC, and sections 2 and 3 of the package leaflet for the 150 mg film-coated tablet presentation to bring it in line with the new dosage form (25 mg granules). The RMP (version 8.3) is updated accordingly. In addition, the MAH took the opportunity to implement minor updates in the product information

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

5.3.19. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0014/G, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of 1) submission of the final report of progression free survival (PFS) in fulfilment of study C16019 (SOB004): a phase 3, randomized, placebo-controlled, double-blind study of oral ixazomib citrate maintenance therapy in patients with multiple myeloma following autologous stem cell transplant; 2) request for an extension of the due date for study C16014 (SOB003): a phase 3, randomized, double-blind, multicentre study comparing oral ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in adult patients with newly diagnosed multiple myeloma (NDMM). As a result, Annex II is amended. The RMP (version 4.0) is updated accordingly

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

5.3.20. Lapatinib - TYVERB (CAP) - EMEA/H/C/000795/II/0062

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report from study EGF117165/LAP016A2206 (listed as an obligation in the Annex II of the product information): an open-label, phase 2 study to evaluate biomarkers associated with response to subsequent therapies in subjects with epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer receiving treatment with trastuzumab in combination with lapatinib or chemotherapy. Annex II and the RMP (version 36.0) are updated accordingly

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

5.3.21. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0013

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include active immunisation of children 1-9 years old. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated based on the results from the two pivotal studies, namely B1971017: a phase 2, randomized, controlled, observer-blinded study to describe the immunogenicity, safety, and tolerability of *Neisseria meningitidis* serogroup b bivalent recombinant lipoprotein 2086 vaccine (bivalent rLP2086 (Trumenba)) in healthy subjects aged ≥24 months to <10 years; and study B1971035: a phase 2, randomized, controlled, observer-blinded study conducted to describe the immunogenicity, safety, and tolerability of a *Neisseria meningitidis* serogroup B bivalent recombinant lipoprotein 2086 vaccine (bivalent rLP2086 (Trumenba)) when administered to healthy toddlers aged 12 to <18 months or 18 to <24 months, and the safety and immunogenicity of a booster dose of bivalent rLP2086. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to submit a corrected version of the final report of study B1971016: a phase 3, randomized, placebo-controlled, observer-blinded, trial to assess the safety, tolerability, and immunogenicity of bivalent rLP2086 vaccine (Trumenba) when administered as a 3-dose regimen in healthy young adults aged >=18 to <26 years, which was included in the initial marketing authorisation application (MAA)/opinion

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

5.3.22. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0029/G

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.8 to adjust the list of adverse drug reactions and their corresponding frequencies in line with the outcome of the PSUSA procedure (PSUSA/00010366/201709) finalised in April 2018 ; 2) update of sections 4.2, 4.4 and 5.2 of the SmPC to add results from a phase 1 open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release combination of

naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning is updated accordingly. The warning related to contraindications is aligned to section 4.3 to add end-stage renal failure patients. As a consequence, the RMP (version 11) is updated accordingly. In addition, the MAH took the opportunity to update the warning on lactose in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.23. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/II/0046/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variations consisting of: 1) update to Annex II to remove the specific obligation (SOB) based on the final results from study NLR506AUS02T (COG-AALL0434): 'intensified methotrexate, nelarabine and augmented Berlin-Frankfurt-Munster (BFM) therapy for children and young adults with newly diagnosed T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL)'. As a consequence, sections 4.8 and 5.1 of the SmPC are updated; 2) update of section 4.6 of the SmPC to revise information on male and female contraception taking into consideration available non-clinical and clinical safety data as well as internal MAH's guidelines based on information from literature, health authority and working group guidelines. Furthermore, the MAH took the opportunity to update details of the local representatives and introduced minor editorial changes in the package leaflet. The RMP (version 10) is updated accordingly

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

5.3.24. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0034, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Submission of the final results of the pivotal study BO21005/GOYA: a phase 3, multicentre, open-label randomized trial comparing the efficacy of obinutuzumab (GA101 (RO5072759)) in combination with cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) (G-CHOP) versus rituximab and CHOP (R-CHOP) in previously untreated patients with CD20-positive diffuse large B-cell lymphoma (DLBCL), to address the additional pharmacovigilance activities required in the EU RMP. The RMP (version 5.0) is updated accordingly

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

5.3.25. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/II/0093

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Submission of an updated RMP (version 23) brought in line with revision 2 of GVP

module V on 'Risk management systems'. In addition, the MAH proposed the removal of some additional risk minimisation measures (aRMM). As a result Annex II is updated. The MAH took the opportunity to update sections 4.2 and 4.4 of the SmPC to include the table on dose modification previously located in section 4.4. In addition, section 4.4 is updated to implement the statement on 'sodium' content in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'. Furthermore, minor corrections are introduced in section 4.8 of the SmPC and in the list of the local representatives

