25 October 2021
EMA/PRAC/544246/2021
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 25-28 October 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

25 October 2021, 13:00 – 19:30, room 1C / via teleconference

26 October 2021, 08:30 – 19:30, room 1C / via teleconference

27 October 2021, 08:30 – 19:30, room 1C / via teleconference

28 October 2021, 08:30 – 16:00, room 1C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

11 November 2021, 09:00 – 12:00, 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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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 25-28 October 2021 12

1.3. Minutes of the previous meeting on 27-30 September 2021 12

2. EU referral procedures for safety reasons: urgent EU procedures 12

2.1. Newly triggered procedures 12

2.2. Ongoing procedures 12

2.3. Procedures for finalisation 12

3. EU referral procedures for safety reasons: other EU referral procedures 12

3.1. Newly triggered procedures 12

3.2. Ongoing procedures 13

3.2.1. Amfepramone (NAP) - EMEA/H/A-31/1501 13

3.3. Procedures for finalisation 13

3.4. Re-examination procedures 13

3.5. Others 13

4. Signals assessment and prioritisation 13

4.1. New signals detected from EU spontaneous reporting systems 13

4.1.1. Alemtuzumab - LEMTRADA (CAP) 13

4.1.2. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) 14

4.1.3. Sacubitril, valsartan – ENTRESTO (CAP), NEPARVIS (CAP) 14

4.1.4. Tocilizumab – ROACTEMRA (CAP) 14

4.2. New signals detected from other sources 14

4.2.1. Olmesartan (NAP) 14

4.3. Signals follow-up and prioritisation 15

4.3.1. Adalimumab - AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/124; HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); YUFLYMA (CAP) 15

4.3.2. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) 15

4.3.3. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) 15

4.3.4. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) – EMEA/H/C/005735/SDA/038, SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/044; coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/SDA/031; coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/088 15

4.3.5. Ertapenem - INVANZ (CAP) - EMEA/H/C/000389/SDA/026; NAP 16

4.3.6. Ibrutinib – IMBRUVICA (CAP) 16

4.3.7. Labetalol (NAP) 16
4.3.8. Lenvatinib – KISPLYX (CAP) - EMEA/H/C/004224/SDA/016; LENVIMA (CAP) - EMEA/H/C/003727/SDA/018 16
4.3.9. Propylthiouracil (NAP) 17
4.4. Variation procedure(s) resulting from signal evaluation 17
4.4.1. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0028 17
4.4.2. Everolimus - AFINITOR (CAP) - EMEA/H/C/001038/II/0076 17

5. Risk management plans (RMPs) 18

5.1. Medicines in the pre-authorisation phase 18
5.1.1. Betulae cortex dry extract (5-10 : 1); extraction solvent: n-heptane 95% (w/w) - EMEA/H/C/005035, Orphan 18
5.1.2. Casirivimab, imdevimab - EMEA/H/C/005814 18
5.1.3. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - EMEA/H/C/005808 18
5.1.4. Dengue tetravalent vaccine (live, attenuated) - EMEA/H/W/005362 18
5.1.5. Dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/005155 18
5.1.6. Formoterol fumarate dihydrate, glycopyrronium, budesonide - EMEA/H/C/005311 18
5.1.7. Pegfilgrastim - EMEA/H/C/004780 18
5.1.8. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/00545119
5.1.9. Regdanvimab - EMEA/H/C/005854 19
5.1.10. Rimegepant - EMEA/H/C/005725 19
5.1.11. Somatrogon - EMEA/H/C/005633, Orphan 19
5.1.12. Sotrovimab - EMEA/H/C/005676 19
5.1.13. Tebentafusp - EMEA/H/C/004929, Orphan 19
5.1.14. Valoctocogene roxaparvovec - EMEA/H/C/005830, Orphan 19
5.2. Medicines in the post-authorisation phase – PRAC-led procedures 20
5.2.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0075 20
5.2.2. Brinzolamide, timolol - AZARGA (CAP) - EMEA/H/C/000960/II/0045 20
5.2.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0040 20
5.2.4. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0022 21
5.2.5. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/II/0054 21
5.2.6. Fesoterodine - TOVIAZ (CAP) - EMEA/H/C/000723/II/0062 21
5.2.7. Influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - FOCLIVIA (CAP) - EMEA/H/C/001208/WS2151/0068; prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - EMEA/H/C/002094/WS2151/0071 21
5.2.8. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0067 22
5.2.9. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS1919/0109; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS1919/0038 22

5.2.10. Varicella vaccine (live) - ZOSTAVAX (CAP) - EMEA/H/C/000674/II/0138 23
5.3. Medicines in the post-authorisation phase – CHMP-led procedures 23
5.3.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0008/G 23
5.3.2. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/X/0004/G, Orphan 23
5.3.3. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0042, Orphan 24
5.3.4. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0010 24
5.3.5. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0023 24
5.3.6. Canakinumab - ILARIS (CAP) - EMEA/H/C/001109/II/0075 25
5.3.7. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/II/0023 25
5.3.8. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/X/0079/G 25
5.3.9. Corifollitropin alfa - ELONVA (CAP) - EMEA/H/C/001106/II/0061 25
5.3.10. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/II/0018/G, Orphan 26
5.3.11. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/X/0145 26
5.3.12. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0056, Orphan 26
5.3.13. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0069/G 27
5.3.14. Doravirine - PIFELTRO (CAP) - EMEA/H/C/004747/WS2065/0019; doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - EMEA/H/C/004746/WS2065/0026 27
5.3.15. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/X/0045/G 27
5.3.16. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0073 28
5.3.17. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0062 28
5.3.18. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0006, Orphan 28
5.3.19. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0031 28
5.3.20. Ibalizumab - TROGARZO (CAP) - EMEA/H/C/004961/II/0015 29
5.3.21. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2113/0090; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2113/0108 29
5.3.22. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2134/0091; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2134/0109 29
5.3.23. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2153/0093; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2153/0111 29
5.3.24. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0033, Orphan 30
5.3.25. Mercaptamine - PROCYSBI (CAP) - EMEA/H/C/002465/X/0035, Orphan 30
5.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0107 30
5.3.27. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0029, Orphan 31
5.3.28. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0110 31
5.3.29. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0111 31
5.3.30. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/X/0063/G 31
5.3.31. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0029 32
5.3.32. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/X/0056/G 32
5.3.33. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/II/0054/G, Orphan 32

5.3.34. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0204 33
5.3.35. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/X/0023 33

6. Periodic safety update reports (PSURs) 33

6.1. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only 33

6.1.1. 5-aminolevulinic acid - GLIOLAN (CAP) - PSUSA/00000009/202103 33
6.1.2. Alogliptin - VIPIDIA (CAP); alogliptin, metformin - VIPDOMET (CAP); alogliptin, pioglitazone - INCRESYNC (CAP) - PSUSA/00010061/202104 34
6.1.3. Avelumab - BAVENCIO (CAP) - PSUSA/00010635/202103 34
6.1.4. Brolucizumab - BEOVU (CAP) - PSUSA/00010829/202104 34
6.1.5. Bupivacaine - EXPAREL LIPOSOMAL (CAP) - PSUSA/00010889/202104 34
6.1.6. Bupivacaine, meloxicam - ZYNRELEF (CAP) - PSUSA/00010880/202103 34
6.1.7. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/202103 34
6.1.8. Ciclosporin - IKERVIS (CAP); VERKAZIA (CAP) - PSUSA/00010362/202103 35
6.1.9. Colesevelam - CHOLESTAGEL (CAP) - PSUSA/00000864/202103 35
6.1.10. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202103 35
6.1.11. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202104 35
6.1.12. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/202103 35
6.1.13. Dimethyl fumarate - TECFIDERA (CAP) - PSUSA/00010143/202103 36
6.1.14. Dimethyl fumarate - SKILARENCE (CAP) - PSUSA/00010647/202103 36
6.1.15. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/202103 36
6.1.16. Ebola vaccine (rDNA, replication-incompetent) - MVABEA (CAP); ZABDENO (CAP) - PSUSA/00010857/202103 36
6.1.17. Enfuvirtide - FUZEON (CAP) - PSUSA/00001217/202103 36
6.1.18. Exenatide - BYDUREON (CAP); BYETTA (CAP) - PSUSA/00009147/202103 36
6.1.19. Filgotinib - JYSELECA (CAP) - PSUSA/00010879/202103 37
6.1.20. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/202103 (with RMP) 37
6.1.21. Gilteritinib - XOSPATA (CAP) - PSUSA/00010832/202103 37
6.1.22. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/202104 37
6.1.23. Ipilimumab - YERVOY (CAP) - PSUSA/00009200/202103 37
6.1.24. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/202103 38
6.1.25. Japanese encephalitis virus (inactivated) - IXIARO (CAP) - PSUSA/00001801/202103 38
6.1.26. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202103 38
6.1.27. Lusutrombopag - MULPLEO (CAP) - PSUSA/00010755/202103 38
6.1.28. Mogamulizumab - POTELIGEO (CAP) - PSUSA/00010741/202103 38
6.1.29. Naldemedine - RIZMOIC (CAP) - PSUSA/00010753/202103 38
6.1.30. Nintedanib - OFEV (CAP) - PSUSA/00010319/202104 39
6.1.31. Niraparib - ZEJULA (CAP) - PSUSA/00010655/202103 39
6.1.32. Ocrelizumab - OCREVUS (CAP) - PSUSA/00010662/202103 39

