



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 January 2019
EMA/PRAC/10734/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 14-17 January 2019

Chair: Sabine Straus – Vice-Chair: Martin Huber

14 January 2019, 13:00 – 19:30, room 3/A

15 January 2019, 08:30 – 19:30, room 3/A

16 January 2019, 08:30 – 19:30, room 3/A

17 January 2019, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

31 January 2019, 09:00 – 12:00, room 9/B, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents ([EMA/127362/2006, Rev. 1](http://www.ema.europa.eu/127362/2006_Rev_1)).



Table of contents

1.	Introduction	13
1.1.	Welcome and declarations of interest of members, alternates and experts	13
1.2.	Agenda of the meeting on 14-17 January 2019	13
1.3.	Minutes of the previous meeting on 26-29 November 2018.....	13
2.	EU referral procedures for safety reasons: urgent EU procedures	13
2.1.	Newly triggered procedures	13
2.2.	Ongoing procedures	13
2.3.	Procedures for finalisation.....	13
2.4.	Planned public hearings	13
3.	EU referral procedures for safety reasons: other EU referral procedures	13
3.1.	Newly triggered procedures	13
3.2.	Ongoing procedures	14
3.2.1.	Methotrexate - JYLAMVO (CAP); NAP - EMEA/H/A-31/1463.....	14
3.3.	Procedures for finalisation.....	14
3.4.	Re-examination procedures.....	14
3.5.	Others	14
4.	Signals assessment and prioritisation	14
4.1.	New signals detected from EU spontaneous reporting systems	14
4.1.1.	Atezolizumab – TECENTRIQ (CAP)	14
4.2.	New signals detected from other sources	15
4.2.1.	Acetylsalicylic acid (NAP)	15
4.2.2.	Dabigatran – PRADAXA (CAP)	15
4.2.3.	Dimethyl fumarate – TECFIDERA (CAP), SKILARENCE (CAP), NAP.....	15
4.2.4.	Dipeptidyl peptidase-4 (DPP-4) inhibitors: alogliptin – VIPIDIA (CAP); linagliptin – TRAJENTA (CAP); saxagliptin – ONGLYZA (CAP); sitagliptin – JANUVIA (CAP), RISTABEN (CAP), TESAVEL (CAP), XELEVIA (CAP); vildagliptin – GALVUS (CAP), JALRA (CAP), XILIARX (CAP); Glucagon-like peptide-1 (GLP-1) receptor agonists: albiglutide – EPERZAN (CAP); dulaglutide – TRULICITY (CAP); exenatide – BYDUREON (CAP), BYETTA (CAP); liraglutide – SAXENDA (CAP), VICTOZA (CAP); lixisenatide – LYXUMIA (CAP); semaglutide – OZEMPIC (CAP)	15
4.2.5.	Pantoprazole – CONTROLLOC CONTROL (CAP), PANTOLOCC CONTROL (CAP), PANTOZOL CONTROL (CAP), SOMAC CONTROL (CAP), NAP	16
4.2.6.	Pregabalin – LYRICA (CAP), PREGABALIN ACCORD (CAP), PREGABALIN MYLAN (CAP), PREGABALIN MYLAN PHARMA (CAP), PREGABALIN PFIZER (CAP), PREGABALIN SANDOZ (CAP), PREGABALIN SANDOZ GMBH (CAP), PREGABALIN ZENTIVA (CAP), PREGABALIN ZENTIVA K.S. (CAP); NAP	16
4.2.7.	Sertraline (NAP)	16
4.2.8.	Temozolomide – TEMODAL (CAP)	17

4.2.9.	Topiramate (NAP)	17
4.3.	Signals follow-up and prioritisation	17
4.3.1.	Apixaban – ELIQUIS (CAP) - EMEA/H/C/002148/SDA/032	17
4.3.2.	Biotin (NAP)	17
4.3.3.	Dolutegravir – TIVICAY (CAP) – EMEA/H/C/002753/SDA/009; abacavir sulfate, dolutegravir sodium, lamivudine – TRIUMEQ (CAP); dolutegravir, rilpivirine – JULUCA (CAP)	18
4.3.4.	Gabapentin (NAP)	18
4.3.5.	Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/SDA/032	18

5. Risk management plans (RMPs) 18

5.1. Medicines in the pre-authorisation phase 18

5.1.1.	Ambrisentan - EMEA/H/C/004955	18
5.1.2.	Autologous CD34 ⁺ cell enriched population that contains hematopoietic stem cells transduced with LentiGlobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - EMEA/H/C/003691, Orphan.....	19
5.1.3.	Cemiplimab - EMEA/H/C/004844	19
5.1.4.	Glutamine - EMEA/H/C/004734, Orphan	19
5.1.5.	Quizartinib - EMEA/H/C/004468, Orphan	19
5.1.6.	Risankizumab - EMEA/H/C/004759	19
5.1.7.	Trientine dihydrochloride - EMEA/H/C/004111, Orphan	19

5.2. Medicines in the post-authorisation phase – PRAC-led procedures..... 20

5.2.1.	Adefovir dipivoxil - HEPSERA (CAP) - EMEA/H/C/000485/II/0081	20
5.2.2.	Aztreonam - CAYSTON (CAP) - EMEA/H/C/000996/II/0075, Orphan.....	20
5.2.3.	Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0072	20
5.2.4.	Corifollitropin alfa - ELONVA (CAP) - EMEA/H/C/001106/II/0043	20
5.2.5.	Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0078/G	21
5.2.6.	Emtricitabine, rilpivirine, tenofovir disoproxil - EVIPLERA (CAP) - EMEA/H/C/002312/II/009821	
5.2.7.	Efavirenz, emtricitabine, tenofovir disoproxil - ATRIPLA (CAP) - EMEA/H/C/000797/WS1509/0138; emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/WS1509/0158	22
5.2.8.	Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/II/0038	22
5.2.9.	Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0026.....	22
5.2.10.	Paclitaxel - ABRAXANE (CAP) - EMEA/H/C/000778/II/0092	23
5.2.11.	Sunitinib - SUTENT (CAP) - EMEA/H/C/000687/II/0073	23

5.3. Medicines in the post-authorisation phase – CHMP-led procedures 23

5.3.1.	Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/X/0117/G	23
5.3.2.	Adalimumab - CYLTEZO (CAP) - EMEA/H/C/004319/II/0006	23
5.3.3.	Adalimumab - HULIO (CAP) - EMEA/H/C/004429/II/0004	24
5.3.4.	Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0042	24
5.3.5.	Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/X/0068.....	24
5.3.6.	Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0018.....	24

5.3.7.	Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0019.....	25
5.3.8.	Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/X/0017	25
5.3.9.	Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/II/0033/G, Orphan.....	25
5.3.10.	Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0106/G	25
5.3.11.	Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/X/0025.....	26
5.3.12.	Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0026	26
5.3.13.	Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/II/0031	26
5.3.14.	Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0020, Orphan	27
5.3.15.	Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/II/0126/G.....	27
5.3.16.	Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/X/0004/G	27
5.3.17.	Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0012	28
5.3.18.	Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/II/0012	28
5.3.19.	Insulin glargine - TOUJEO (CAP) - EMEA/H/C/000309/II/0105/G	28
5.3.20.	Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0063	29
5.3.21.	Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/X/0018	29
5.3.22.	Methoxy polyethylene glycol-epoetin beta - MIRCERA (CAP) - EMEA/H/C/000739/II/0068	29
5.3.23.	Modified vaccinia Ankara virus - IMVANEX (CAP) - EMEA/H/C/002596/II/0035	29
5.3.24.	Pemetrexed - PEMETREXED FRESENIUS KABI (CAP) - EMEA/H/C/003895/X/0009	30
5.3.25.	Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0074/G	30
5.3.26.	Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0003/G	30
5.3.27.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0150	31
5.3.28.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0157	31
5.3.29.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0158	31
5.3.30.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0012	32
5.3.31.	Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/II/0012	32
5.3.32.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/II/0045/G	32