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

5.3.26. Pegfilgrastim - PELGRAZ (CAP) - EMEA/H/C/003961/II/0005

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: Change in the immediate packaging of Pelgraz (pegfilgrastim) finished product solution for injection 6mg/0.6 mL to add an additional presentation as a solution for injection in pre-filled injector in addition to the existing approved solution for injection in Pre-filled syringe. The RMP (version 1.4) is updated accordingly

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

5.3.27. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0017, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.4, 4.5 and 4.6 of the SmPC in order to reflect available information of co-administration of pitolisant with cytochrome P450 3A4 (CYP3A4) substrates based on the results from the following studies: 1) study R-B478-2.649: a drug-drug interaction in-vitro study of CYP450 3A induction: effect of BF2.649 (pitolisant), BP2.951 (pitolisant metabolite), BP1.8054(pitolisant metabolite) and BP1.4787 (modafinil); 2) study R.BF2.649-SK-005: evaluation of the induction potential of CYP3A4 by BF2.649, P2.951 and BP1.8054 gene expression analysis in human primary hepatocytes; 3) study R-B472-1.11413: quantification of 4β-hydroxycholesterol (BP1.11413) in human serum from a two-part, open label, one sequence, cross-over pharmacokinetic study to evaluate: study part I: at steady-state, the pitolisant (40 mg) interaction (as inducer) on both a single dose of midazolam and of bupropion in eighteen healthy male volunteers; study to assess the tolerance and pharmacokinetic profile of repeated 20 mg oral doses of BF2.649, in healthy elderly subjects and a young adult control group; a study to assess the potential impact of drug-drug interaction of rifampicin on the relative bioavailability of BF2.649 in healthy male subjects; B28-day repeated dose study, to evaluate pharmacokinetic parameters and accumulation rate of BF2.649, administered once a day, in six ambulatory healthy male volunteers. The MAH took the opportunity to update section 5.2 of the SmPC to more accurately reflect information previously assessed during procedure II/0004/G finalised in 2017. The RMP (version 6.0) is updated accordingly. In addition, the MAH took the opportunity to clarify details on the manufacturers of the finished product in the package leaflet

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

5.3.28. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0074/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) extension of indication to include a new indication for the vial presentation 'treatment of retinopathy of prematurity (ROP) in preterm infants'. As a consequence, sections 2, 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet, labelling and the RMP (version 18.0) are updated accordingly; 2) introduction of a low volume high accuracy syringe, as a stand-alone medical device for the administration of the Lucentis (ranibizumab) 0.2 mg paediatric dose (corresponding to 0.02 mL of the Lucentis 10 mg/mL solution for injection in vial presentation)

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

5.3.29. Telotristat ethyl - XERMELO (CAP) - EMEA/H/C/003937/II/0015, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 5.1 of the SmPC based on final results from study LX1606.1-302.CS (TELEPATH) (listed as a category 3 study in the RMP): a multicentre, phase 3, long-term extension study to further evaluate the safety and tolerability of telotristat etiprate in patients with carcinoid syndrome (CS). The RMP (version 4.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.30. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/II/0020

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.8 and 5.1 of the SmPC based on safety information from interim results at week 48 of study GS-US-320-4018 (listed as a category 3 study in the RMP): a phase 3, randomized, double blind study conducted to evaluate the efficacy and safety of switching from tenofovir disoproxil fumarate (TDF) 300 mg once a day (QD) to tenofovir alafenamide (TAF) 25 mg QD in subjects with chronic Hepatitis B (CHB) who are virologically suppressed. The package leaflet and the RMP (version 4.1) are updated accordingly

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

5.3.31. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/X/0040

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new strength (108 mg) and a new route of administration (subcutaneous

use). The RMP (version 5.0) is updated accordingly

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. Adalimumab[8] - AMGEVITA (CAP); HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HYRIMOZ (CAP); IMRALDI (CAP) - PSUSA/00010589/201812

Applicant(s): Amgen Europe B.V. (Amgevita), Mylan S.A.S (Hulio), Sandoz GmbH (Halimatoz, Hefiya, Hyrimoz), Samsung Bioepis NL B.V. (Imraldi)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201812

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alectinib - ALECENSA (CAP) - PSUSA/00010581/201901

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Allopurinol, lesinurad - DUZALLO (CAP) - PSUSA/00010704/201812

Applicant: Grunenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[8] Biosimilar medicinal product(s) only

6.1.5. Amifampridine - FIRDAPSE (CAP) - PSUSA/00000141/201812

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201901

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Asparaginase[9] - SPECTRILA (CAP) - PSUSA/00010445/201901

Applicant: Medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/201901

Applicant(s): Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/201812

Applicant: Pierre Fabre Medicament

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. Birch bark extract[10] - EPISALVAN (CAP) - PSUSA/00010446/201901