6.1.33. Risankizumab - SKYRIZI (CAP) - PSUSA/00010765/202103 39
6.1.34. Siponimod - MAYZENT (CAP) - PSUSA/00010818/202103 39
6.1.35. Sodium zirconium cyclosilicate - LOKELMA (CAP) - PSUSA/00010675/202103 40
6.1.36. Solriamfetol - SUNOSI (CAP) - PSUSA/00010831/202103 40
6.1.37. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/202103 40
6.1.38. Tolcapone - TASMAR (CAP) - PSUSA/00002985/202103 40
6.1.39. Tucatinib - TUKYSA (CAP) - PSUSA/00010918/202104 40
6.1.40. Vandetanib - CAPRELSA (CAP) - PSUSA/00009327/202104 40
6.1.41. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/202103 41
6.1.42. Vildagliptin - GALVUS (CAP), JALRA (CAP), XILIARX (CAP); vildagliptin, metformin - EUCREAS (CAP), ICANDRA (CAP), ZOMARIST (CAP) - PSUSA/00003113/202102 41
6.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs) 41
6.2.1. Bimatoprost - LUMIGAN (CAP); NAP - PSUSA/00000413/202103 41
6.2.2. Enoxaparin - INHIXA (CAP); NAP - PSUSA/00010833/202104 41
6.2.3. Esomeprazole - NEXIUM CONTROL (CAP); NAP - PSUSA/00001269/202103 41
6.2.4. Voriconazole - VFEND (CAP); NAP - PSUSA/00003127/202102 42
6.3. PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only 42
6.3.1. Ampicillin, sulbactam (NAP) - PSUSA/00000197/202102 42
6.3.2. Bilastine (NAP) - PSUSA/00003163/202103 42
6.3.3. Butoconazole (NAP) - PSUSA/00000471/202102 42
6.3.4. Calcium chloride, glutamic acid, glutathione, histidine, lactobionic acid, magnesium chloride, mannitol, potassium chloride, sodium hydroxide (NAP) - PSUSA/00009162/202103 42
6.3.5. Citrulline malate (NAP) - PSUSA/00010579/202103 43
6.3.6. Dobutamine (NAP) - PSUSA/00001151/202103 43
6.3.7. Ethinylestradiol, gestodene (NAP) - PSUSA/00001308/202103 43
6.3.8. Fluorodopa (^{18}F) (NAP) - PSUSA/00010002/202103 43
6.3.9. Gliclazide (NAP) - PSUSA/00001532/202102 43
6.3.10. Metamizole (NAP) - PSUSA/00001997/202103 43
6.3.11. Nitrazepam (NAP) - PSUSA/00002170/202103 44
6.3.12. Nitrofurantoin, nifurtoinol (NAP) - PSUSA/00002174/202102 44
6.3.13. Olodaterol (NAP) - PSUSA/00010245/202103 44
6.3.14. Ondansetron (NAP) - PSUSA/00002217/202102 44
6.3.15. Rabies vaccine (NAP) - PSUSA/00009277/202103 44
6.3.16. Spironolactone (NAP) - PSUSA/00002780/202103 44
6.3.17. Tenoxicam (NAP) - PSUSA/00002893/202102 45
6.3.18. Terlipressin (NAP) - PSUSA/00002905/202104 45
6.4. Follow-up to PSUR/PSUSA procedures 45
6.4.1. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.4 45

6.4.2. Fentanyl - EFFENTORA (CAP) - EMEA/H/C/000833/LEG 019.1 45
6.4.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 030.1 46
6.4.4. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/LEG 021.1 46
6.4.5. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/LEG 159.2 46
6.4.6. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/LEG 002.2 46
6.4.7. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/LEG 003.2 47
6.5. Variation procedure(s) resulting from PSUSA evaluation 47
6.5.1. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0015/G 47
6.5.2. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0026 47
6.5.3. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/II/0049 48
6.5.4. Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/II/0042, Orphan 48
6.6. Expedited summary safety reviews 48
6.6.1. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.9 48
6.6.2. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.8 49
6.6.3. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 014.6 49
6.6.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 027.6 49

7. Post-authorisation safety studies (PASS) 49

7.1. Protocols of PASS imposed in the marketing authorisation(s) 49
7.1.1. Elivaldogene autotemcel - SKYSONA (CAP) - EMEA/H/C/PSA/S/0079 49
7.1.2. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/PSP/S/0095 50
7.1.3. Tolvaptan - JINARC (CAP) - EMEA/H/C/PSA/S/0078 50
7.1.4. Valproate (NAP) - EMEA/H/N/PSP/J/0072.5 50
7.1.5. Valproate (NAP) - EMEA/H/N/PSP/J/0075.6 50
7.1.6. Valproate (NAP) - EMEA/H/N/PSP/J/0094.1 51
7.2. Protocols of PASS non-imposed in the marketing authorisation(s) 51
7.2.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/MEA 002.1 51
7.2.2. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.1 51
7.2.3. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.2 51
7.2.4. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037 52
7.2.5. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.3 52
7.2.6. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 011 52
7.2.7. Drospirenone, estetrol - DROVELIS (CAP) - EMEA/H/C/005336/MEA 001 52

7.2.8. Drospirenone, estetrol - LYDISILKA (CAP) - EMEA/H/C/005382/MEA 001 53
7.2.9. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.11 53
7.2.10. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003.8 53
7.2.11. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/MEA 001.1 54
7.2.12. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.2 54
7.3. Results of PASS imposed in the marketing authorisation(s) 54
7.3.1. Dexketoprofen, tramadol (NAP) - EMEA/H/N/PSR/S/0035 54
7.3.2. Valproate (NAP) - EMEA/H/N/PSR/J/0036 55
7.4. Results of PASS non-imposed in the marketing authorisation(s) 55
7.4.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0038 55
7.4.2. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0078 55
7.4.3. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/II/0047 55
7.4.4. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0034 56
7.5. Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation 56
7.5.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.3 56
7.5.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.5 56
7.5.3. Coronavirus (COVID-19) mRNA vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.3 57
7.5.4. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/LEG 011.2 57
7.5.5. Imiglucerase - CEREZYME (CAP) - EMEA/H/C/000157/MEA 040.11 57
7.5.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 009 57
7.5.7. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 010 58
7.5.8. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.11 58
7.5.9. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/LEG 006.2 58
7.5.10. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.12 58
7.5.11. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/LEG 013.3 59
7.6. Others 59
7.6.1. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/MEA 004 59
7.6.2. Somatropin - OMNITROPE (CAP) - EMEA/H/C/000607/MEA 010.3 59
7.7. New Scientific Advice 59
7.8. Ongoing Scientific Advice 59
7.9. Final Scientific Advice (Reports and Scientific Advice letters) 60

8. Renewals of the marketing authorisation, conditional renewal and annual reassessments 60

8.1. Annual reassessments of the marketing authorisation 60
8.1.1. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0087 (without RMP) 60
8.1.2. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/S/0055 (without RMP) 60

8.1.3. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/S/0069 (without RMP) 60
8.1.4. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/S/0025 (without RMP) 60
8.2. Conditional renewals of the marketing authorisation 61
8.2.1. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/R/0045 (without RMP) 61
8.2.2. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0027 (without RMP) 61
8.2.3. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0050 (without RMP) 61
8.3. Renewals of the marketing authorisation 61
8.3.1. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/R/0034 (without RMP)..... 61
8.3.2. Chlormethine - LEDAGA (CAP) - EMEA/H/C/002826/R/0030 (with RMP)..... 61
8.3.3. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/R/0054 (without RMP) 62
8.3.4. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/R/0030 (with RMP) 62
8.3.5. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/R/0029 (without RMP)..... 62
8.3.6. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL KRKA D.D. (CAP) - EMEA/H/C/004686/R/0017 (without RMP) 62
8.3.7. Etanercept - ERELZI (CAP) - EMEA/H/C/004192/R/0037 (with RMP)..... 62
8.3.8. Miglustat - YARGESA (CAP) - EMEA/H/C/004016/R/0011 (with RMP) 62
8.3.9. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/R/0025 (with RMP) 63
8.3.10. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/R/0025 (without RMP) 63
8.3.11. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/R/0044 (with RMP) 63
8.3.12. Pentosan polysulfate sodium - ELMIRON (CAP) - EMEA/H/C/004246/R/0024 (without RMP)63
8.3.13. Umeclidinium - ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/R/0019 (without RMP)..... 63

9. Product related pharmacovigilance inspections 64
9.1. List of planned pharmacovigilance inspections 64
9.2. Ongoing or concluded pharmacovigilance inspections 64
9.3. Others 64

10. Other safety issues for discussion requested by the CHMP or the EMA 64
10.1. Safety related variations of the marketing authorisation 64
10.2. Timing and message content in relation to Member States' safety announcements64
10.3. Other requests 64
10.3.1. Tirbanibulin – KLISYRI (CAP) - EMEA/H/C/005183/ANX 001 64
10.4. Scientific Advice 65

11. Other safety issues for discussion requested by the Member States65
11.1. Safety related variations of the marketing authorisation 65
11.2. Other requests 65
11.2.1. Fentanyl (NAP) - FR/H/PSUFU/00001369/202004 65
11.2.2. Methotrexate (NAP) - DE/H/PSUFU/00002014/201910 65

12. Organisational, regulatory and methodological matters 66

12.1. Mandate and organisation of the PRAC 66

12.1.1. PRAC membership 66

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q3 2021 66

12.1.3. Vote by proxy 66

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

12.2.1. Advanced therapy medicinal products (ATMP) - Impact of tocilizumab shortages on the use of chimeric antigen receptor-T (CAR-T) cell-based ATMPs in the EU 66