6. Periodic safety update reports (PSURs) 33

6.1.	PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only	33
6.1.1.	Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201806.....	33
6.1.2.	Alectinib - ALECENSA (CAP) - PSUSA/00010581/201807	33
6.1.3.	Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201807	33
6.1.4.	Atazanavir - REYATAZ (CAP) - PSUSA/00000258/201806	33
6.1.5.	Autologous CD34 ⁺ enriched cell fraction that contains CD34 ⁺ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) cDNA sequence - STRIMVELIS (CAP) - PSUSA/00010505/201805	34
6.1.6.	Azacitidine - VIDAZA (CAP) - PSUSA/00000274/201805	34
6.1.7.	Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/201806	34
6.1.8.	Brinzolamide, brimonidine tartrate - SIMBRINZA (CAP) - PSUSA/00010273/201806	34

6.1.9.	Budesonide - JORVEZA (CAP) - PSUSA/00010664/201807	34
6.1.10.	Cabazitaxel - JEVTANA (CAP) - PSUSA/00000476/201806	35
6.1.11.	Canakinumab - ILARIS (CAP) - PSUSA/00000526/201806	35
6.1.12.	Cenegermin - OXERVATE (CAP) - PSUSA/00010624/201807	35
6.1.13.	Chlorhexidine - UMBIPRO (Art 58) - EMEA/H/W/003799/PSUV/0004	35
6.1.14.	Cladribine - MAVENCLAD (CAP) - PSUSA/00010634/201807	35
6.1.15.	Daclatasvir - DAKLINZA (CAP) - PSUSA/00010295/201807	35
6.1.16.	Dasatinib - SPRYCEL (CAP) - PSUSA/00000935/201806	36
6.1.17.	Dimethyl fumarate - SKILARENCE (CAP) - PSUSA/00010647/201806	36
6.1.18.	Edotreotide - SOMAKIT TOC (CAP) - PSUSA/00010552/201806	36
6.1.19.	Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/201806	36
6.1.20.	Elotuzumab - EMPLICITI (CAP) - PSUSA/00010500/201805	36
6.1.21.	Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/201806	37
6.1.22.	Ertugliflozin, metformin - SEGLUROMET (CAP) - PSUSA/00010680/201806	37
6.1.23.	Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010681/201806	37
6.1.24.	Fluciclovine (¹⁸ F) - AXUMIN (CAP) - PSUSA/00010594/201805	37
6.1.25.	Follitropin delta - REKOVELLE (CAP) - PSUSA/00010554/201805	37
6.1.26.	Galsulfase - NAGLAZYME (CAP) - PSUSA/00001515/201805	37
6.1.27.	Human fibrinogen, human thrombin - EVICEL (CAP); TACHOSIL (CAP); VERASEAL (CAP) - PSUSA/00010297/201806	38
6.1.28.	Human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/201806	38
6.1.29.	Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - GARDASIL (CAP); SILGARD (CAP) - PSUSA/00001634/201805	38
6.1.30.	Hydroxycarbamide - SIKLOS (CAP) - PSUSA/00001692/201806 (with RMP)	38
6.1.31.	Icatibant - FIRAZYR (CAP) - PSUSA/00001714/201807	38
6.1.32.	Imiglucerase - CEREZYME (CAP) - PSUSA/00001727/201805	39
6.1.33.	Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/201806	39
6.1.34.	Levofloxacin - QUINSAIR (CAP) - PSUSA/00010429/201805	39
6.1.35.	Lonocotocog alfa - AFSTYLA (CAP) - PSUSA/00010559/201807	39
6.1.36.	Lutetium (¹⁷⁷ Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/201806	39
6.1.37.	Migalastat - GALAFOLD (CAP) - PSUSA/00010507/201805	39
6.1.38.	Mirabegron - BETMIGA (CAP) - PSUSA/00010031/201806	40
6.1.39.	Mixture of polynuclear iron(III)-oxyhydroxide, sucrose, and starches - VELPHORO (CAP) - PSUSA/00010296/201805	40
6.1.40.	Nevirapine - VIRAMUNE (CAP) - PSUSA/00002147/201805	40
6.1.41.	Nivolumab - OPDIVO (CAP) - PSUSA/00010379/201807	40
6.1.42.	Nonacog beta pegol - REFIXIA (CAP) - PSUSA/00010608/201806	40
6.1.43.	Nonacog gamma - RIXUBIS (CAP) - PSUSA/00010320/201806	41
6.1.44.	Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/201805	41

6.1.45.	Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/201805	41
6.1.46.	Opicapone - ONGENTYS (CAP) - PSUSA/00010516/201806.....	41
6.1.47.	Pentosan polysulfate sodium - ELMIRON (CAP) - PSUSA/00010614/201806.....	41
6.1.48.	Peramivir - ALPIVAB (CAP) - PSUSA/00010687/201806.....	41
6.1.49.	Pertuzumab - PERJETA (CAP) - PSUSA/00010125/201806	42
6.1.50.	Rilpivirine - EDURANT (CAP) - PSUSA/00009282/201805 (with RMP)	42
6.1.51.	Rotavirus vaccine monovalent (live, oral) - ROTARIX (CAP) - PSUSA/00002665/201807...	42
6.1.52.	Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201806	42
6.1.53.	Semaglutide - OZEMPIC (CAP) - PSUSA/00010671/201805	42
6.1.54.	Sildenafil - REVATIO (CAP) - PSUSA/00002700/201805.....	43
6.1.55.	Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/201806	43
6.1.56.	Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201806	43
6.1.57.	Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/201807	43
6.1.58.	Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/201807.....	43
6.1.59.	Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/201806.....	43
6.1.60.	Trametinib - MEKINIST (CAP) - PSUSA/00010262/201805.....	44
6.1.61.	Venetoclax - VENCLYXTO (CAP) - PSUSA/00010556/201806.....	44
6.2.	PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)	44
6.2.1.	Capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); ECANSYA (CAP); XELODA (CAP); NAP - PSUSA/00000531/201804.....	44
6.2.2.	Imatinib - GLIVEC (CAP); NAP - PSUSA/00001725/201805.....	44
6.2.3.	Lutetium (¹⁷⁷ Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/201806	45
6.2.4.	Measles, mumps, rubella vaccine (live, attenuated) - M-M-RVAXPRO (CAP); NAP - PSUSA/00001937/201805	45
6.2.5.	Naloxone - NYXOID (CAP); NAP - PSUSA/00010657/201805.....	45
6.2.6.	Olopatadine - OPATANOL (CAP); NAP - PSUSA/00002211/201804	45
6.3.	PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only	45
6.3.1.	5 fluorouracil, salicylic acid - PSUSA/00000008/201805	45
6.3.2.	Acemetacin - PSUSA/00000026/201805	46
6.3.3.	Acipimox (NAP) - PSUSA/00000050/201805	46
6.3.4.	Bismuth subcitrate potassium, metronidazole, tetracycline (NAP) - PSUSA/00010199/201805	46
6.3.5.	Carmustine (NAP) - PSUSA/00010349/201804.....	46
6.3.6.	Ceftriaxone (NAP) - PSUSA/00000613/201805.....	46
6.3.7.	Cefuroxime sodium (NAP) - PSUSA/00010206/201805.....	46
6.3.8.	Chlorphenoxamine hydrochloride (NAP) - PSUSA/00010361/201805.....	47
6.3.9.	Cidofovir (NAP) - PSUSA/00010558/201806.....	47