Applicant: Amryt AG

[9] Centrally authorised product(s) only
[10] Centrally authorised product(s) only

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/201901

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Budesonide[11] - JORVEZA (CAP) - PSUSA/00010664/201901

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/201901

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cholic acid[12] - ORPHACOL (CAP) - PSUSA/00010208/201809

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Cladribine[13] - MAVENCLAD (CAP) - PSUSA/00010634/201901

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

[11] Centrally authorised product(s) only
[12] Treatment of inborn errors in primary bile acid synthesis due to 3β-hydroxy-Δ5-C27-steroid oxidoreductase deficiency or Δ4-3-oxosteroid-5β-reductase indication(s) only
[13] Treatment of multiple sclerosis (MS) only

Action: For adoption of recommendation to CHMP

6.1.16. Clofarabine - EVOLTRA (CAP) - PSUSA/00000805/201812

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - PSUSA/00010028/201812

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dasabuvir - EXVIERA (CAP) - PSUSA/00010363/201901

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Dimethyl fumarate[14] - SKILARENCE (CAP) - PSUSA/00010647/201812

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/201812

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[14] Treatment of psoriasis only

6.1.21. Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/201812

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ertugliflozin, metformin - SEGLUROMET (CAP) - PSUSA/00010680/201812

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010681/201812

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/201901

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/201812

Applicant: MSD Vaccins

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201901

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.27. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/201901

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/201812

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Lamivudine[15] - EPIVIR (CAP); lamivudine, zidovudine - COMBIVIR (CAP) - PSUSA/00009207/201811

Applicant(s): ViiV Healthcare B.V. (Combivir, Epivir)

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Lesinurad - ZURAMPIC (CAP) - PSUSA/00010470/201812

Applicant: Grunenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Liraglutide - SAXENDA (CAP); VICTOZA (CAP) - PSUSA/00001892/201812

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Treatment of human immunodeficiency virus (HIV) infections only

6.1.32. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/201901

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/201812

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Neratinib - NERLYNX (CAP) - PSUSA/00010712/201901

Applicant: Puma Biotechnology B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/201901

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/201812

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - PSUSA/00010367/201901

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Peramivir - ALPIVAB (CAP) - PSUSA/00010687/201812

Applicant: BioCryst Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/201812

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Sarilumab - KEVZARA (CAP) - PSUSA/00010609/201901

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/201901

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Secukinumab - COSENTYX (CAP) - PSUSA/00010341/201812

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201812

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/201812

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/201901

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

I wonScope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201812

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/201901 (with RMP)

Applicant: CO.DON AG, ATMP[16]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.48. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/201901

Applicant: Vanda Pharmaceuticals Germany GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[16] Advanced therapy medicinal product

6.1.49. Thyrotropin alfa - THYROGEN (CAP) - PSUSA/00002940/201811

Applicant: Genzyme Europe BV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Umeclidinium bromide - INCRUSE ELLIPTA (CAP); ROLUFTA ELLIPTA (CAP) - PSUSA/00010263/201812

Applicant(s): GlaxoSmithKline (Ireland) Limited (Incruse Ellipta), GlaxoSmithKline Trading Services Limited (Rolufta Ellipta)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Umeclidinium bromide, vilanterol - ANORO ELLIPTA (CAP); LAVENTAIR ELLIPTA (CAP) - PSUSA/00010264/201812

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Ustekinumab - STELARA (CAP) - PSUSA/00003085/201812

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/201812

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Ziconotide - PRIALT (CAP) - PSUSA/00003142/201812

Applicant: Riemser Pharma GmbH

PRAC Rapporteur: Jean-Michel Dogné

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. Bimatoprost, timolol - GANFORT (CAP); NAP - PSUSA/00002961/201811

Applicant(s): Allergan Pharmaceuticals Ireland (Ganfort), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Caspofungin - CANCIDAS (CAP); CASPOFUNGIN ACCORD (CAP); NAP - PSUSA/00000576/201812

Applicant(s): Merck Sharp & Dohme B.V. (Cancidas), Accord Healthcare S.L.U. (Caspofungin Accord), various

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Doxorubicin - CAELYX (CAP); MYOCET (CAP), NAP - PSUSA/00001172/201811

Applicant(s): Janssen-Cilag International NV (Caelyx), Teva B.V. (Myocet), various

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Edotreotide - SOMAKIT TOC (CAP); NAP - PSUSA/00010552/201812

Applicant(s): Advanced Accelerator Applications (SomaKit TOC), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Levetiracetam - KEPPRA (CAP); NAP - PSUSA/00001846/201811

Applicant(s): UCB Pharma S.A. (Keppra), various

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Lutetium (^{177}Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/201812

Applicant(s): ITG Isotope Technologies Garching GmbH (EndolucinBeta), I.D.B. Holland B.V. (Lumark), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. Nitric oxide - INOMAX (CAP); NAP - PSUSA/00002172/201812