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

12.4. Cooperation within the EU regulatory network 66

12.4.1. Coronavirus (COVID-19) pandemic - update 66

12.5. Cooperation with International Regulators 66

12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee 66

12.7. PRAC work plan 67

12.7.1. PRAC work plan 2022 67

12.8. Planning and reporting 67

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q3 2021 and predictions 67

12.8.2. PRAC workload statistics – Q3 2021 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 67

12.10.1. Periodic safety update reports 67

12.10.2. Granularity and Periodicity Advisory Group (GPAG) 67

12.10.3. PSURs repository 68

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

12.10.5. PSUR single assessment (PSUSA) recommendation for nationally approved products (NAP) - outcome of EMA survey on recommendation implementation 68

12.11. Signal management 68

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

12.12. Adverse drug reactions reporting and additional reporting 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 68

12.13. EudraVigilance database 68

12.13.1. Activities related to the confirmation of full functionality 68

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 69
12.18.1. Public participation in pharmacovigilance 69
12.18.2. Safety communication 69
12.19. Continuous pharmacovigilance 70
12.19.1. Incident management 70
12.20. Impact of pharmacovigilance activities 70
12.21. Others 70
12.21.1. EU pharmaceutical legislation – revision of Directive 2001/83/EC and Regulation (EC) No 726/2004 70
12.21.2. Lifecycle regulatory submissions metadata project (LRSM) 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 25-28 October 2021. See November 2021 PRAC minutes (to be published post December 2021 PRAC meeting).

1.2. Agenda of the meeting on 25-28 October 2021

Action: For adoption

1.3. Minutes of the previous meeting on 27-30 September 2021

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Amfepramone (NAP) - EMEA/H/A-31/1501

Applicant(s): Artegodan GmbH, Temmler Pharma GmbH

PRAC Rapporteur: Anette Kirstine Stark; PRAC Co-rapporteur: Eva Jirsová

Scope: Review of the benefit-risk balance following notification by Romania 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

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Alemtuzumab - LEMTRADA (CAP)

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of vitiligo

Action: For adoption of PRAC recommendation

EPITT 19737 – New signal

Lead Member State(s): DK

[1] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[2] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

4.1.2. Coronavirus (COVID-19) mRNA[3] vaccine (nucleoside-modified) - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of capillary leak syndrome

Action: For adoption of PRAC recommendation

EPITT 19743 – New signal

Lead Member State(s): DK

4.1.3. Sacubitril, valsartan – ENTRESTO (CAP), NEPARVIS (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of vasoplegia syndrome

Action: For adoption of PRAC recommendation

EPITT 19739 – New signal

Lead Member State(s): DK

4.1.4. Tocilizumab – ROACTEMRA (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of encephalopathy including posterior reversible encephalopathy syndrome (PRES)

Action: For adoption of PRAC recommendation

EPITT 19731 – New signal

Lead Member State(s): DE

4.2. New signals detected from other sources

4.2.1. Olmesartan (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of autoimmune hepatitis

Action: For adoption of PRAC recommendation

EPITT 19258 – Related to December 2018[4]

[3] Messenger ribonucleic acid
[4] Held 26-29 November 2018

Lead Member State(s): DE

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab - AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/124; HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); YUFLYMA (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Celltrion Healthcare Hungary Kft. (Yuflyma), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S (Hulio), Pfizer Europe MA EEIG (Amsparity), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Hefiya, Hyrimoz)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of acquired haemophilia

Action: For adoption of PRAC recommendation

EPITT 19688 – Follow-up to June 2021

4.3.2. Coronavirus (COVID-19) mRNA[5] vaccine (nucleoside-modified) - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of myocarditis and pericarditis

Action: For adoption of PRAC recommendation

EPITT 19712 – Follow-up to October 2021

4.3.3. Coronavirus (COVID-19) mRNA[6] vaccine (nucleoside-modified) - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of myocarditis and pericarditis

Action: For adoption of PRAC recommendation

EPITT 19713 – Follow-up to October 2021

4.3.4. Coronavirus (COVID-19) mRNA[7] vaccine (nucleoside-modified) - COMIRNATY (CAP) – EMEA/H/C/005735/SDA/038, SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/044; coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/SDA/031; coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/088

Applicant(s): AstraZeneca AB (Vaxzevria), BioNTech Manufacturing GmbH (Comirnaty),

[5] Messenger ribonucleic acid
[6] Messenger ribonucleic acid
[7] Messenger ribonucleic acid

Janssen-Cilag International N.V. (Covid-19 vaccine Janssen), Moderna Biotech Spain, S.L. (Spikevax)

PRAC Rapporteur (lead): Menno van der Elst

Scope: Signal of multisystem inflammatory syndrome

Action: For adoption of PRAC recommendation

EPITT 19732 – Follow-up to September 2021

4.3.5. Ertapenem - INVANZ (CAP) - EMEA/H/C/000389/SDA/026; NAP

Applicant(s): Merck Sharp & Dohme B.V., various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Signal of toxic encephalopathy in patients with renal impairment

Action: For adoption of PRAC recommendation

EPITT 19498 – Follow-up to July 2021

4.3.6. Ibrutinib – IMBRUVICA (CAP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of sudden death/cardiac death with ibrutinib and concomitant angiotensin-converting enzyme (ACE) inhibitors[8] from a clinical trial[9]

Action: For adoption of PRAC recommendation

EPITT 19726 – Follow-up to September 2021

4.3.7. Labetalol (NAP)

Applicant(s): various

PRAC Rapporteur: Karen Pernille Harg

Scope: Signal of nipple pain and suppressed lactation

Action: For adoption of PRAC recommendation

EPITT 19639 – Follow-up to May 2021

4.3.8. Lenvatinib – KISPLYX (CAP) - EMEA/H/C/004224/SDA/016; LENVIMA (CAP) - EMEA/H/C/003727/SDA/018

Applicant(s): Eisai GmbH

PRAC Rapporteur: Annika Folin

[8] Benazepril, captopril, cilazapril, enalapril, enalaprilat, fosinopril, imidapril, lisinopril, perindopril, quinapril, ramipril, trandolapril, zofenopril and combinations
[9] Study 2013-001944-76 (FLAIR): a phase 3 study evaluating first-line treatment with ibrutinib+rituximab versus fludarabine, cyclophosphamide and rituximab in patients with chronic lymphocytic leukaemia who are up to 75 years of age

Scope: Signal of colitis

Action: For adoption of PRAC recommendation

EPITT 19691 – Follow-up to June 2021

4.3.9. Propylthiouracil (NAP)

Applicant(s): various

PRAC Rapporteur: Krõõt Aab

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

Action: For adoption of PRAC recommendation

EPITT 19692 – Follow-up to July 2021

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Coronavirus (COVID-19) mRNA[10] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0028

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.1) to include myocarditis and pericarditis in the list of the safety concerns as an important identified risk, as requested in the outcome of the signal procedure on myocarditis and pericarditis (EPITT 19713) adopted in July 2021 (SDA 033)

Action: For adoption of PRAC Assessment Report

4.4.2. Everolimus - AFINITOR (CAP) - EMEA/H/C/001038/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to include lymphoedema as an adverse drug reaction based on post-marketing data and related to the outcome of a signal procedure (EPITT 18197) adopted in February 2015. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

[10] Messenger ribonucleic acid

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Betulae cortex dry extract (5-10 : 1); extraction solvent: n-heptane 95% (w/w) - EMEA/H/C/005035, Orphan

Applicant: Amryt Pharmaceuticals DAC

Scope: Treatment to achieve accelerated healing of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in patients from birth onwards

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

5.1.2. Casirivimab, imdevimab - EMEA/H/C/005814

Scope: Prevention and treatment of coronavirus disease-2019 (COVID-19)

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

5.1.3. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - EMEA/H/C/005808

Scope: Prevention of coronavirus disease-2019 (COVID-19)

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

5.1.4. Dengue tetravalent vaccine (live, attenuated) - EMEA/H/W/005362

Scope (accelerated assessment): Prevention of dengue disease

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

5.1.5. Dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/005155

Scope (accelerated assessment): Prevention of dengue disease

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

5.1.6. Formoterol fumarate dihydrate, glycopyrronium, budesonide - EMEA/H/C/005311

Scope: Maintenance treatment of chronic obstructive pulmonary disease (COPD)

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

5.1.7. Pegfilgrastim - EMEA/H/C/004780

Scope: Treatment of neutropenia

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

5.1.8. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451

Scope: Prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F

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

5.1.9. Regdanvimab - EMEA/H/C/005854

Scope: Treatment of coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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

5.1.10. Rimegepant - EMEA/H/C/005725

Scope: Management of migraine

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

5.1.11. Somatrogon - EMEA/H/C/005633, Orphan

Applicant: Pfizer Europe MA EEIG

Scope: Long-term treatment of paediatric patients with growth disturbance due to insufficient secretion of growth hormone

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

5.1.12. Sotrovimab - EMEA/H/C/005676

Scope: Treatment of coronavirus disease 2019 (COVID-19)

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

5.1.13. Tebentafusp - EMEA/H/C/004929, Orphan

Applicant: Immunocore Ireland Limited

Scope (accelerated assessment): Treatment of uveal melanoma

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

5.1.14. Valoctocogene roxaparvovec - EMEA/H/C/005830, Orphan

Applicant: BioMarin International Limited, ATMP[11]