6.3.10.	Clevipidine (NAP) - PSUSA/00010288/201805	47
6.3.11.	Ebastine (NAP) - PSUSA/00001191/201805	47
6.3.12.	Fentanyl (NAP) - PSUSA/00001370/201804	47
6.3.13.	Flunarizine (NAP) - PSUSA/00001416/201805	48
6.3.14.	Human hemin (NAP) - PSUSA/00001629/201805	48
6.3.15.	Iodine (¹³¹ I) iobenguane (NAP) - PSUSA/00001764/201805	48
6.3.16.	Loperamide (NAP); loperamide, simeticone (NAP) - PSUSA/00010665/201805	48
6.3.17.	Methoxyflurane (NAP) - PSUSA/00010484/201805	48
6.3.18.	Milnacipran (NAP) - PSUSA/00002063/201804	48
6.3.19.	Misoprostol (NAP) - PSUSA/00010353/201805	49
6.3.20.	Nalbuphine (NAP) - PSUSA/00002110/201805	49
6.3.21.	Nitrous oxide (NAP); nitrous oxide, oxygen (NAP) - PSUSA/00010572/201806	49
6.3.22.	Olodaterol, tiotropium (NAP) - PSUSA/00010489/201805	49
6.3.23.	Ozenoxacin (NAP) - PSUSA/00010651/201805	49
6.3.24.	Pamidronate (NAP) - PSUSA/00002269/201805	49
6.3.25.	Patent blue V sodium (NAP) - PSUSA/00002320/201804	50
6.3.26.	Pelargonium sidoides DC and/or pelargonium reniforme Curt., radix (NAP) - PSUSA/00002329/201806	50
6.3.27.	Pholcodine (NAP) - PSUSA/00002396/201805	50
6.3.28.	Pholcodine, biclotymol, chlorphenamine maleate (NAP) - PSUSA/00010437/201804	50
6.3.29.	Praziquantel (NAP) - PSUSA/00002503/201804	50
6.3.30.	Ranitidine (NAP) - PSUSA/00002610/201805	51
6.3.31.	Tafluprost (NAP) - PSUSA/00002843/201804	51
6.3.32.	Terlipressin (NAP) - PSUSA/00002905/201804	51
6.3.33.	Thiamphenicol (NAP) - PSUSA/00002925/201805	51
6.3.34.	Treprostinil (NAP) - PSUSA/00003013/201805	51
6.4.	Follow-up to PSUR/PSUSA procedures	51
6.4.1.	Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/LEG 018	51
6.4.2.	Dibotermis alfa - INDUCTOS (CAP) - EMEA/H/C/000408/LEG 074	52
6.4.3.	Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/LEG 037	52
6.4.4.	Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/MEA 027	52
6.4.5.	Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 066.1	52
6.4.6.	Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/LEG 020	53

7. Post-authorisation safety studies (PASS) 53

7.1.	Protocols of PASS imposed in the marketing authorisation(s)	53
7.1.1.	Acitretin (NAP), alitretinoin (NAP), isotretinoin (NAP) - EMEA/H/N/PSP/J/0069	53
7.1.2.	Dexketoprofen, tramadol (NAP) - EMEA/H/N/PSP/S/0062.1	53
7.1.3.	Hydroxyethyl starch (NAP) - EMEA/H/N/PSP/J/0067	54
7.1.4.	Hydroxyethyl starch (NAP) - EMEA/H/N/PSP/S/0068	54

7.1.5.	Lesinurad – ZURAMPIC (CAP) - EMEA/H/C/PSA/S/0036	54
7.1.6.	Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSP/S/0064.1	54
7.2.	Protocols of PASS non-imposed in the marketing authorisation(s)	55
7.2.1.	Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/MEA 019.3	55
7.2.2.	Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/MEA 007.3.....	55
7.2.3.	Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/MEA 003.1.....	55
7.2.4.	Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/REC 001.1	56
7.2.5.	Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/MEA 004.3	56
7.2.6.	Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 002	56
7.2.7.	Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/MEA 006.2.....	57
7.2.8.	Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.....	57
7.2.9.	Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 002.....	57
7.2.10.	Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002.3	57
7.2.11.	Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/MEA 017.3	58
7.2.12.	Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.....	58
7.2.13.	Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/MEA 003.1	58
7.2.14.	Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 004.1	58
7.2.15.	Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/MEA 007.3	59
7.2.16.	Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/MEA 054	59
7.2.17.	Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/MEA 024.3	59
7.2.18.	Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/MEA 008.3	60
7.2.19.	Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/MEA 002.2.....	60
7.2.20.	Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/MEA 021.3	60
7.2.21.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 007.2	61
7.2.22.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 024.....	61
7.2.23.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 028.....	61
7.2.24.	Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/MEA 001	61
7.3.	Results of PASS imposed in the marketing authorisation(s).....	62
7.3.1.	Domperidone (NAP) - EMEA/H/N/PSR/J/0015.....	62
7.3.2.	Mannitol – BRONCHITOL (CAP) - EMEA/H/C/PSR/S/0020.....	62
7.3.3.	Piperaquine tetraphosphate, arteminol – EURARTESIM (CAP) - EMEA/H/C/PSR/S/0018	62
7.4.	Results of PASS non-imposed in the marketing authorisation(s).....	63
7.4.1.	Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0185.....	63
7.4.2.	Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0040.....	63
7.4.3.	Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0041.....	63
7.4.4.	Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0074/G.....	63
7.4.5.	Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1270/0216; LIFMIOR (CAP) - EMEA/H/C/004167/WS1270/0013	64

7.4.6.	Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0054	64
7.4.7.	Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0085	64
7.4.8.	Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0218.....	65
7.4.9.	Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/II/0030.....	65
7.4.10.	Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/II/0042/G	65
7.4.11.	Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0041	66
7.4.12.	Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0082	66
7.5.	Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation.....	66
7.5.1.	Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 046.8	66
7.5.2.	Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.7.....	67
7.5.3.	Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 006.4	67
7.5.4.	Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/MEA 024.1	67
7.5.5.	Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/MEA 010.4	67
7.5.6.	Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 008.1	68
7.5.7.	Human rotavirus, live attenuated - ROTARIX (CAP) - EMEA/H/C/000639/MEA 094.....	68
7.5.8.	Infliximab - REMICADE (CAP) - EMEA/H/C/000240/MEA 114.10	68
7.5.9.	Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.5.....	68
7.5.10.	Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.6.....	69
7.5.11.	Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/ANX 001.1.....	69
7.5.12.	Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/MEA 003.6	69
7.5.13.	Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.15	69
7.5.14.	Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.3	70
7.6.	Others	70
7.6.1.	Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/LEG 031	70
7.6.2.	Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/LEG 031	70
7.6.3.	Desloratadine - AERIUS (CAP) - EMEA/H/C/000313/MEA 065.4	70
7.6.4.	Desloratadine - AZOMYR (CAP) - EMEA/H/C/000310/MEA 065.4.....	71
7.6.5.	Desloratadine - NEOCLARITYN (CAP) - EMEA/H/C/000314/MEA 065.4	71
7.6.6.	Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 047.6	71
7.6.7.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 023.....	71
7.6.8.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 025.....	72
7.6.9.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 026.....	72
7.6.10.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 027.....	72
7.6.11.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 029.....	72
7.7.	New Scientific Advice	73
7.8.	Ongoing Scientific Advice	73
7.9.	Final Scientific Advice (Reports and Scientific Advice letters)	73