Applicant(s): Linde Healthcare AB (INOmax), various

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.8. Paclitaxel – APEALEA (CAP); NAP - PSUSA/00002264/201812

Applicant(s): Oasmia Pharmaceutical AB, various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.9. Raloxifene - EVISTA (CAP); OPTRUMA (CAP); RALOXIFENE TEVA (CAP), NAP - PSUSA/00002603/201812

Applicant(s): Daiichi Sankyo Europe GmbH (Evista), Eli Lilly Nederland B.V. (Optruma), Teva B.V. (Raloxifene Teva), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.10. Sufentanil - DZUVEO (CAP); ZALVISO (CAP); NAP - PSUSA/00002798/201811

Applicant(s): FGK Representative Service GmbH (Dzuveo), Grunenthal GmbH (Zalviso), various

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Acetylsalicylic acid, bisoprolol (NAP) - PSUSA/00010287/201811

Applicant(s): various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amino acid combinations, glucose, triglyceride combinations[17], with or without electrolytes, mineral compounds[18] [19] (NAP) - PSUSA/00010190/201812

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Anti-T lymphocyte immunoglobulin (horse) (NAP) - PSUSA/00010433/201811

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Atomoxetine (NAP) - PSUSA/00000262/201811

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Azathioprine (NAP) - PSUSA/00000275/201812

Applicant(s): various

PRAC Lead: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

[17] E.g. olive oil, soya bean oil, fish oil
[18] Intravenous (I.V.) application only
[19] Nationally authorised product Numeta only

Action: For adoption of recommendation to CMDh

6.3.6. Cefotaxime (NAP) - PSUSA/00000599/201812

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Clevidipine (NAP) - PSUSA/00010288/201811

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Danaparoid (NAP) - PSUSA/00000923/201812

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Hydromorphone (NAP) - PSUSA/00001686/201811

Applicant(s): various

PRAC Lead: Gabriela Jazbec

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Hydroxycarbamide[20] (NAP) - PSUSA/00009182/201812

Applicant(s): various

PRAC Lead: Nikica Mirosevic Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[20] Non-centrally authorised product(s) only

6.3.11. Iron[21] (NAP) - PSUSA/00010236/201901

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Iron dextran (NAP) - PSUSA/00010696/201901

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Ketamine (NAP) - PSUSA/00001804/201812

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Levonorgestrel, ethinylestradiol; ethinylestradiol[22] (NAP) - PSUSA/00010442/201901

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Metoclopramide (NAP) - PSUSA/00002036/201811

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Naltrexone (NAP) - PSUSA/00002117/201811

Applicant(s): various

[21] Parenteral preparation(s) only, except iron dextran
[22] Combination pack

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Sertindole (NAP) - PSUSA/00002695/201901

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Tapentadol (NAP) - PSUSA/00002849/201811

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Terazosin (NAP) - PSUSA/00002895/201811

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Valaciclovir (NAP) - PSUSA/00003086/201812

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Yellow fever vaccine (live) (NAP) - PSUSA/00003135/201812

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Capecitabine - XELODA (CAP) - EMEA/H/C/000316/LEG 034

Applicant: Roche Registration GmbH

PRAC Rapporteur: Martin Huber

Scope: Review of all cases of hyperammonaemia and hyperammonaemic encephalopathy as requested in the conclusions of PSUSA/00000531/201804 adopted in January 2019

Action: For adoption of advice to CHMP

6.4.2. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/LEG 005

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Review of the risk of colitis as requested in the conclusions of PSUSA/00010450/201808 adopted in March 2019

Action: For adoption of advice to CHMP

6.4.3. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/LEG 013

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Detailed review on events of alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, gamma-glutamyl-transferase increased, blood bilirubin increased and hepatitis observed in clinical studies and post-authorisation safety studies. The total number of exposed patients in the respective studies and pooled data should also be provided; as well as a proposal for relevant frequency for 'hepatic disorders' as an undesirable effect, as requested in the conclusions of PSUSA/00010412/201809 adopted in April 2019

Action: For adoption of advice to CHMP

6.4.4. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 069

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Detailed analyses of skin melanoma and malignant melanoma as requested in the conclusions of PSUSA/00002127/201808 adopted in February 2019

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[23]

7.1.1. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/PSP/S/0070.1

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSP/S/0070 [protocol for an observational study to assess the effectiveness and long term safety of prophylaxis with damoctocog alfa pegol in real-world settings through the collection of total bleeding events and analysis of the annualised bleeding rate (ABR) in the different prophylaxis regimens (following approved local label or any other regimen prescribed by the physician as part of normal clinical practice) in patients with haemophilia A] as per the request for supplementary information (RSI) adopted in February 2019