Scope (accelerated assessment): Treatment of severe haemophilia A

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

[11] Advanced therapy medicinal product

and CHMP

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

5.2.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0075

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: Submission of an updated RMP (version 30.1) to include a follow-up questionnaire on intraocular pressure (IOP) increase and timing of IOP increase report submission. In addition, the MAH proposed to simplify the educational material consisting of a prescriber guide and injection video based on collected data and following consultation with a panel of ophthalmologists, as per the conclusions of variation II/0068 concluded in March 2021

Action: For adoption of PRAC Assessment Report

5.2.2. Brinzolamide, timolol - AZARGA (CAP) - EMEA/H/C/000960/II/0045

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 3.0) to remove important identified risks (respiratory disorders, cardiovascular disorders, corneal decompensation and metabolic acidosis), important potential risk (long term use of preserved eye drops) and missing information (use in paediatric patients)

Action: For adoption of PRAC Assessment Report

5.2.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0040

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP (version 4.1) in order to add 'thrombosis in combination with thrombocytopenia' as an important potential risk as requested in the outcome of the signal procedure on immune thrombocytopenia (ITP) (EPITT 19678) adopted in July 2021 (SDA/034.1), to add acute macular neuroretinopathy, acute macular outer retinopathy, paracentral acute middle maculopathy, paresthesia and dysaesthesia in the list of adverse events of special interest (AESI) as requested in the outcome of the signal procedure on acute macular outer retinopathy (EPITT 19703) adopted in July 2021 (SDA/065). In addition, the updated RMP include the removal of the enhanced active surveillance (EAS) studies D8111R00003 [EU], D8110R00001 [US], D8111C00004 [UK], the update of the important potential risk of 'nervous system disorders, including immune-mediated neurological conditions' to reflect the recent product information on Guillain-Barré syndrome (IB/0034) as requested in the outcome of fourth monthly summary safety update (MSSR) (MEA 027.3) adopted in July 2021. Finally, the updated RMP includes the addition of the UK effectiveness study D8111R00007 as per the CHMP conclusion (MEA 010.1) dated June 2021 and the addition of study D8111R00010 to assess the relationship between the

exposure to COVID-19 vaccines and the risk of thrombotic thrombocytopenia syndrome

Action: For adoption of PRAC Assessment Report

5.2.4. Coronavirus (COVID-19) mRNA[12] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0022

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.0) to include clinical safety data from study mRNA-1273 P203 (NCT04649151): a phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ⩾ 12 to < 18 years

Action: For adoption of PRAC Assessment Report

5.2.5. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/II/0054

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 7.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with another centrally authorised product containing fentanyl. As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

5.2.6. Fesoterodine - TOVIAZ (CAP) - EMEA/H/C/000723/II/0062

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated RMP (version 10.0) in order to bring the important identified risks, important potential risks and missing information in line with revision 2 of GVP module V on 'Risk management systems' and in line with the PRAC outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00001387/202004) adopted in December 2020 by removing safety in paediatric patients as missing information

Action: For adoption of PRAC Assessment Report

5.2.7. Influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - FOCLIVIA (CAP) - EMEA/H/C/001208/WS2151/0068; prepandemic

[12] Messenger ribonucleic acid

influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - EMEA/H/C/002094/WS2151/0071

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 3.9) in order to align safety concerns of Aflunov (prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)) and Foclivia (influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1)) and to reclassify some potential risks in line with revision 2 of GVP module V on 'Risk management systems'. In addition, reference to adverse drug reaction follow-up forms for routine pharmacovigilance activity are removed

Action: For adoption of PRAC Assessment Report

5.2.8. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0067

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of the conditions of the non-interventional PASS (listed as a specific obligation in Annex II) by using different criteria of patient exposure and long term follow up to assess the relevant safety data, with consequential amendment of the study completion date. The RMP (version 13) is updated accordingly and submitted together with an amended global registry protocol (amendment 8). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

5.2.9. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS1919/0109; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS1919/0038

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 13.2) to include results from recently completed PASS, namely: 1) study A0081359: a population-based cohort study of pregabalin to characterize pregnancy outcomes; 2) study A0081106: a 12-month open-label study to evaluate the safety and tolerability of pregabalin as adjunctive therapy in paediatric subjects 1 month to 16 years of age with partial onset seizures and paediatric and adult subjects 5 to 65 years of age with primary generalized tonic-clonic seizures; 3) study A0081042: a double-blind, placebo-controlled, parallel-group, multicentre study of the efficacy and safety of pregabalin as adjunctive therapy in children 1 month through <4 years of age with partial onset seizures; 4) study A0081105: a randomized, double-blind, placebo-controlled, parallel group, multicentre trial of pregabalin as adjunctive therapy in paediatric and adult subjects with primary generalized tonic-clonic seizures. In addition, information on study A0081096: a prospective randomized 12-week controlled study of visual field change in subjects with partial seizures receiving pregabalin or placebo has been updated as well as study A0081365: a phase 4, randomised, double-blind, double-dummy,

placebo- and active-controlled, single-dose, six-way crossover study to evaluate the potential for abuse with pregabalin. In light of the results from the pregnancy outcomes study (study A0081359), section 4.6 of the SmPC is updated on the risks of pregabalin treatment during pregnancy. In addition, section 4.4 of the SmPC is updated to highlight that pregabalin should not be used during pregnancy unless clearly necessary and women of childbearing potential use effective contraception

Action: For adoption of PRAC Assessment Report

5.2.10. Varicella vaccine (live) - ZOSTAVAX (CAP) - EMEA/H/C/000674/II/0138

Applicant: MSD Vaccins

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 9.1) in order to reflect the completion of study V211-024: a post-licensure observational study of the long-term effectiveness of Zostavax (varicella vaccine (live)) and to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0008/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 5.1 of the SmPC based on final results from study CBYL719C2301 (SOLAR-1) (listed as a post-authorisation efficacy study (PAES) in Annex II): a phase 3, randomized, double-blind, placebo controlled study of alpelisib in combination with fulvestrant for men and postmenopausal women with hormone receptor positive, epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer which progressed on or after aromatase inhibitor treatment. Annex II is updated accordingly. In addition, the MAH is updating the anatomical therapeutic chemical (ATC) code in the SmPC. The RMP (version 5.0) is also updated in accordance

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

5.3.2. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/X/0004/G, Orphan

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Grouped applications consisting of: 1) line extension to add two new strengths of film-coated tablets (25 mg and 50 mg); 2) introduction of a new therapeutic indication to include treatment of adult patients with advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) and mast cell leukaemia (MCL), after at least one systemic therapy for Ayvakyt (avapritinib) based on the results of study BLU-285-2101: a

phase 1 study of avapritinib in patients with AdvSM and relapsed or refractory myeloid malignancies and study BLU-285-2202: an open-label, single arm, phase 2 study to evaluate efficacy and safety of avapritinib in patients with AdvSM. The new indication is applicable to the new and existing presentations (25 mg, 50 mg, 100 mg and 200 mg film-coated tablets). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2, 5.3, 6.1 and 8 of the SmPC are updated. The labelling, package leaflet and the RMP (version 1.1) are updated in accordance

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

5.3.3. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0042, Orphan

Applicant: Kite Pharma EU B.V., ATMP[13]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the package leaflet are updated. The RMP (version 5.1) is updated in accordance. In addition, the applicant took the opportunity to make minor editorial corrections throughout the SmPC and package leaflet to align with the latest quality review of documents (QRD) template (version 10.2)

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

5.3.4. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0010

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of visual impairment due to diabetic macular oedema (DME). As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated in accordance

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

5.3.5. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0023

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include monotherapy treatment of adults and adolescent patients aged 12 years and older, with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 6.0) are updated in accordance

[13] Advanced therapy medicinal product

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

5.3.6. Canakinumab - ILARIS (CAP) - EMEA/H/C/001109/II/0075

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with Schnitzler syndrome. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance

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

5.3.7. Cariprazine - REAGILA (CAP) - EMEA/H/C/002770/II/0023

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.4, 4.5, 4.6 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from RGH-188-302 (CAROLA) study (listed as a category 3 study in the RMP): an open-label, single-arm, fixed-sequence, phase 1 trial in female schizophrenia patients to investigate the effect of multiple-dose administration of cariprazine on the pharmacokinetics of a combined oral contraceptive containing ethinylestradiol and levonorgestrel. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and the package leaflet

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

5.3.8. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/X/0079/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (90 mg/90 mg/120 mg/6 mg film-coated tablets); 2) to include treatment of human immunodeficiency virus 1 (HIV 1) infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir in paediatric patients aged from 2 years and with body weight at least 14 kg. Sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated to support the extended indication. The RMP (version 5.1) is updated in accordance

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

5.3.9. Corifollitropin alfa - ELONVA (CAP) - EMEA/H/C/001106/II/0061

Applicant: Organon N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adolescent males (14 to less than 18

years) with hypogonadotropic hypogonadism in combination with human chorionic gonadotropin (hCG) based on final results of paediatric study P043: an open-label, non-comparative, multicentre safety and efficacy study of corifollitropin in association with hCG in male adolescents with hypogonadotropic hypogonadism, part of the paediatric investigation plan (PIP). As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 9.2) are updated in accordance. In addition, the MAH took the opportunity to implement some minor editorial and formatting changes throughout the product information