8.	Renewals of the marketing authorisation, conditional renewal and annual reassessments	73
8.1.	Annual reassessments of the marketing authorisation	73
8.1.1.	Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0012 (without RMP)	73
8.1.2.	Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0032 (without RMP)	73
8.2.	Conditional renewals of the marketing authorisation	73
8.2.1.	Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/R/0029 (without RMP)	73
8.2.2.	Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0033 (without RMP)	74
8.2.3.	Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - EMEA/H/C/003963/R/0019 (with RMP)	74
8.2.4.	Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0016 (without RMP)	74
8.2.5.	Pixantrone - PIXUVRI (CAP) - EMEA/H/C/002055/R/0046 (with RMP)	74
8.2.6.	Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/R/0008 (without RMP)	74
8.3.	Renewals of the marketing authorisation	75
8.3.1.	Budesonide, formoterol - BIRESPIROMAX (CAP) - EMEA/H/C/003890/R/0027 (without RMP)	75
8.3.2.	Budesonide, formoterol - DUORESP SPIROMAX (CAP) - EMEA/H/C/002348/R/0027 (without RMP)	75
8.3.3.	Capsaicin - QUTENZA (CAP) - EMEA/H/C/000909/R/0047 (with RMP)	75
8.3.4.	Everolimus - AFINITOR (CAP) - EMEA/H/C/001038/R/0060 (without RMP)	75
8.3.5.	Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/R/0049 (with RMP)	75
8.3.6.	Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - EMEA/H/C/002705/R/0018 (without RMP)	76
8.3.7.	Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/R/0031 (without RMP)	76
8.3.8.	Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/R/0051 (without RMP)	76
8.3.9.	Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/R/0027 (without RMP)	76
8.3.10.	Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/R/0029 (without RMP)	76
8.3.11.	Tacrolimus - ENVARSUS (CAP) - EMEA/H/C/002655/R/0014 (with RMP)	76
9.	Product related pharmacovigilance inspections	77
9.1.	List of planned pharmacovigilance inspections	77
9.2.	Ongoing or concluded pharmacovigilance inspections	77
9.3.	Others	77
10.	Other safety issues for discussion requested by the CHMP or the EMA	77
10.1.	Safety related variations of the marketing authorisation	77
10.1.1.	Dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/II/0032	77
10.2.	Timing and message content in relation to Member States’ safety announcements	77
10.3.	Other requests	77
10.4.	Scientific Advice	78

11. Other safety issues for discussion requested by the Member States 78

11.1. Safety related variations of the marketing authorisation.....	78
11.1.1. Methylphenidate hydrochloride (NAP) - DE/H/XXXX/WS/547	78
11.1.2. Valproate (NAP) - NL/H/xxxx/WS/0312	78
11.2. Other requests.....	78
11.2.1. Phenylephrine hydrochloride, tropicamide (NAP) - DK/H/PSUFU/00010430/201711	78
11.2.2. Rosuvastatin (NAP) - NL/H/PSUFU/00002664/201711	79
11.2.3. Ulipristal acetate - AT/H/0862/001/DC, AT/H/0863/001/DC.....	79

12. Organisational, regulatory and methodological matters 79

12.1. Mandate and organisation of the PRAC.....	79
12.2. Coordination with EMA Scientific Committees or CMDh-v	79
12.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups	79
12.3.1. Working Party with Patients' and Consumers' Organisations (PCWP) – revised mandate and composition	79
12.3.2. Working Party with Healthcare Professionals' Organisations (HCPWP) - revised mandate and composition	80
12.3.3. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP) - revised rules of procedure.....	80
12.4. Cooperation within the EU regulatory network.....	80
12.5. Cooperation with International Regulators.....	80
12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee.....	80
12.7. PRAC work plan	80
12.7.1. PRAC work plan 2019.....	80
12.8. Planning and reporting	80
12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q4 2018 and predictions	80
12.8.2. Marketing authorisation applications (MAA) forecast for 2019 – planning update dated Q4 2018	80
12.9. Pharmacovigilance audits and inspections	81
12.9.1. Pharmacovigilance systems and their quality systems	81
12.9.2. Pharmacovigilance inspections	81
12.9.3. Pharmacovigilance audits.....	81
12.10. Periodic safety update reports (PSURs) & Union reference date (EURD) list	81
12.10.1. Periodic safety update reports	81
12.10.2. Granularity and Periodicity Advisory Group (GPAG).....	81
12.10.3. PSURs repository	81
12.10.4. Union reference date list – consultation on the draft list	81
12.11. Signal management	81

12.11.1.	Signal management – feedback from Signal Management Review Technical (SMART) Working Group	81
12.12.	Adverse drug reactions reporting and additional monitoring.....	82
12.12.1.	Management and reporting of adverse reactions to medicinal products.....	82
12.12.2.	Additional monitoring	82
12.12.3.	List of products under additional monitoring – consultation on the draft list	82
12.13.	EudraVigilance database	82
12.13.1.	Activities related to full functionality	82
12.14.	Risk management plans and effectiveness of risk minimisations.....	82
12.14.1.	Risk management systems	82
12.14.2.	Tools, educational materials and effectiveness measurement of risk minimisations	82
12.15.	Post-authorisation safety studies (PASS)	82
12.15.1.	Post-authorisation Safety Studies – imposed PASS	82
12.15.2.	Post-authorisation Safety Studies – non-imposed PASS	82
12.16.	Community procedures.....	83
12.16.1.	Referral procedures for safety reasons	83
12.17.	Renewals, conditional renewals, annual reassessments.....	83
12.18.	Risk communication and transparency	83
12.18.1.	Public participation in pharmacovigilance	83
12.18.2.	Safety communication	83
12.19.	Continuous pharmacovigilance	83
12.19.1.	Incident management	83
12.20.	Others	83
12.20.1.	Drug induced hepatotoxicity – PRAC review status update	83
12.20.2.	Strategy on measuring the impact of pharmacovigilance - PRAC interest group (IG) Impact work plan 2019	83
13.	Any other business	83
14.	Explanatory notes	84

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held on 14-17 January 2019. See January 2019 PRAC minutes (to be published post February 2019 PRAC meeting).

1.2. Agenda of the meeting on 14-17 January 2019

Action: For adoption

1.3. Minutes of the previous meeting on 26-29 November 2018

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

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. Methotrexate¹ - JYLAMVO (CAP); NAP - EMEA/H/A-31/1463

Applicants: Therakind Limited (Jylamvo), various

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

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

Action: For discussion on the organisation of a stakeholder meeting

3.3. Procedures for finalisation

None

3.4. Re-examination procedures²

None

3.5. Others

None

4. Signals assessment and prioritisation³

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Atezolizumab – TECENTRIQ (CAP)

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19335 – New signal

Lead Member State(s): PT

¹ For oral use

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

³ Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

4.2. New signals detected from other sources

4.2.1. Acetylsalicylic acid (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Evaluation of data on cancer-related mortality from a single study in elderly adults

Action: For adoption of PRAC recommendation

EPITT 19317 – New signal

Lead Member State(s): HU

4.2.2. Dabigatran – PRADAXA (CAP)

Applicant(s): Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of alopecia

Action: For adoption of PRAC recommendation

EPITT 19337 – New signal

Lead Member State(s): DK

4.2.3. Dimethyl fumarate – TECFIDERA (CAP), SKILARENCE (CAP), NAP

Applicant(s): Almirall S.A (Skilarence), Biogen Netherlands B.V. (Tecfidera), various

PRAC Rapporteur: To be appointed

Scope: Signal of arthritis and arthralgia

Action: For adoption of PRAC recommendation

EPITT 19338 – New signal

Lead Member State(s): DE

4.2.4. Dipeptidyl peptidase-4 (DPP-4) inhibitors: alogliptin – VIPIDIA (CAP); linagliptin – TRAJENTA (CAP); saxagliptin – ONGLYZA (CAP); sitagliptin – JANUVIA (CAP), RISTABEN (CAP), TESAVEL (CAP), XELEVIA (CAP); vildagliptin – GALVUS (CAP), JALRA (CAP), XILIARX (CAP); Glucagon-like peptide-1 (GLP-1) receptor agonists: albiglutide – EPERZAN (CAP); dulaglutide – TRULICITY (CAP); exenatide – BYDUREON (CAP), BYETTA (CAP); liraglutide – SAXENDA (CAP), VICTOZA (CAP); lixisenatide – LYXUMIA (CAP); semaglutide – OZEMPIC (CAP)