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

7.1.2. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/PSA/S/0039

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Amendment to a protocol initially endorsed by PRAC in April 2017 (EMEA/H/C/PSP/S/0049.2) for a post-marketing, observational safety study in patients with cystic fibrosis to evaluate the long-term safety of Quinsair (levofloxacin) over a five-year period (2017 to 2021) compared to other inhaled approved antibiotic therapies in cystic fibrosis (CF) patients who are enrolled in the United Kingdom (UK) CF registry. The primary objective is extended to evaluate the safety profile of Quinsair (levofloxacin) over a three-year period (2019 to 2021) compared to other inhaled approved antibiotic therapies in CF patients who are enrolled in the German CF registry

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

7.1.3. Radium (Ra^{223}) dichloride - XOFIGO (CAP) - EMEA/H/C/PSP/S/0076.1

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: MAH's response to PSP/S/0076 [protocol for a PASS to estimate the incidence rate of symptomatic bone fractures among users of Xofigo (radium-223) in routine clinical practice] as per the request for supplementary information (RSI) adopted in March 2019

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

[23] In accordance with Article 107n of Directive 2001/83/EC

7.1.4. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/PSP/S/0077.1

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSP/S/0077 [protocol for a study evaluating the long-term safety of Adynovi (rurioctocog alfa pegol) in adults and adolescents ⩾12 years of age with haemophilia A] as per the request for supplementary information (RSI) adopted in March 2019

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

7.1.5. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/PSA/S/0040

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Amendment to a protocol previously agreed in July 2013 for study TED-R-13-002: an international short bowel syndrome registry: a prospective, long-term observational cohort study of patients with short bowel syndrome

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

7.1.6. Umeclidinium bromide – INCRUSE ELLIPTA (CAP), ROLUFTA ELLIPTA (CAP); umeclidinium bromide, vilanterol – ANORO ELLIPTA (CAP), LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/PSA/S/0032.2

Applicant(s): GlaxoSmithKline (Ireland) Limited (Incruse Ellipta, Anoro Ellipta, Laventair Ellipta), GlaxoSmithKline Trading Services Limited (Rolufta Ellipta)

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to PSA/S/0032.1 [amendment to a protocol initially endorsed by PRAC in March 2015 (EMEA/H/C/PSP/J/003.1) for study 201038: a post-authorisation safety (PAS) observational cohort study to quantify the incidence of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients using inhaled umeclidinium bromide/vilanterol (UMEC/VI) combination, inhaled UMEC, or tiotropium] as per the request for supplementary information (RSI) adopted in March 2019

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

7.1.7. Valproate (NAP) - EMEA/H/N/PSP/J/0072.1

Applicant: Sanofi-aventis Recherche & Development (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0072 [protocol for a retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in February 2019

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

7.1.8. Valproate (NAP) - EMEA/H/N/PSP/J/0073.1

Applicant: Sanofi-aventis Recherche & Development (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0073 [protocol for a survey among healthcare professionals (HCP) to assess the knowledge of HCP and behaviour with regard to the pregnancy prevention programme (PPP), the receipt/use of direct healthcare professional communication (DHPC) and educational materials as well as for a survey among patients to assess the knowledge of patients with regards to PPP and receipt/use of educational materials, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in February 2019

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

7.1.9. Valproate (NAP) - EMEA/H/N/PSP/J/0075.1

Applicant: Sanofi-aventis Recherche & Development (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0075 [protocol for a drug utilisation study (DUS) to assess the effectiveness of the new risk minimisation measures (RMMs) and to further characterise the prescribing patterns for valproate as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in February 2019

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

7.1.10. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/PSP/S/0078.1

Applicant: Novartis Europharm Limited, ATMP[24]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSP/S/0078 [protocol for a post-authorisation observational study to collect long-term safety information (i.e., for 5 years after treatment) associated with voretigene neparvovec (vector and/or transgene), its subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products] as per the request for supplementary information (RSI) adopted in April 2019

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

[24] Advanced therapy medicinal product

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[25]

7.2.1. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.2

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: MAH's response to MEA 004.1 [protocol for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.2.2. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/MEA 002

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Protocol for study DFIDM-1801 (ARCANGELO (itAlian pRospective study on CANGrELOr)): a multicentre prospective observational study of acute coronary syndrome patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelor

Action: For adoption of advice to CHMP

7.2.3. Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/MEA 001.1

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to MEA 001 [protocol and feasibility study for a case-control study linked to existing cancer registries to understand the data sources and analytic methods available to quantify the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin)] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.2.4. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/MEA 001

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for study CAMG334A2023: a non-interventional study to examine patient characteristics and drug utilisation patterns in migraine patients treated with prophylactic drugs in the Nordic registries [final clinical study report (CSR) expected end of data collection + 1 year] (from the initial opinion/MA)