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

5.3.10. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/II/0018/G, Orphan

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) extension of indication to add treatment of relapsed/refractory acute myeloid leukaemia (AML) in paediatric patients. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the new safety and efficacy data from the paediatric clinical study AAML1421: a phase 1/2 study of liposomal daunorubicin/cytarabine alone followed by fludarabine, cytarabine, and granulocyte colony-stimulating factor (G-CSF) (FLAG) for children with relapsed AML. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the product information is updated in line with the latest quality review of documents (QRD) template (version 10.2); 2) submission of the final data from paediatric clinical study CPX-MA-1201: a phase 1/pilot study of liposomal daunorubicin/cytarabine for children, adolescents and young adults with recurrent or refractory hematologic malignancies, in support of the extension of indication

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

5.3.11. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/X/0145

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension application to introduce a new pharmaceutical form (gastro-resistant tablets). The RMP (version 14.0) is updated in accordance

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

5.3.12. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0056, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 15-007 (listed as a specific obligation in Annex II): a phase 3, randomised, adaptive study of defibrotide vs. best supportive care in the prevention of hepatic veno-occlusive disease in adult and paediatric patients undergoing hematopoietic stem cell transplant (HSCT). The RMP (version 9) is updated accordingly. The

MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) (template 10.2). In addition, the MAH introduced some minor correction throughout the product information

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

5.3.13. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0069/G

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC in order to add rhinorrhoea to the list of adverse drug reactions (ADRs) with frequency not known based on a systematic review of information from clinical and non-clinical studies, post-marketing data and scientific literature. The package leaflet is updated accordingly; 2) update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 109MS303 (ENDORSE) (listed as a category 3 study in the RMP): a dose-blind, multicentre, extension study to determine the long-term safety and efficacy of two doses of BG00012 (dimethyl fumarate) monotherapy in subjects with relapsing-remitting multiple sclerosis. The RMP (version 11.1) is updated accordingly

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

5.3.14. Doravirine - PIFELTRO (CAP) - EMEA/H/C/004747/WS2065/0019; doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - EMEA/H/C/004746/WS2065/0026

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include the new indication to the paediatric population weighing at least 35 kg. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated in accordance. In addition, the MAH took the opportunity to make minor editorial corrections and to update the list of local representatives in the package leaflet

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

5.3.15. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/X/0045/G

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped applications consisting of: 1) extension of application to add a new strength (100 mg solution for injection) consisting of: one presentation containing 2 pre-filled syringes and one presentation containing 6 pre-filled syringes (multipack of 3 packs of 2); 2) extension of indication to include treatment of paediatric patients with severe asthma with type 2 inflammation aged 6 to 11 years old. The RMP (version 6.0) are updated accordingly

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

5.3.16. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0073

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include the treatment of adolescents and children aged 10 years and above based on the results from study BCB114 (D5551C00002): a phase 3, double-blind, placebo-controlled, randomised, multicentre study to assess the safety and efficacy of exenatide once weekly in adolescents with type 2 diabetes (T2DM), which was initially submitted and assessed by the CHMP as part of post-authorisation measure (PAM) P46 028. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 35s1) are updated in accordance

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

5.3.17. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0062

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to amend an existing warning on the drug-drug interaction information with mercaptopurine/azathioprine based on final results from study FAI-01 (listed as a category 3 study in the RMP): a phase 1, drug-drug interaction study investigating the pharmacokinetic (PK) profile of 6-mercaptopurine following coadministration of two doses febuxostat and azathioprine in healthy subjects. The RMP (version 9.0) is updated accordingly

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

5.3.18. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0006, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add 'blood homocysteine increase' as a new adverse drug reaction (ADR) and update of section 4.4 of the SmPC to add a related warning. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH took the opportunity to make editorial changes to the product information and to update the local representative details for Malta and Cyprus

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

5.3.19. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0031

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC based on 2-year data from study CNTO1959PSA3002: a phase 3, multicentre, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of guselkumab administered subcutaneously in subjects with active psoriatic arthritis. The RMP (version 8.2) is updated accordingly

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

5.3.20. Ibalizumab - TROGARZO (CAP) - EMEA/H/C/004961/II/0015

Applicant: Theratechnologies Europe Limited

PRAC Rapporteur: David Olsen

Scope: Updated timelines for a post-authorisation efficacy study (PAES) to further characterise the efficacy of ibalizumab in combination with other anti-retroviral medicinal products, for the treatment of adults infected with multidrug resistant human immunodeficiency virus-1 (HIV-1) infection for whom it is otherwise not possible to construct a suppressive antiviral regimen (PROMISE study) to provide the final study report from October 2025 to October 2026. Annex II of the product information is updated accordingly. The RMP (version 2.0) is updated accordingly and in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010797/202009) adopted in April 2021

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

5.3.21. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2113/0090; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2113/0108

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for Opdivo (nivolumab) in combination with Yervoy (ipilimumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 24.0 for Opdivo and version 33.0 for Yervoy) are updated in accordance

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

5.3.22. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2134/0091; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2134/0109

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC based on final results from study CA209908: a phase 1b/2 clinical trial of nivolumab monotherapy and nivolumab in combination with ipilimumab in paediatric subjects with high grade primary central nervous system (CNS) malignancies. The RMP (version 22.3 for Opdivo) is updated in accordance

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

5.3.23. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2153/0093; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2153/0111

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2 and 6.6 of the SmPC to change the infusion time for ipilimumab when used as monotherapy or in combination with nivolumab in the melanoma indications. The package leaflet for Yervoy (ipilimumab) is updated in accordance. The RMP (version 26.0 for Opdivo and version 34.0 for Yervoy) are updated accordingly. In addition, the MAH took the opportunity to introduce an administrative update in Annex II of Yervoy (ipilimumab)

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

5.3.24. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0033, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report for the final analysis of overall survival (OS) for study C16010 (listed as an obligation in Annex II): a phase 3, randomised, double-blind multicentre study comparing ixazomib in combination with lenalidomide and dexamethasone (LenDex) versus placebo plus LenDex in adult patients with relapsed and/or refractory multiple myeloma. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 7.0) are updated accordingly

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

5.3.25. Mercaptamine - PROCYSBI (CAP) - EMEA/H/C/002465/X/0035, Orphan

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new pharmaceutical form associated with two new strengths (75 and 300 mg gastro-resistant granules). The RMP (version 7.2) is updated in accordance

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

5.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0107

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include in combination with fluoropyrimidine- and platinum-based combination chemotherapy the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for OPDIVO based on study CA209648: a randomized phase 3 study of nivolumab plus ipilimumab or nivolumab combined with fluorouracil plus cisplatin versus fluorouracil plus cisplatin in subjects with unresectable advanced, recurrent or metastatic previously untreated oesophageal squamous cell carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 25.0) are updated in accordance

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

5.3.27. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0029, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final results of study SHP634-101: an open-label, randomised, crossover study to assess the pharmacokinetic and pharmacodynamic profiles of once-daily and twice-daily dose regimens of recombinant human parathyroid hormone (rhPTH[1-84]) administered subcutaneously to subjects with hypoparathyroidism. Further clinical evaluation of an alternative dosing regimen is no longer warranted, as outlined in the current specific obligation (study SHP634-403). The conditional marketing authorisation can therefore be converted into a standard marketing authorisation (no longer subject to a specific obligation) valid for 5 years. The RMP (version 3.2) is updated accordingly

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

5.3.28. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0110

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery of adults with locally advanced, inflammatory, or early-stage triple-negative breast cancer at high-risk of recurrence; as a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 37.1) are updated in accordance

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

5.3.29. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0111

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the adjuvant treatment of adults and adolescents aged 12 years and older with stage IIB, stage IIC or stage III melanoma and to include the treatment of adolescents aged 12 years and older with advanced melanoma. As a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 36.1) are updated in accordance

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

5.3.30. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/X/0063/G

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form (gastro-resistant powder and solvent for oral suspension); 2) extension of indication to the paediatric population. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 17.1) are

updated in accordance

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

5.3.31. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0029

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from study CO-338-043 (ARIEL4) (listed as a specific obligation in Annex II): a phase 3, multicentre, open-label, randomised study evaluating the efficacy and safety of rucaparib versus chemotherapy for treatment of relapsed ovarian cancer/ The package leaflet and the RMP (version 6.1) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes and bring the product information in line with the latest bring the product information in line with the latest quality review of documents (QRD) template (version 10.2 Rev.1)

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

5.3.32. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/X/0056/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form (coated granules in sachet) associated with strengths 200mg/50mg and 150mg/37.5mg. The new presentations are indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients 3 years of age and older; 2) inclusion of paediatric use in patients 3 years of age and older to the existing presentations of the film-coated tablets. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.1) are updated accordingly. In addition, the MAH took the opportunity to implement minor updates and corrections throughout the product information

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

5.3.33. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/II/0054/G, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variations consisting of: 1) extension of indication to include patients from 4 months corrected gestational aged 1 year and above. Consequently sections 4.1, 4.2, 4.8, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 9.1) are updated accordingly; 2) update of Annex II-D on 'Conditions or restrictions with regards to the safe and effective use of the medicinal product' to amend the date of completion of the imposed post authorisation study: an international short bowel syndrome registry, from Q3 2031 to Q2 2032. In addition, the MAH took the opportunity to amend the list of local representatives