Applicant(s): AstraZeneca AB (Bydureon, Byetta, Onglyza), Boehringer Ingelheim (Trajenta), Eli Lilly Nederland B.V. (Trulicity), GlaxoSmithKline Trading Services limited (Eperzan), Merck Sharp & Dohme B. V. (Januvia, Ristaben, Tesavel, Xelevia), Novartis Europharm Limited (Galvus, Jalra, Xiliarx), Novo Nordisk A/S (Ozempic, Saxenda, Victoza),

Sanofi-aventis groupe (Lyxumia), Takeda Pharma A/S (Vipidia)

PRAC Rapporteur: To be appointed

Scope: Signal of increased risk of cholangiocarcinoma in adults with type 2 diabetes (T2DM)

Action: For adoption of PRAC recommendation

EPITT 19343 – New signal

Lead Member State(s): IT, NL, SE, UK

4.2.5. [Pantoprazole – CONTROLOC CONTROL \(CAP\), PANTOLOC CONTROL \(CAP\), PANTOZOL CONTROL \(CAP\), SOMAC CONTROL \(CAP\), NAP](#)

Applicant(s): Takeda GmbH (Controloc Control, Pantoloc Control, Pantozol Control, Somac Control), various

PRAC Rapporteur: To be appointed

Scope: Signal of colitis microscopic

Action: For adoption of PRAC recommendation

EPITT 19342 – New signal

Lead Member State(s): UK

4.2.6. [Pregabalin – LYRICA \(CAP\), PREGABALIN ACCORD \(CAP\), PREGABALIN MYLAN \(CAP\), PREGABALIN MYLAN PHARMA \(CAP\), PREGABALIN PFIZER \(CAP\), PREGABALIN SANDOZ \(CAP\), PREGABALIN SANDOZ GMBH \(CAP\), PREGABALIN ZENTIVA \(CAP\), PREGABALIN ZENTIVA K.S. \(CAP\); NAP](#)

Applicant(s): Accord Healthcare Limited (Pregabalin Accord), Mylan S.A.S. (Pregabalin Mylan, Pregabalin Mylan Pharma), Pfizer Europe MA EEIG (Lyrica, Pregabalin Pfizer), Sandoz GmbH (Pregabalin Sandoz, Pregabalin Sandoz GmbH), Zentiva k.s. (Pregabalin Zentiva, Pregabalin Zentiva k.s.), various

PRAC Rapporteur: To be appointed

Scope: Signal of respiratory depression with and without concomitant opioid use

Action: For adoption of PRAC recommendation

EPITT 19339 – New signal

Lead Member State(s): NL

4.2.7. [Sertraline \(NAP\)](#)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of maculopathy

Action: For adoption of PRAC recommendation

EPITT 19341 – New signal

Lead Member State(s): NL

4.2.8. Temozolomide – TEMODAL (CAP)

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

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC recommendation

EPITT 19332 – New signal

Lead Member State(s): DE

4.2.9. Topiramate (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of uveitis

Action: For adoption of PRAC recommendation

EPITT 19345 – New signal

Lead Member State(s): SE

4.3. Signals follow-up and prioritisation

4.3.1. Apixaban – ELIQUIS (CAP) - EMEA/H/C/002148/SDA/032

Applicant(s): Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of pancreatitis

Action: For adoption of PRAC recommendation

EPITT 19265 – Follow up to September 2018

4.3.2. Biotin (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of interference with clinical laboratory tests

Action: For adoption of PRAC recommendation

EPITT 19156 – Follow up to June 2018

4.3.3. Dolutegravir – TIVICAY (CAP) – EMEA/H/C/002753/SDA/009; abacavir sulfate, dolutegravir sodium, lamivudine – TRIUMEQ (CAP); dolutegravir, rilpivirine – JULUCA (CAP)

Applicant(s): ViiV Healthcare B.V. (Tivicay), ViiV Healthcare UK Limited (Juluca, Triumeq)

PRAC Rapporteur: Julie Williams

Scope: Evaluation of preliminary data from an observational study on birth outcomes in human immunodeficiency virus (HIV)-infected women

Action: For adoption of PRAC recommendation

EPITT 19244 – Follow-up to October 2018

4.3.4. Gabapentin (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of dysphagia

Action: For adoption of PRAC recommendation

EPITT 19296 – Follow up to September 2018

4.3.5. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/SDA/032

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of scleroderma

Action: For adoption of PRAC recommendation

EPITT 19282 – Follow up to September 2018

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Ambrisentan - EMEA/H/C/004955

Scope: Treatment of pulmonary arterial hypertension (PAH)

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

5.1.2. Autologous CD34⁺ cell enriched population that contains hematopoietic stem cells transduced with LentiGlobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - EMEA/H/C/003691, Orphan

Applicant: Bluebird bio GmbH, ATMP⁴

Scope (accelerated assessment): Treatment of transfusion-dependent β -thalassaemia (TDT)

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

5.1.3. Cemiplimab - EMEA/H/C/004844

Scope: Treatment in monotherapy of patients with metastatic cutaneous squamous cell carcinoma

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

5.1.4. Glutamine - EMEA/H/C/004734, Orphan

Applicant: Emmaus Medical Europe Ltd

Scope: Treatment of Sickle cell disease (SCD)

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

5.1.5. Quizartinib - EMEA/H/C/004468, Orphan

Applicant: Daiichi Sankyo Europe GmbH

Scope (accelerated assessment): Treatment of acute myeloid leukaemia (AML)

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

5.1.6. Risankizumab - EMEA/H/C/004759

Scope: Treatment of psoriasis in adults

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

5.1.7. Trientine dihydrochloride - EMEA/H/C/004111, Orphan

Applicant: Univar BV

Scope: Treatment of Wilson's disease

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

⁴ Advanced therapy medicinal product

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

5.2.1. Adefovir dipivoxil - HEPSERA (CAP) - EMEA/H/C/000485/II/0081

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Update of the RMP (version 2.1) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.2. Aztreonam - CAYSTON (CAP) - EMEA/H/C/000996/II/0075, Orphan

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of the RMP (version 7.1) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.3. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0072

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 14.0) in order to revise the distribution list of educational materials (addition of dermatologists) and to revise the RMP in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template), including the update of the important identified risks and important potential risks. The PASS protocol for study UP0038 designed to assess the effectiveness of the educational material is updated to add dermatologists to the healthcare professional study population, to remove Italy and Spain from the study participation and to make additional administrative changes. In addition, the MAH took the opportunity to introduce some administrative changes in the RMP

Action: For adoption of PRAC Assessment Report

5.2.4. Corifollitropin alfa - ELONVA (CAP) - EMEA/H/C/001106/II/0043

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 8.1) in order to implement changes in line with revision 2 of the guidance on the format of RMP in the EU (template), to include data following the completion of study P017: a phase 3 follow-up trial to collect outcome and safety of frozen-thawed embryo transfer (FTET) cycles performed with the embryos cryopreserved in studies

P016 (a phase 3, randomized, double-blind, active-controlled, non-inferiority trial to investigate the efficacy and safety of a single injection of corifollitropin alfa to induce multifollicular development for controlled ovarian stimulation (COS) using daily recombinant FSH (recFSH) as a reference in women aged 35 to 42 years) and P031 (a phase 3, multicentre, open label trial to evaluate the efficacy and safety of corifollitropin alfa in combination with human chorionic gonadotropin (hCG) in inducing testicular development and spermatogenesis in adult azoospermic men with hypogonadotropic hypogonadism), as requested in the conclusion of PSUSA/00000875/201407 adopted in February 2015, and to delete the important potential risks of 'hypersensitivity' and 'lack of effect due to immunogenicity' from the list of safety concerns as requested in the conclusion of PSUSA/00000875/201707 adopted in March 2018. In addition, the MAH took the opportunity to include some data from ongoing study P043: a multicentre, open label, single-group trial to investigate the efficacy and safety of corifollitropin alfa in combination with hCG for initiation or restoration of puberty assessed by increased testicular volume in adolescent males 14 to <18 years old with hypogonadotropic hypogonadism (HH)