[25] 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

7.2.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.12

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Substantial amendment to a protocol previously agreed in May 2015 for ongoing US study B2311060 (listed as a category 3 study in the RMP): a study to estimate the incidence and to compare the risks of endometrial hyperplasia and endometrial cancer in postmenopausal women initiating either Duavive (estrogens conjugated/bazedoxifene) or estrogen + progestin (E+P) combination hormone replacement therapy (HRT)

Action: For adoption of advice to CHMP

7.2.6. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.1

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 014 [protocol for study E7080-G000-508: an observational study to characterise hepatic related toxicity and overall safety profile in real-life conditions in the EU (Western population) in hepatocellular carcinoma (HCC) patients, including patients with Child-Pugh B] as per the request for supplementary information (RSI) adopted in January 2019

Action: For adoption of advice to CHMP

7.2.7. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/MEA 001

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for a PASS to characterise the safety of allogeneic haematopoietic stem cell transplantation (HSCT) in patients with cutaneous t-cell lymphoma (CTCL) treated with mogamulizumab [final clinical study report expected in July 2024] (from the initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.8. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 002

Applicant: Puma Biotechnology B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study PUMA-NER-6202: a randomized study to characterize the incidence and severity of diarrhoea in patients with early stage epidermal growth factor receptor 2 + (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis versus neratinib and intensive loperamide prophylaxis plus a bile acid sequestrant in the first month of treatment to characterise the incidence and severity of

diarrhoea in patients with early-stage HER2+ breast cancer treated with Nerlynx (neratinib) and intensive loperamide prophylaxis with/without a bile acid sequestrant [final study results expected in December 2021] (from the initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.9. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 003

Applicant: Puma Biotechnology B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study PUMA-NER-7402: a non-interventional study exploring the safety of neratinib among breast cancer patients to characterise the incidence and duration of diarrhoea in a real world setting, to describe patient characteristics, incidence rates and duration of diarrhoea, to describe use of loperamide and other concomitant antidiarrhoeal medication, describe adherence to neratinib therapy, assess the impact of neratinib therapy on patient self-reported, health related quality of life and their ability to perform their activities of daily living and to further assess and characterize adverse events hepatic, cardiac, pulmonary, reproductive and developmental toxicity [final study results expected in December 2023] (from the initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.10. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 004

Applicant: Puma Biotechnology B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study PUMA-NER-7403: a study to evaluate the availability, interpretability, and impact of Nerlynx (neratinib) educational materials [final study results expected in December 2021] (from the initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.11. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 002.1

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 002 [Protocol for study ALN-TTR02-0009: a prospective observational study to monitor and assess the safety of Onpattro (patisiran) in a real-world cohort of hereditary transthyretin amyloidosis (hATTR) patients] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.2.12. Ropeginterferon alfa-2b - BESREMI (CAP) - EMEA/H/C/004128/MEA 001

Applicant: AOP Orphan Pharmaceuticals AG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Protocol for EUPAS29462 study: a prospective, multicentre, non-interventional observational PASS to further investigate the safety and tolerability of ropeginterferon alfa-2b in polycythaemia vera patients with a special focus on hepatotoxicity to evaluate the effectiveness of risk minimisation measures and to evaluate cardiovascular safety during titration phase [final study report expected in Q3 2023] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.13. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.3

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.2 [PASS protocol for a safety surveillance programme using existing EU rheumatoid arthritis (RA) registries conducted in four countries: Germany (German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (OBS15180)), Spain (Spanish Registry for Adverse Events for Biological Therapy in Rheumatic Diseases (BIOBASASER) (6R88-RA-1720)), Sweden (Register for Antirheumatic Therapies in Sweden (ARTIS) (OBS15220)) and UK (British Society for Rheumatology Biologicals Register (BSRBR) (6R88-RA-1634))] as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.2.14. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 008.1 [protocol for study A3921312 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.2.15. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 009.1 [protocol for study A3921314 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Swedish (ARTIS) register] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.2.16. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 010.1 [protocol for study A3921316 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Spanish registry of adverse events of biological therapies and biosimilars in rheumatoid diseases (BIOBADASER)] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 011.1 [Protocol for study A3921317 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)] as per the request for supplementary information (RSI) adopted in February 2019

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[26]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[27]

7.4.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0124/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variations consisting of: 1) submission of the final reports from studies (listed as category 3 studies in the RMP), namely, study IM101125: a nationwide post-marketing study on the safety of abatacept treatment in Sweden Using the 'Antirheumatic Therapies in Sweden (ARTIS)' register, study IM101127: a long-term observation of treatment with biologics in rheumatoid arthritis (Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)), study IM101211: a multinational surveillance of abatacept-