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

5.3.34. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0204

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nathalie Gault

Scope: Submission of final study report for study GS-US-174-0144 (listed as category 3 study in the RMP): a randomised, double-blind evaluation of the antiviral efficacy, safety and tolerability of tenofovir disporoxil fumarate. This application fulfils the Article 46 commitment to provide the final week 192 study results for clinical measure 'study 5' (study GS_US_174-0144) listed in the paediatric investigation plan (PIP). As a consequence, section 5.1 of the SmPC is updated accordingly. Additionally, the risk minimisation measures for paediatrics are removed from the RMP and Annex II of the product information. The package leaflet and the RMP (version 25.1) are updated accordingly. In addition, the MAH took the opportunity to implement minor linguistic amendments throughout the product information. Furthermore, the expression of lactose content in Annex I for the tablets was changed to refer to lactose base (not as monohydrate) in line with current practice

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

5.3.35. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/X/0023

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new strength (200 mg solution for injection). The RMP (version 1.0) 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. 5-aminolevulinic acid[14] - GLIOLAN (CAP) - PSUSA/00000009/202103

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[14] Indicated for the treatment of glioma only

6.1.2. Alogliptin - VIPIDIA (CAP); alogliptin, metformin - VIPDOMET (CAP); alogliptin, pioglitazone - INCRESYNC (CAP) - PSUSA/00010061/202104

Applicant(s): Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Avelumab - BAVENCIO (CAP) - PSUSA/00010635/202103

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Brolucizumab - BEOVU (CAP) - PSUSA/00010829/202104

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Bupivacaine - EXPAREL LIPOSOMAL (CAP) - PSUSA/00010889/202104

Applicant: Pacira Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bupivacaine, meloxicam - ZYNRELEF (CAP) - PSUSA/00010880/202103

Applicant: Heron Therapeutics, B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/202103

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Ciclosporin[15] - IKERVIS (CAP); VERKAZIA (CAP) - PSUSA/00010362/202103

Applicant(s): Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Colesevelam - CHOLESTAGEL (CAP) - PSUSA/00000864/202103

Applicant: Cheplapharm arzneimittel GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202103

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202104

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/202103

Applicant: Takeda Pharma A/S, ATMP[16]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

[15] Topical use only
[16] Advanced therapy medicinal product

6.1.13. Dimethyl fumarate[17] - TECFIDERA (CAP) - PSUSA/00010143/202103

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Dimethyl fumarate[18] - SKILARENCE (CAP) - PSUSA/00010647/202103

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/202103

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Ebola vaccine (rDNA[19], replication-incompetent) - MVABEA (CAP); ZABDENO (CAP) - PSUSA/00010857/202103

Applicant(s): Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Enfuvirtide - FUZEON (CAP) - PSUSA/00001217/202103

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Exenatide - BYDUREON (CAP); BYETTA (CAP) - PSUSA/00009147/202103

Applicant(s): AstraZeneca AB

[17] Indicated for the treatment of multiple sclerosis only
[18] Indicated for the treatment of psoriasis only
[19] Recombinant deoxyribonucleic acid

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Filgotinib - JYSELECA (CAP) - PSUSA/00010879/202103

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/202103 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Gilteritinib - XOSPATA (CAP) - PSUSA/00010832/202103

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/202104

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ipilimumab - YERVOY (CAP) - PSUSA/00009200/202103

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/202103

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Japanese encephalitis virus (inactivated) - IXIARO (CAP) - PSUSA/00001801/202103

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202103

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Lusutrombopag - MULPLEO (CAP) - PSUSA/00010755/202103

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Mogamulizumab - POTELIGEO (CAP) - PSUSA/00010741/202103

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Naldemedine - RIZMOIC (CAP) - PSUSA/00010753/202103

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Nintedanib[20] - OFEV (CAP) - PSUSA/00010319/202104

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Niraparib - ZEJULA (CAP) - PSUSA/00010655/202103

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Ocrelizumab - OCREVUS (CAP) - PSUSA/00010662/202103

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Risankizumab - SKYRIZI (CAP) - PSUSA/00010765/202103

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Siponimod - MAYZENT (CAP) - PSUSA/00010818/202103

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[20] Respiratory indication(s) only

6.1.35. Sodium zirconium cyclosilicate - LOKELMA (CAP) - PSUSA/00010675/202103

Applicant: AstraZeneca AB

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Solriamfetol - SUNOSI (CAP) - PSUSA/00010831/202103

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/202103

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Tolcapone - TASMAR (CAP) - PSUSA/00002985/202103

Applicant: Meda AB

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Tucatinib - TUKYSA (CAP) - PSUSA/00010918/202104

Applicant: Seagen B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Vandetanib - CAPRELSA (CAP) - PSUSA/00009327/202104

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/202103

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Vildagliptin - GALVUS (CAP), JALRA (CAP), XILIARX (CAP); vildagliptin, metformin - EUCREAS (CAP), ICANDRA (CAP), ZOMARIST (CAP) - PSUSA/00003113/202102

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

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 - LUMIGAN (CAP); NAP - PSUSA/00000413/202103

Applicants: Allergan Pharmaceuticals Ireland (Lumigan), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Enoxaparin - INHIXA (CAP); NAP - PSUSA/00010833/202104

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

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Esomeprazole - NEXIUM CONTROL (CAP); NAP - PSUSA/00001269/202103

Applicants: GlaxoSmithKline Dungarvan Ltd (Nexium Control), various

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Voriconazole - VFEND (CAP); NAP - PSUSA/00003127/202102

Applicants: Pfizer Europe MA EEIG (Vfend), various

PRAC Rapporteur: Liana Gross-Martirosyan

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. Ampicillin, sulbactam (NAP) - PSUSA/00000197/202102

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Bilastine (NAP) - PSUSA/00003163/202103

Applicant(s): various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Butoconazole (NAP) - PSUSA/00000471/202102

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Calcium chloride, glutamic acid, glutathione, histidine, lactobionic acid, magnesium chloride, mannitol, potassium chloride, sodium hydroxide (NAP) - PSUSA/00009162/202103

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Citrulline malate (NAP) - PSUSA/00010579/202103

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Dobutamine (NAP) - PSUSA/00001151/202103

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Ethinylestradiol, gestodene (NAP) - PSUSA/00001308/202103

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Fluorodopa (^{18}F) (NAP) - PSUSA/00010002/202103

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Gliclazide (NAP) - PSUSA/00001532/202102

Applicant(s): various

PRAC Lead: Gudrun Stefansdottir

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Metamizole (NAP) - PSUSA/00001997/202103

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Nitrazepam (NAP) - PSUSA/00002170/202103

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Nitrofurantoin, nifurtoinol (NAP) - PSUSA/00002174/202102

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Olodaterol (NAP) - PSUSA/00010245/202103

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Ondansetron (NAP) - PSUSA/00002217/202102

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Rabies vaccine (NAP) - PSUSA/00009277/202103

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Spironolactone (NAP) - PSUSA/00002780/202103

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Tenoxicam (NAP) - PSUSA/00002893/202102

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Terlipressin (NAP) - PSUSA/00002905/202104

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For preliminary discussion

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.4

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 016.3 [analysis of available mortality data from controlled clinical trials in the dexmedetomidine development programme as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000998/201903) adopted in November 2019] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

6.4.2. Fentanyl - EFFENTORA (CAP) - EMEA/H/C/000833/LEG 019.1

Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 019 [review of the current labelling for fentanyl transmucosal route of administration regarding off-label use, misuse and accidental exposure as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) adopted in January 2021] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

6.4.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 030.1

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to LEG 030 [review of the current labelling for fentanyl transmucosal route of administration regarding off-label use, misuse and accidental exposure as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) adopted in January 2021] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

6.4.4. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/LEG 021.1

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 021 [review of the current labelling for fentanyl transmucosal route of administration regarding off-label use, misuse and accidental exposure as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) adopted in January 2021] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

6.4.5. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/LEG 159.2

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 0159.1 [review on administration of live vaccines, including a literature review on postnatal clearance of tumour necrosis factor alfa (TNFα) inhibitors in the newborn, particularly of infliximab and of cases of disseminated BCG vaccinations associated with administration of BCG after birth as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010759/201908) adopted in April 2020] as per the conclusions adopted in May 2021

Action: For adoption of advice to CHMP

6.4.6. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/LEG 002.2

Applicant: Therakind (Europe) Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 002.1 [comprehensive review of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002014/201910) adopted in May 2020] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

6.4.7. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/LEG 003.2

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 003.1 [comprehensive review of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002014/201910) adopted in May 2020] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Coronavirus (COVID-19) mRNA[21] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0015/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variations to address PRAC requests as per the conclusions of the second and third monthly safety summary report (MSSR) procedures (MEA 011.1 and MEA 011.2) respectively: 1) update of sections 4.4 of the SmPC to provide additional safety information regarding hypersensitivity and anaphylaxis, as requested by the PRAC in the second MSSR. The package leaflet is updated accordingly; 2) update of section 4.8 of the SmPC to include 'delayed injection site reaction' as an adverse reaction with a frequency 'common', as requested by the PRAC in the third MSSR. The package leaflet is updated accordingly. In addition, the MAH submitted a justification for not adding diarrhoea to the product information as an adverse reaction as requested by the PRAC in the third MSSR and took the opportunity to introduce minor editorial changes in the product information

Action: For adoption of PRAC Assessment Report

6.5.2. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0026

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 4.8 of the SmPC to include new data related to hypersensitivity as per the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010668/202011) adopted in June 2021. The package leaflet is updated in accordance

Action: For adoption of PRAC Assessment Report

[21] Messenger ribonucleic acid

6.5.3. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/II/0049

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of section 4.8 of SmPC to include new symptoms of trigeminal neuralgia as per the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00001352/202001) finalised in September 2020. The package leaflet is updated accordingly. The MAH introduced further editorial updates including an update of the product information in line with the latest quality review of documents (QRD) template (version 10.2) and an update of the contact details of the local representatives