Action: For adoption of PRAC Assessment Report

5.2.5. [Denosumab - PROLIA \(CAP\) - EMEA/H/C/001120/II/0078/G](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of an update of the RMP (version 25) in order to: 1) bring it in line with revision 2 of GVP module V on 'Risk management systems'; 2) add study 20170534 (listed as category 3 study in the RMP): an open-label extension of the currently ongoing study 20130173 involving paediatric subjects with osteogenesis imperfecta, based on the MAH's commitment arising from Prolia (denosumab) approved paediatric investigation plan (PIP: EMEA-000145-PIP02-12): open-label, prospective, extension study; 3) add a study (listed as category 3 study in the RMP) to further characterize potential increased risk of cerebrovascular events (stroke) and other serious cardiovascular events in subjects with osteoporosis, as per the conclusion of procedure PSUSA/00000954/201709 adopted in April 2018

Action: For adoption of PRAC Assessment Report

5.2.6. [Emtricitabine, rilpivirine, tenofovir disoproxil - EVIPLERA \(CAP\) - EMEA/H/C/002312/II/0098](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 13.1) in order: to 1) implement revision 2 of the guidance on the format of RMP in the EU (template); 2) reflect changes in the categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' based on exposure data from clinical studies and post-marketing use; 3) change the MAH name from Gilead Sciences International Ltd., Cambridge, UK (GSIL) to Gilead Sciences Ireland UC, Cork, Ireland (GSIUC)

Action: For adoption of PRAC Assessment Report

5.2.7. [Efavirenz, emtricitabine, tenofovir disoproxil - ATRIPLA \(CAP\) - EMEA/H/C/000797/WS1509/0138;](#)
[emtricitabine, tenofovir disoproxil - TRUVADA \(CAP\) - EMEA/H/C/000594/WS1509/0158](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Worksharing variation consisting of an update of the RMPs (version 17.1 for Atripla and version 15.5 for Truvada) in order to: 1) reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template); 2) remove the additional risk minimisation measures for tenofovir disoproxil fumarate in the form of education materials regarding renal toxicity and bone events, with the resulting amendment of Annex II of the product information; 3) add clinical data from study GS-US-104-0352: a phase 3, randomized, open-label study comparing the safety and efficacy of switching stavudine or zidovudine to tenofovir disoproxil fumarate versus continuing stavudine or zidovudine in virologically suppressed human immunodeficiency virus (HIV)-infected children taking highly active antiretroviral therapy; 4) revise the due dates for study GS-US-276-0103 (listed as category 3 study in the RMP): a prospective, observational study of individuals who seroconvert while taking Truvada (emtricitabine/tenofovir disoproxil) for pre exposure prophylaxis (PrEP), and study GS-EU-276-4027 (listed as category 3 study in the RMP): a cross-sectional post authorisation safety study to assess healthcare provider's level of awareness of risk minimisation materials for Truvada (emtricitabine/tenofovir disoproxil) for PrEP in the European Union; 5) implement already approved administrative changes

Action: For adoption of PRAC Assessment Report

5.2.8. [Micafungin - MYCAMINE \(CAP\) - EMEA/H/C/000734/II/0038](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of the RMP (version 20.0) in order to streamline and improve the educational programme and communication to prescribing physicians as requested in the conclusion of variation II/0035 adopted in June 2018

Action: For adoption of PRAC Assessment Report

5.2.9. [Osimertinib - TAGRISSO \(CAP\) - EMEA/H/C/004124/II/0026](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 12.0) following the completion of study D6030C00001 (BLOOM study): a phase 1, open-label, multicentre study to assess the safety, tolerability, pharmacokinetics and preliminary anti-tumour activity of osimertinib (AZD9291) in patients with epidermal growth factor receptor (EGFR) mutation positive advanced stage non-small cell lung cancer (NSCLC) in order to remove 'use in patients with Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2 ' and 'use in patients with symptomatic brain metastases' as missing information

Action: For adoption of PRAC Assessment Report

5.2.10. Paclitaxel - ABRAXANE (CAP) - EMEA/H/C/000778/II/0092

Applicant: Celgene Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 17.0) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.11. Sunitinib - SUTENT (CAP) - EMEA/H/C/000687/II/0073

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Amelia Cupelli

Scope: Update of the RMP (version 17.0) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

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

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

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

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

5.3.2. Adalimumab - CYLTEZO (CAP) - EMEA/H/C/004319/II/0006

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 1297.12 (listed as a category 3 study in the RMP): efficacy, safety and immunogenicity of Cyltezo (BI 695501, adalimumab) versus Humira (adalimumab) in patients with moderate to severe chronic plaque psoriasis: a randomized, double-blind, parallel-arm, multiple-dose, active comparator trial. The RMP (version 3.0) is updated accordingly

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

5.3.3. [Adalimumab - HULIO \(CAP\) - EMEA/H/C/004429/II/0004](#)

Applicant: Mylan S.A.S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study FKB327-003 (listed as a category 3 study in the RMP): an open-label extension study to compare the long term efficacy, safety, immunogenicity and pharmacokinetics of Hulio (adalimumab) and Humira (adalimumab) in patients with rheumatoid arthritis on concomitant methotrexate (ARABESC-OLE). The RMP (version 2.0) is updated accordingly. In addition, the MAH took the opportunity to remove the product information text from Annex 6 of the RMP and proposed to only keep the text for patient alert card in the RMP as an additional risk minimisation measure

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

5.3.4. [Alirocumab - PRALUENT \(CAP\) - EMEA/H/C/003882/II/0042](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease based on the final study report of study EFC11570: a randomized, double-blind, placebo-controlled, parallel-group study to evaluate the effect of alirocumab on the occurrence of cardiovascular events in patients who have recently experienced an acute coronary syndrome. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.5. [Arsenic trioxide - TRISENOX \(CAP\) - EMEA/H/C/000388/X/0068](#)

Applicant: Teva B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application to add a new strength of 2 mg/mL. The RMP (version 2.0) is updated accordingly

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

5.3.6. [Atezolizumab - TECENTRIQ \(CAP\) - EMEA/H/C/004143/II/0018](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include Tecentriq (atezolizumab), in combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.7. [Atezolizumab - TECENTRIQ \(CAP\) - EMEA/H/C/004143/II/0019](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include Tecentriq (atezolizumab), in combination with nab-paclitaxel and carboplatin, for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have epidermal growth factor receptor (EGFR) mutant or ALK-positive NSCLC. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.8. [Atezolizumab - TECENTRIQ \(CAP\) - EMEA/H/C/004143/X/0017](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension application to add a new strength of 840 mg (60 mg/mL) for Tecentriq (atezolizumab) concentrate for solution for infusion in a vial and to add a new indication for the treatment of metastatic triple-negative breast cancer (TNBC). The new indication applies only to the 840 mg strength. The RMP (version 7.0) is updated accordingly

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

5.3.9. [Bedaquiline - SIRTURO \(CAP\) - EMEA/H/C/002614/II/0033/G, Orphan](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) extension of indication to include patients 12 years of age and older based on week 24 analysis of cohort 1 (adolescent subjects aged ≥ 12 to < 18 years) for study TMC207-C211: a phase 2, open-label, multicentre, single-arm study to evaluate the pharmacokinetics, safety, tolerability and anti-mycobacterial activity of bedaquiline (TMC207) in combination with a background regimen (BR) of multidrug resistant tuberculosis (MDR-TB) medications for the treatment of children and adolescents 0 months to < 18 years of age who have confirmed or probable pulmonary MDR-TB. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated accordingly; 2) update of section 4.9 of the SmPC to remove reference to the use of activated charcoal as an aid to remove unabsorbed bedaquiline in case of overdose