[26] In accordance with Article 107p-q of Directive 2001/83/EC
[27] 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

treated patients during disease registries, study IM101213: a post-marketing observational study assessing the long-term safety of abatacept using a population-based cohort of rheumatoid arthritis patients in the province of British Columbia, Canada, as well as the interim report from study IM101121: Abatacept Pregnancy Exposure Registry 'Organization of Teratology Information Specialists (OTIS)' autoimmune diseases in pregnancy project as an extension study. These are biologic registries and pharmacoepidemiology studies to assess the risk associated with the use of abatacept during post-marketing in geographically diverse populations and subgroups; 2) submission of the final study report from study IM101488: a retrospective cohort study assessing the long-term safety of abatacept; 3) The deadline for submission of the final study report from study IM101121 (pregnancy registry) is proposed to be extended. The RMP (version 26) is updated accordingly and also include the addition of two epidemiological studies as category 3 studies in the RMP, namely: study IM101803: a nationwide post-marketing study on the safety of abatacept treatment in Denmark using the DANBIO[28] register and IM101W52: a nationwide post-marketing study on the safety of abatacept treatment in Sweden using the ARTIS register. In addition, the RMP is updated to remove the following missing information: combination therapy, including biologic therapy, and elderly patients

Action: For adoption of PRAC Assessment Report

7.4.2. Bosentan - STAYVEER (CAP) - EMEA/H/C/002644/II/0027

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study AC-052-516 (listed as a category 1 study in Annex II and the RMP): a non-interventional observational study of the disease characteristics and outcomes of pulmonary arterial hypertension (PAH) in children and adolescents in real-world clinical settings. The RMP (version 10) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

7.4.3. Bosentan - TRACLEER (CAP) - EMEA/H/C/000401/II/0091

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study AC-052-516 (listed as a category 1 study in Annex II and the RMP): a non-interventional observational study of the disease characteristics and outcomes of pulmonary arterial hypertension (PAH) in children and adolescents in real-world clinical settings. The RMP (version 10) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

7.4.4. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0059

Applicant: AstraZeneca AB

[28] A nationwide registry of biological therapies in Denmark

PRAC Rapporteur: Annika Folin

Scope: Submission of the final clinical study report (CSR) for study H80-MC-B016: a modified prescription-event monitoring programme (modified PEM) to be conducted in the UK enrolling patients with type 2 diabetes mellitus (T2DM) to quantify the incidence of acute pancreatitis in the first 12 months after initiating treatment with prescription exenatide once weekly. The RMP (version 33) is updated accordingly (in fulfilment of post-authorisation measures (PAM) MEA 010.5)

Action: For adoption of PRAC Assessment Report

7.4.5. Pegvisomant - SOMAVERT (CAP) - EMEA/H/C/000409/II/0089

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final clinical study report (CSR) from study A6291010 (ACROSTUDY) (listed as a category 3 study in the RMP): an open-label, global, non-interventional PASS performed to monitor the long-term safety and outcomes of pegvisomant treatment in clinical practice (in fulfilment of post approval measure (PAM) MEA 059)

Action: For adoption of PRAC Assessment Report

7.4.6. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/WS1557/0120; PROMETAX (CAP) - EMEA/H/C/000255/WS1557/0121

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final report for study CENA713D2409: a drug utilisation study (DUS) aimed to assess the extent of inappropriate use of Exelon/Prometax (rivastigmine) (fulfilment of post-authorisation measures (PAM) Exelon MEA 034 and Prometax MEA 035)

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. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017.4

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's responses to MEA 017.3 [second interim report for study ALIROC07997: a PASS using healthcare databases, in order to monitor the safety of Praluent (alirocumab) in patients affected with the human immunodeficiency virus (HIV)] as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.5.2. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 005.5

Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Three year report for apremilast psoriasis registry in the EU, long-term benefits and safety of systemic psoriasis therapy: German registry on the treatment of psoriasis with biologics and systemic therapeutics (PsoBest) (from initial MA/opinion)

Action: For adoption of advice to CHMP

7.5.3. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.5

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Four-year interim report for study PTC124-GD-025o-DMD (listed as a category 3 study in the RMP): a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting [final clinical study report (CSR) expected in April 2023]

Action: For adoption of advice to CHMP

7.5.4. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.4

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Fifth annual report (reporting period: 14 February 2018 to 13 February 2019) for the multicentre, multinational, observational Morquio A registry study (MARS): a voluntary observational registry study to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population and to evaluate the long-term effectiveness and safety of Vimizim (elosulfase alfa) [final clinical study report (CSR) expected by March 2025]

Action: For adoption of advice to CHMP

7.5.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 003.6

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.5 [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. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 002.1

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for an established nationwide prospective study (listed as a category 3 study in the RMP) from the use of biological agents to treat patients with rheumatological disorders in routine clinical practice using the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR): an established nationwide register [final clinical study report expected in 2027]