Action: For adoption of PRAC Assessment Report

6.5.4. Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/II/0042, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of Annex II of the product information and of the RMP (version 12.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010115/202010) adopted in June 2021 to remove the controlled distribution system and prescriber kit (prescribing check list and healthcare professional (HCP) brochure) as additional risk minimisation measures (aRMM) while the patient alert card is kept as an aRMM. In addition, the RMP is updated to remove off-label use from the list of safety concerns, elderly patients aged over 75 years, patients with moderate to severe hepatic impairment and patients with severe renal impairment and/or undergoing dialysis as missing information. The MAH took the opportunity to include in the RMP updated specific follow-up questionnaires forms (in line with internal company template. Finally, the MAH the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[22]

6.6.1. Coronavirus (COVID-19) mRNA[23] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.9

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Tenth expedited monthly summary safety report (MSSR) for Comirnaty (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

[22] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC
[23] Messenger ribonucleic acid

6.6.2. Coronavirus (COVID-19) mRNA[24] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.8

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Ninth expedited monthly summary safety report (MSSR) for Spikevax (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.3. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 014.6

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Seventh expedited monthly summary safety report (MSSR) for COVID-19 Vaccine Janssen (COVID-19 vaccine (Ad26.COV2-S, recombinant)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 027.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Seventh expedited monthly summary safety report (MSSR) for Vaxzevria (COVID-19 vaccine (ChAdOx1-S [recombinant])) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[25]

7.1.1. Elivaldogene autotemcel - SKYSONA (CAP) - EMEA/H/C/PSA/S/0079

Applicant: bluebird bio (Netherlands) B.V, ATMP[26]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment to a protocol previously agreed in the initial marketing authorisation application (MAA)/marketing authorisation for study REG-502 (listed as an obligation in Annex II and RMP): a prospective, multicentre, international, observational, long-term safety and effectiveness registry study of patients with cerebral

[24] Messenger ribonucleic acid
[25] In accordance with Article 107n of Directive 2001/83/EC
[26] Advanced therapy medicinal product

adrenoleukodystrophy (CALD) treated with elivaldogene autotemcel or allogeneic hematopoietic stem cell transplantation (Stargazer)

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

7.1.2. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/PSP/S/0095

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Protocol for a PASS of paediatric patients initiating selumetinib: a multiple-country prospective cohort study

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

7.1.3. Tolvaptan - JINARC (CAP) - EMEA/H/C/PSA/S/0078

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Substantial amendment to a protocol previously agreed in March 2016 (PSP/0028.2) for a 7.5-year, multicentre, non-interventional PASS to characterise and quantify the identified risk of idiosyncratic liver injury in Jinarc (tolvaptan) treated patients with autosomal dominant polycystic kidney disease (ADPKD) in routine clinical practice

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

7.1.4. Valproate (NAP) - EMEA/H/N/PSP/J/0072.5

Applicant: Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Progress report for a joint 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)]

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

7.1.5. Valproate (NAP) - EMEA/H/N/PSP/J/0075.6

Applicant: Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Second interim report for a joint 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)

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

7.1.6. Valproate (NAP) - EMEA/H/N/PSP/J/0094.1

Applicant(s): Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0094 [protocol for a joint retrospective study of multiple European data sources characterising neurodevelopmental disorders in children exposed in utero to valproate and/or other antiepileptic drugs with long-term follow-up] as per the request for supplementary information (RSI) adopted in June 2021

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

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

7.2.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/MEA 002.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study CBYL719C2404: a non-interventional study of Piqray (alpelisib) in combination with fulvestrant in postmenopausal women and men with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative, locally advanced or metastatic breast cancer with a PIK3CA mutation in the real-world setting in European countries, as per the outcome of variation II/001 finalised in March 2021. The safety concerns addressed are hyperglycaemia and osteonecrosis of the jaw] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.2.2. Coronavirus (COVID-19) mRNA[28] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to a protocol previously agreed in the initial marketing authorisation application (MAA)/marketing authorisation for study C4591012 assessing the occurrence of safety events of interest, including severe or atypical COVID-19 in real-world use of COVID-19 mRNA vaccine [final clinical study report (CSR) expected in December-2023]

Action: For adoption of advice to CHMP

7.2.3. Coronavirus (COVID-19) mRNA[29] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.2

Applicant: BioNTech Manufacturing GmbH

[27] 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
[28] Messenger ribonucleic acid
[29] Messenger ribonucleic acid

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 011.1 [protocol for study C4591010: assessment of occurrence of safety events in real-world use of COVID-19 mRNA vaccine [final clinical study report (CSR) expected in September 2024] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

7.2.4. Coronavirus (COVID-19) mRNA[30] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study C4591009: a non-interventional PASS in US to assess the occurrence of safety events of interest, including myocarditis and pericarditis (from variation II/0059 finalised in October 2021)

Action: For adoption of advice to CHMP

7.2.5. Coronavirus (COVID-19) mRNA[31] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.3

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: MAH's response to MEA 003 [protocol for a study (listed as a category 3 study in the RMP): an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals - post authorisation safety of SARS-CoV-2 mRNA-1273 vaccine in the US [final clinical study report (CSR) expected in June 2023] (from initial opinion/marketing authorisation)] as adopted in March 2021

Action: For adoption of advice to CHMP

7.2.6. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 011

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Protocol for study AMY2009: a Multicentre, prospective study of daratumumab-based therapy in newly diagnosed patients with AL amyloidosis (from variation II/0043)

Action: For adoption of advice to CHMP

7.2.7. Drospirenone, estetrol - DROVELIS (CAP) - EMEA/H/C/005336/MEA 001

Applicant: Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.)

[30] Messenger ribonucleic acid
[31] Messenger ribonucleic acid

PRAC Rapporteur: Martin Huber

Scope: Protocol for an international active surveillance study (INAS-NEES): a prospective non-interventional comparative cohort observational study to characterize and compare the risks of estetrol/drospirenone with combined oral contraceptive-containing levonorgestrel (COC-LNG) in a study population that is representative of the actual users of these preparations. The main clinical outcome of interest is venous thromboembolism (VTE), specifically deep venous thrombosis (DVT) and pulmonary embolism (PE) [final study report expected in December 2029] (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.2.8. Drospirenone, estetrol - LYDISILKA (CAP) - EMEA/H/C/005382/MEA 001

Applicant: Estetra SRL

PRAC Rapporteur: Martin Huber

Scope: Protocol for an international active surveillance study (INAS-NEES): a prospective non-interventional comparative cohort observational study to characterize and compare the risks of estetrol/drospirenone with combined oral contraceptive-containing levonorgestrel (COC-LNG) in a study population that is representative of the actual users of these preparations. The main clinical outcome of interest is venous thromboembolism (VTE), specifically deep venous thrombosis (DVT) and pulmonary embolism (PE) [final study report expected in December 2029] (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.2.9. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.11

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Amendment to a protocol previously agreed in September 2019 for study 1245.96 (version 8.0): a non-interventional PASS in patients with type 2 diabetes mellitus (T2DM) to assess the risk of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infections, and diabetic ketoacidosis among patients treated with empagliflozin compared to patients treated with dipeptidyl peptidase 4 (DPP-4) inhibitors

Action: For adoption of advice to CHMP

7.2.10. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003.8

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Amendment to a protocol previously agreed in September 2019 for study 1245.96 (version 8.0): a non-interventional PASS in patients with type 2 diabetes mellitus (T2DM) to assess the risk of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infections, and diabetic ketoacidosis among patients treated with empagliflozin compared to patients treated with dipeptidyl peptidase 4

(DPP-4) inhibitors

Action: For adoption of advice to CHMP

7.2.11. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/MEA 001.1

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 001 [protocol for study AT1001-030: a prospective, multicentre, multinational, observational disease registry in Fabry disease patients treated with migalastat and untreated patients to evaluate the long-term safety and effectiveness of migalastat in Fabry disease patients in real-world setting] as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.12. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.2

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 001.1 [protocol for study RPC-1063-MS-004 (listed as a category 3 study in the RMP): a post authorisation multinational long-term non-interventional study (ORION) study on ozanimod real world safety [final clinical study report (CSR) expected in December 2031]] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[32]

7.3.1. Dexketoprofen, tramadol (NAP) - EMEA/H/N/PSR/S/0035

Applicant: Menarini International Operations Luxembourg S.A. (Dextradol, Enanplus, Skudexa, Takudex)

PRAC Rapporteur: Eva Segovia

Scope: Results of a drug utilisation study (DUS) and PASS on dexketoprofen-tramadol (DKP-TRAM) fixed combination to evaluate the pattern of prescriptions of DKP-TRAM and assess the risk of adverse events (AE) (e.g. nausea, vomiting, diarrhoea, vertigo) in DKP-TRAM *vs.* tramadol monotherapy (including tramadol-paracetamol combinations) users, with a special focus on patients 75 years old and over

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI))

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

7.3.2. Valproate (NAP) - EMEA/H/N/PSR/J/0036

Applicant(s): Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Results for a joint survey among healthcare professionals (HCP) to assess knowledge of HCP and behaviour with regards to pregnancy prevention programme (PPP) as well as receipt/use of a direct healthcare professional communication (DHPC) and educational materials and survey among patients to assess knowledge of the patients with regards to PPP as well as 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)]

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI))