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

5.3.10. [Bevacizumab - AVASTIN \(CAP\) - EMEA/H/C/000582/II/0106/G](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of: 1) update of section 5.1 of the SmPC to reflect final overall survival data from the long-term follow-up study JO25567 (erlotinib alone or with bevacizumab as first-line therapy in patients with advanced non-squamous non-small-cell lung cancer (NSCLC) harbouring epidermal growth factor receptor (EGFR) mutations: an open-label, randomised, multicentre, phase 2 study) in order to fulfil ANX 085 for study JO29424 (survival follow up of JO25567); 2) change in the deadline for the fulfilment of ANX 086 (discussion on any further outcome data on the combination of bevacizumab and erlotinib in the first-line treatment of patients with non-squamous NSCLC harbouring EGFR activating mutations) from Q4 2018 to Q2 2019. Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 29.0) are updated accordingly. The RMP is submitted in line with revision 2 of the guidance on the format of RMP in the EU (template) and consolidates the approved versions (versions 27.1 and 28.1)

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

5.3.11. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/X/0025

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Extension application to introduce a new pharmaceutical form (film-coated tablets). The RMP (version 12) is updated accordingly

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

5.3.12. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0026

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.5 of the SmPC in order to update the safety information based on the final results from study CLDK378A2103 (listed as a category 3 study in the RMP, MEA 002): a phase 1, multicentre, open label, drug-drug interaction study to assess the effect of ceritinib on the pharmacokinetics of warfarin and midazolam administered as a two-drug cocktail in patients with anaplastic lymphoma kinase (ALK)-positive advanced tumours including non-small cell lung cancer (NSCLC). The package leaflet and the RMP (version 14) are updated accordingly

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

5.3.13. Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/II/0031

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of section 5.1 of the SmPC in order to add information on long-term efficacy and drug resistance based on final results from study AI444046 (listed as a category 3 study in the RMP): a phase 3 non-randomized, open-label, long-term follow-up and

observational study of durability of efficacy, resistance and characterization of progression of liver disease in subjects with chronic hepatitis C previously treated with daclatasvir and/or asunaprevir. In addition, the MAH took the opportunity to postpone the due date of safety study AI444427: a post-authorisation safety study of early recurrence of hepatocellular carcinoma in hepatitis C virus (HCV)-infected patients after direct-acting antiviral therapy (DAA PASS) evaluating recurrence of hepatocellular carcinoma from Q2 2021 to Q2 2023. Annex II and the RMP (version 6.0) are updated accordingly

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

5.3.14. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0020, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

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

5.3.15. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/II/0126/G

Applicant: Apotex Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of an update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update safety information on the use of Ferriprox (deferiprone) in patients with renal or hepatic impairment, based on the final results of two clinical studies (listed as category 3 studies in the RMP): 1) study LA39-0412: an open-label study to compare the pharmacokinetic profiles of a single dose of Ferriprox (deferiprone) in subjects with impaired renal function and healthy volunteers; 2) study LA40-0412: an open-label study to compare the pharmacokinetic profiles of a single dose of Ferriprox in subjects with impaired hepatic function and healthy volunteers. The package leaflet and labelling are updated accordingly. The RMP (version 13.1) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to introduce minor editorial changes in the product information

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

5.3.16. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/X/0004/G

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP); 2) extensions of indication to add as indications: 'add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal

product for maintenance treatment, including those with or without an eosinophilic phenotype', 'maintenance therapy to improve lung function' and 'maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients' based on pivotal studies, namely study DRI12544: a randomized, double-blind, placebo-controlled, dose-ranging study to evaluate dupilumab in patients with moderate to severe uncontrolled asthma; study LIBERTY ASTHMA QUEST: a randomized, double blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of dupilumab in patients with persistent asthma; and study VENTURE: a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of dupilumab in patients with severe steroid dependent asthma. As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths

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

5.3.17. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0012

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to extend the adult atopic dermatitis indication to the paediatric, 12 years to 17 years (adolescent) patients under Article 8 of Regulation (EC) No 1901/2006 on medicinal products for paediatric use. The package leaflet and the RMP (version 3.0) are updated accordingly

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

5.3.18. Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/II/0012

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to extend the Maviret (glecaprevir/pibrentasvir) indication to adolescents from 12 to 18 years of age with chronic hepatitis C infection, based on new clinical data from study M16-123: an open-label, multicentre study to evaluate the pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in paediatric subjects with genotypes 1-6 chronic hepatitis C virus infection (DORA), using the adult co-formulated tablets in adolescents. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. In addition, the RMP (version 4.0) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

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

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations to introduce a new 3 mL pre-filled pen. Introduction of four new

pack sizes: packs of 1, 3, 6 (multipack) and 9 pens (multipack). As a consequence, Annex A, I, IIA and IIIB are amended. In addition, the RMP (version 5.0) in line with revision 2 of the guidance on the format of RMP in the EU (template) is updated accordingly

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

5.3.20. [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/II/0063](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4 and 4.8 of the SmPC and of Annex II in order to add safety information regarding graft versus host disease (GVHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients after treatment with ipilimumab. The update is based on a review of post-marketing data. The package leaflet and the RMP (version 25.0) are updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes in the product information and to reflect changes to the RMP as requested in the conclusions of previous procedures

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

5.3.21. [Mepolizumab - NUCALA \(CAP\) - EMEA/H/C/003860/X/0018](#)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen). The RMP (version 4.0) is updated accordingly

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

5.3.22. [Methoxy polyethylene glycol-epoetin beta - MIRCERA \(CAP\) - EMEA/H/C/000739/II/0068](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report for study BH21260 (listed as a category 3 study in the RMP): a randomized, controlled, open-label, multicentre, parallel-group study to assess all-cause mortality and cardiovascular morbidity in patients with chronic kidney disease (CKD) on dialysis and those not on renal replacement therapy under treatment with Mircera (methoxy polyethylene glycol-epoetin beta) or erythropoiesis-stimulating agents (ESAs) of reference (in fulfilment of post-approval commitment MEA 008.5). The RMP (version 12.0) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.23. [Modified vaccinia Ankara virus - IMVANEX \(CAP\) - EMEA/H/C/002596/II/0035](#)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and to add urticaria as an adverse reaction following the final results from study POX-MVA-037 (listed as a category 3 study in the RMP (post-authorisation measure MEA 007)): a phase 2, randomized, open-label, multicentre trial designed to evaluate the safety and immunogenicity of Imvanex (modified vaccinia Ankara-Bavarian Nordic (MVA-BN) live virus smallpox vaccine) when increasing the dose or the number of injections compared with the standard 2-dose regimen in a population of adult, vaccinia naive, immunocompromised subjects with human immunodeficiency virus (HIV) infection. The RMP (version 7.1) is updated accordingly. Furthermore, the product information is brought in line with the latest the quality review of documents (QRD) template (version 10)

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

5.3.24. Pemetrexed - PEMETREXED FRESENIUS KABI (CAP) - EMEA/H/C/003895/X/0009

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/mL. The RMP (version 2.0) is updated accordingly

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

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

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

5.3.26. Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0003/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of: 1) update of section 5.2 of the SmPC in order to reflect results from study CLEE011A2109: a phase 1, open label, multicentre, parallel cohort, single dose study to evaluate the pharmacokinetics (PK) of ribociclib (LEE011) in healthy subjects with normal hepatic function and subjects with impaired hepatic function;

2) update of sections 4.2 and 5.2 of the SmPC in order to reflect results from study CLEE011A2116-Part I: a phase 1, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of ribociclib (LEE011) in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function. The RMP (version 2.0) is updated accordingly

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

5.3.27. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0150

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the treatment of patients with moderate to severe pemphigus vulgaris (PV). As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 17.0) are updated accordingly