Action: For adoption of advice to CHMP

7.5.7. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 005.1

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 study in the RMP): a prospective, observational cohort study whose objectives are to evaluate the long-term effectiveness, safety, and costs associated with tumour necrosis factor-inhibitor therapies in the treatment of rheumatoid arthritis (RA) and to compare this to a cohort of RA patients who are treated with non-biologic disease-modifying antirheumatic drugs (DMARDs) using the German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) [final clinical study report planned expected in 2027]

Action: For adoption of advice to CHMP

7.5.8. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 006.1

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 in the RMP) conducted in the Spanish register of adverse events of biological therapies in rheumatic diseases (BIOBADASER) to identify relevant adverse events occurring during treatment of rheumatic diseases with biological therapies, to estimate the frequency of their occurrence; to identify unexpected adverse events; to identify relevant adverse events that occur following the suspension of the treatment, to estimate the relative risk of occurrence of adverse events with biological therapies in patients with rheumatoid arthritis (RA) compared to those not exposed to these treatments; to identify risk factors for suffering adverse reactions with these treatments; to evaluate, under non-experimental conditions, the treatment duration before the biological medications had been suspended in patients with rheumatic diseases, as well as the reasons for the interruption of the treatment [final clinical study report planned expected in 2027]

Action: For adoption of advice to CHMP

7.5.9. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.3

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second annual report for study VX14 809 108: an observational study to evaluate the utilisation patterns and long-term effects of lumacaftor/ivacaftor therapy in patients with cystic fibrosis (CF) [final report expected: December 2021]

Action: For adoption of advice to CHMP

7.5.10. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 023.11

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Ninth annual interim report for study CNTO1275PSO4005 (Nordic database initiative): a prospective cohort registry, five-year observational study of adverse events (AEs) observed in patients exposed to ustekinumab

Action: For adoption of advice to CHMP

7.5.11. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.12

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Ninth annual interim report for study CNTO1275PSO4007 (Nordic pregnancy research initiative) (C0743T): exposure to ustekinumab during pregnancy in patients with psoriasis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 038 [amendment to the previously agreed protocol for study D2311: a phase 3, double-blind, double dummy, randomized, multicentre, active controlled study evaluating efficacy and safety of fingolimod once daily versus interferon β-1a once weekly in paediatric patients with multiple sclerosis (MS) aged 10 to <18 years old (from X/44/G)] as per the request for supplementary information (RSI) adopted in April 2019

Action: For adoption of advice to CHMP

7.6.2. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 006

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Interim study report for study M12-175: a phase 1 study evaluating the safety and pharmacokinetics of venetoclax (ABT-199) in subjects with relapsed or refractory chronic lymphocytic leukaemia and non-Hodgkin lymphoma

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

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)

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/S/0010 (without RMP)

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0080 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Menno van der Elst

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. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0067 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/R/0017 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/R/0026 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Dalbavancin - XYDALBA (CAP) - EMEA/H/C/002840/R/0028 (without RMP)

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/R/0045 (without RMP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Dronedarone - MULTAQ (CAP) - EMEA/H/C/001043/R/0042 (with RMP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/R/0022 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Lapatinib - TYVERB (CAP) - EMEA/H/C/000795/R/0060 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/R/0028 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/R/0025 (without RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/R/0029 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/R/0054 (without RMP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/R/0028 (without RMP)

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/R/0094 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Ramucirumab - CYRAMZA (CAP) - EMEA/H/C/002829/R/0031 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Rasagiline - RASAGILINE RATIOPHARM (CAP) - EMEA/H/C/003957/R/0014 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.15. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/R/0032 (without RMP)

Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.16. Sevelamer carbonate - SEVELAMER CARBONATE WINTHROP (CAP) - EMEA/H/C/003971/R/0022 (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

8.3.17. Tilmanocept - LYMPHOSEEK (CAP) - EMEA/H/C/002085/R/0016 (with RMP)

Applicant: Norgine B.V.

PRAC Rapporteur: Rugile Pilviniene

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

None

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

None

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

None

11.2. Other requests

None

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

12.3.1. Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products on requirements for previously untreated patients (PUPs) - PRAC and PDCO flow for paediatric investigation plans (PIPs) of authorised medicinal products with studies on PUPs

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

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

12.6.1. International Conference on Harmonisation (ICH) E2B(R3) on electronic transmission of individual case safety reports - data elements and message specification - stakeholder readiness for mandatory use

Action: For discussion

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) forecast for 2019 – planning update dated Q2 2019

Action: For information

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

12.11. 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 - monitoring EudraVigilance data by MAHs – experience from the pilot period

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

12.13.2. EudraVigilance – EMA data management and quality activities

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

12.14.2. 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 policy on handling of competing interests for scientific committees' members and experts – reminder training

Action: For discussion

12.20.2. EMA reimbursement rules for delegates - update

Action: For discussion

12.20.3. Rapid data analytical process - pilot

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/