7.4. Results of PASS non-imposed in the marketing authorisation(s)[33]

7.4.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0038

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study MS1222-0003 (listed as a category 3 study in the RMP) as assessment of anti-platelet factor 4 (PF4) antibodies prior to, and following, vaccination with AZD1222: a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria (COVID-19 vaccine) leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesised mechanism underlying thrombosis with thrombocytopenia syndrome (TTS)

Action: For adoption of PRAC Assessment Report

7.4.2. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0078

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 20101102 (listed as a category 3 study in the RMP) as 'osteonecrosis of the jaw (ONJ) case registry': an observational PASS with the primary objective to estimate the rate and describe the time course of resolution of ONJ, in subjects 18 years of age with cancer who had newly diagnosed, positively adjudicated ONJ

Action: For adoption of PRAC Assessment Report

7.4.3. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/II/0047

Applicant: Amryt Pharmaceuticals DAC

[33] 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

PRAC Rapporteur: Menno van der Elst

Scope: Introduction of an enhanced pharmacovigilance system to evaluate the occurrence and outcomes of pregnancy in females of reproductive potential treated with lomitapide who decide to continue the pregnancy following advice from a teratologist/clinician, replacing the currently agreed pregnancy exposure register (PER) (listed as part of Annex II-E on 'specific obligation to complete post-authorisation measures for the marketing authorisation under exceptional circumstances'). The RMP (version 6.5) is updated accordingly. In addition, the MAH took the opportunity to introduce minor administrative changes

Action: For adoption of PRAC Assessment Report

7.4.4. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0034

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from study D3820R00006 (listed as a category 3 study in the RMP): an observational drug utilisation in selected European populations. The RMP (version 7.0) is updated accordingly

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. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.3

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 050.2 [first interim report for study C18477-ONC-50025: a post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox (arsenic trioxide) to assess the long-term safety of all-trans retinoic acid (ATRA) + arsenic trioxide (ATO) in newly diagnosed low to intermediate risk APL patients in a real-world clinical practice setting [final report expected in 2Q 2023]] as as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.5

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BEL115467/HGS1006-C1113: a randomized, double-blind placebo-controlled large safety study, based on a protocol agreed with CHMP, evaluating over a minimum of one year the incidence of all-cause mortality and adverse events of special interest (AESI) in patients with systemic lupus erythematosus receiving belimumab [three years' malignancy and mortality follow-up.] [final report with 5-year follow-up data expected in December 2023]

Action: For adoption of advice to CHMP

7.5.3. Coronavirus (COVID-19) mRNA[34] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.3

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591010: assessment of occurrence of safety events in real-world use of COVID-19 mRNA vaccine [final clinical study report (CSR) expected in September 2024] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.5.4. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/LEG 011.2

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 011.1 [second interim report for a national, post-registration observational study of the long-term safety and health outcome of patients treated with Defitelio (defibrotide), including patients with severe hepatic veno-occlusive disease (VOD) after hematopoietic stem-cell transplantation (HSCT) (DEFIFRANCE registry)] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

7.5.5. Imiglucerase - CEREZYME (CAP) - EMEA/H/C/000157/MEA 040.11

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Ninth interim report from the Gaucher pregnancy and lactation sub-registry to assess the pregnancy outcomes including adverse events in women with Gaucher disease, untreated and treated with Cerezyme (imiglucerase) during pregnancy. This report covers the period from 01 June 2018 to 31 May 2021

Action: For adoption of advice to CHMP

7.5.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 009

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Biennial interim report for the Chronisch Entzündliche Darmerkrankungen, ein Unabhängiges Register (CEDUR) to describe the long-term effectiveness of treatment with inflammatory bowel disease (IBD) therapies such as drug survival, effectiveness, side effects of treatment combination, and disease activity achieved

[34] Messenger ribonucleic acid

Action: For adoption of advice to CHMP

7.5.7. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 010

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Biennial interim report for the Czech Register of inflammatory bowel disease (IBD) Patients on Biological Therapy (CREDIT) to monitor effectiveness of total population of IBD patients on biological medication in the Czech Republic and regular analytical evaluation of the effectiveness

Action: For adoption of advice to CHMP

7.5.8. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.11

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Interim progress report for study D3820R00009 (EUPAS12669): an observational PASS of Moventig (naloxegol) among patients aged 18 years and older treated with opioids chronically

Action: For adoption of advice to CHMP

7.5.9. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/LEG 006.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Third yearly progress report for PASS NN7999-4031 (Paradigm 8): a non-interventional study in male haemophilia B patients receiving nonacog beta pegol (N9-GP) prophylaxis treatment to investigate the potential effects of polyethylene glycol (PEG) accumulation in the choroid plexus of the brain and other tissues/organs

Action: For adoption of advice to CHMP

7.5.10. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.12

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 0044.11 [third interval safety registry for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.11. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/LEG 013.3

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Annual report 2021 from the post-marketing Gaucher disease outcome survey (GOS) to assess the long-term safety and effectiveness of velaglucerase alfa in patients with Gaucher disease

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/MEA 004

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Interim report for study ALN-AS1-003 (ENVISION): a phase 3 randomised, double-blind, placebo-controlled, multicentre study with an open-label extension to evaluate the efficacy and safety of givosiran in patients with acute hepatic porphyrias (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.6.2. Somatropin - OMNITROPE (CAP) - EMEA/H/C/000607/MEA 010.3

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Fourth interim report for study EP00-401: a phase 4 multicentre study on the safety and efficacy of Omnitrope (somatropin) in short children born small for gestational age (SGA) and MAH's proposal to terminate interventional study EP00-401 and provide the final study report in 2022

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

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

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0087 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/S/0055 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/S/0069 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/S/0025 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

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. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/R/0045 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0027 (without RMP)

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0050 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/R/0034 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Chlormethine - LEDAGA (CAP) - EMEA/H/C/002826/R/0030 (with RMP)

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/R/0054 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/R/0030 (with RMP)

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/R/0029 (without RMP)

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL KRKA D.D. (CAP) - EMEA/H/C/004686/R/0017 (without RMP)

Applicant: KRKA, d.d., Novo mesto

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Etanercept - ERELZI (CAP) - EMEA/H/C/004192/R/0037 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Miglustat - YARGESA (CAP) - EMEA/H/C/004016/R/0011 (with RMP)

Applicant: Piramal Critical Care B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/R/0025 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/R/0025 (without RMP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/R/0044 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Pentosan polysulfate sodium - ELMIRON (CAP) - EMEA/H/C/004246/R/0024 (without RMP)

Applicant: bene-Arzneimittel GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Umeclidinium - ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/R/0019 (without RMP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ilaria Baldelli

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

10.3.1. Tirbanibulin – KLISYRI (CAP) - EMEA/H/C/005183/ANX 001

Applicant: Almirall S.A.

PRAC Rapporteur: Michal Radik; PRAC Co-Rapporteur: Rhea Fitzgerald

Scope: PRAC consultation on an interventional imposed PASS protocol for study M-14789-41 (listed as a category 1 study in Annex II): a phase 4, multicentre, randomized, evaluator-blinded, active-controlled study to determine the incidence of squamous cell carcinoma and evaluate the long-term safety and efficacy of tirbanibulin 10 mg/g ointment and diclofenac sodium 3% gel for the treatment of adult patients with actinic keratosis on the face or scalp

Action: For adoption of advice to CHMP

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

11.2.1. Fentanyl (NAP) - FR/H/PSUFU/00001369/202004

Applicant(s): Angelini farmaceutica S.A., Aurobindo, Gedeon Richter PLC, Grünenthal, Kyowa Mylan, Sandoz, Stada, Teva B.V., Yes Pharmaceuticals

PRAC Lead: Tiphaine Vaillant

Scope: Further PRAC consultation on a PSUR follow-up (PSU FU) procedure evaluating off-label use, misuse and accidental exposure, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) concluded in January 2021, following advice in July 2021, on request of France

Action: For adoption of advice to Member States

11.2.2. Methotrexate[35] (NAP) - DE/H/PSUFU/00002014/201910

Applicant(s): Addenda Pharma, Especialidades Farmacéuticas Centrum S.A., Gebro Pharma, medac, Morningside Healthcare Limited, Mylan, Nordic Group, Orion Pharma, Pfizer, Remedica, Rompharm, Sandoz, Teva

PRAC Lead: Martin Huber

Scope: Further PRAC consultation on a PSUR follow-up (PSU FU) procedure evaluating comprehensive reviews of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00002014/201910) concluded in May 2020, following advice in January 2021, on request of Germany

Action: For adoption of advice to Member States

[35] In non-oncology indication(s)

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q3 2021

Action: For discussion

12.1.3. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. Advanced therapy medicinal products (ATMP) - Impact of tocilizumab shortages on the use of chimeric antigen receptor-T (CAR-T) cell-based ATMPs in the EU

Action: For discussion

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2022

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q3 2021 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q3 2021

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.10.5. PSUR single assessment (PSUSA) recommendation for nationally approved products (NAP) - outcome of EMA survey on recommendation implementation

Action: For discussion

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

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

12.14.2. 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. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. EU pharmaceutical legislation – revision of Directive 2001/83/EC and Regulation (EC) No 726/2004

PRAC lead: Sabine Straus, Martin Huber, Amelia Cupelli, Menno van der Elst, Liana Gross-Martirosyan, Maria del Pilar Rayon, Eva Segovia, Ulla Wändel Liminga

Action: For discussion

12.21.2. Lifecycle regulatory submissions metadata project (LRSM)

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/