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

5.3.28. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0157

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

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

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

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product', resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1,400 mg by the submission of the final

clinical study report for study BO25341 (SAWYER, listed as a category 1 study) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SAWYER is a phase Ib adaptive, comparative, randomized, parallel-group, multicentre study of subcutaneous (SC) rituximab versus intravenous (IV) rituximab both in combination with chemotherapy (fludarabine and cyclophosphamide), in patients with previously untreated chronic lymphocytic leukaemia (CLL). The RMP (version 19.0) is updated accordingly. In addition, the MAH took the opportunity to include the changes on the concluded commitment such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation

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

5.3.30. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0012

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension application to introduce a new pharmaceutical form (prolonged-release tablet) associated with a new strength (11 mg), and presented in pack sizes of 28, 30, 90 and 91 tablets. The extension of indication includes a change in pharmacokinetics. The RMP (version 4.0) is updated accordingly

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

5.3.31. Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/II/0012

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, platinum-, and either a taxane- or irinotecan-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. The RMP (version 6.1) is also updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.32. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/II/0045/G

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of final study reports from five mechanistic in vitro studies, namely, 3083-N03-050: inhibition of multidrug resistance-associated protein 2 (MRP2) in vitro in membrane vesicles (PAM MEA 020), 3083-N04-050: cell viability in 3D spheroid micro-tissues (PAM MEA 021), 3083-N05-050: cell viability in 'sandwich' (PAM MEA 022), 3083-N01-050: effects of ulipristal acetate (UPA) and its main metabolite PGL4002 on

mitochondrial function and cell health markers in vitro in HepG2⁵ cells (PAM REC) and 3083-N02-050: in vitro interaction studies of UPA and PGL4002 test articles with human bile salt export pump (BSEP), MRP3 (multidrug resistance-associated protein 3) and multidrug resistance-associated protein 4 (MRP4) efflux (ABC) transporters and with the human sodium/taurocholate co-transporting polypeptide (NTCP) uptake transporter (PAM REC), as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMA/H/A-20/1460). The RMP (version 16.1) 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. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201806

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alectinib - ALECENSA (CAP) - PSUSA/00010581/201807

Applicant: Roche Registration GmbH

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201807

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Atazanavir - REYATAZ (CAP) - PSUSA/00000258/201806

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Adrien Inoubli

⁵ Human liver cancer cell line

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. [Autologous CD34⁺ enriched cell fraction that contains CD34⁺ cells transduced with retroviral vector that encodes for the human adenosine deaminase \(ADA\) cDNA sequence - STRIMVELIS \(CAP\) - PSUSA/00010505/201805](#)

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP⁶

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.6. [Azacitidine - VIDAZA \(CAP\) - PSUSA/00000274/201805](#)

Applicant: Celgene Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. [Blinatumomab - BLINCYTO \(CAP\) - PSUSA/00010460/201806](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. [Brinzolamide, brimonidine tartrate - SIMBRINZA \(CAP\) - PSUSA/00010273/201806](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. [Budesonide⁷ - JORVEZA \(CAP\) - PSUSA/00010664/201807](#)

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

⁶ Advanced therapy medicinal product

⁷ Centrally authorised product(s) only

6.1.10. Cabazitaxel - JEVTANA (CAP) - PSUSA/00000476/201806

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Canakinumab - ILARIS (CAP) - PSUSA/00000526/201806

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/201807

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Chlorhexidine - UMBIPRO (Art 58⁸) - EMEA/H/W/003799/PSUV/0004

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cladribine⁹ - MAVENCLAD (CAP) - PSUSA/00010634/201807

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Daclatasvir - DAKLINZA (CAP) - PSUSA/00010295/201807

Applicant: Bristol-Myers Squibb Pharma EEIG

⁸ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

⁹ Indicated in the treatment of multiple sclerosis (MS)

PRAC Rapporteur: Ana Sofia Diniz Martins
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.16. Dasatinib - SPRYCEL (CAP) - PSUSA/00000935/201806

Applicant: Bristol-Myers Squibb Pharma EEIG
PRAC Rapporteur: Doris Stenver
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.17. Dimethyl fumarate¹⁰ - SKILARENCE (CAP) - PSUSA/00010647/201806

Applicant: Almirall S.A
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.18. Edotreotide - SOMAKIT TOC (CAP) - PSUSA/00010552/201806

Applicant: Advanced Accelerator Applications
PRAC Rapporteur: Ronan Grimes
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.19. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/201806

Applicant: Swedish Orphan Biovitrum AB (publ)
PRAC Rapporteur: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.20. Elotuzumab - EMLICITI (CAP) - PSUSA/00010500/201805

Applicant: Bristol-Myers Squibb Pharma EEIG
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹⁰ Indicated in the treatment of psoriasis

6.1.21. Ertugliflozin - STEGLATRO (CAP) - PSUSA/00010682/201806

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ertugliflozin, metformin - SEGLUROMET (CAP) - PSUSA/00010680/201806

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - PSUSA/00010681/201806

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Fluciclovine (¹⁸F) - AXUMIN (CAP) - PSUSA/00010594/201805

Applicant: Blue Earth Diagnostics Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Follitropin delta - REKOVELLE (CAP) - PSUSA/00010554/201805

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Galsulfase - NAGLAZYME (CAP) - PSUSA/00001515/201805

Applicant: BioMarin International Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. [Human fibrinogen, human thrombin - EVICEL \(CAP\); TACHOSIL \(CAP\); VERASEAL \(CAP\) - PSUSA/00010297/201806](#)

Applicants: Instituto Grifols, S.A. (VeraSeal), Omrix Biopharmaceuticals N. V. (Evicel), Takeda Austria GmbH (TachoSil)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. [Human papillomavirus vaccine \[types 6, 11, 16, 18, 31, 33, 45, 52, 58\] \(recombinant, adsorbed\) - GARDASIL 9 \(CAP\) - PSUSA/00010389/201806](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. [Human papillomavirus vaccine \[types 6, 11, 16, 18\] \(recombinant, adsorbed\) - GARDASIL \(CAP\); SILGARD \(CAP\) - PSUSA/00001634/201805](#)

Applicant: Merck Sharp & Dohme Limited (Silgard), MSD Vaccins (Gardasil)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. [Hydroxycarbamide¹¹ - SIKLOS \(CAP\) - PSUSA/00001692/201806 \(with RMP\)](#)

Applicant: Addmedica S.A.S.

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. [Icatibant - FIRAZYR \(CAP\) - PSUSA/00001714/201807](#)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹¹ Centrally authorised product(s) only

6.1.32. Imiglucerase - CERZYME (CAP) - PSUSA/00001727/201805

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/201806

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Levofloxacin¹² - QUINSAIR (CAP) - PSUSA/00010429/201805

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Lonococog alfa - AFSTYLA (CAP) - PSUSA/00010559/201807

Applicant: CSL Behring GmbH

PRAC Rapporteur: Daniela Philadelphly

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Lutetium (¹⁷⁷Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/201806

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Migalastat - GALAFOLD (CAP) - PSUSA/00010507/201805

Applicant: Amicus Therapeutics UK Ltd

PRAC Rapporteur: Ulla Wändel Liminga

¹² Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. [Mirabegron - BETMIGA \(CAP\) - PSUSA/00010031/201806](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. [Mixture of polynuclear iron\(III\)-oxyhydroxide, sucrose, and starches - VELPHORO \(CAP\) - PSUSA/00010296/201805](#)

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. [Nevirapine - VIRAMUNE \(CAP\) - PSUSA/00002147/201805](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. [Nivolumab - OPDIVO \(CAP\) - PSUSA/00010379/201807](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. [Nonacog beta pegol - REFIXIA \(CAP\) - PSUSA/00010608/201806](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Nonacog gamma - RIXUBIS (CAP) - PSUSA/00010320/201806

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/201805

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/201805

Applicant: Intercept Pharma Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Opicapone - ONGENTYS (CAP) - PSUSA/00010516/201806

Applicant: Bial - Portela & C^a, S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Pentosan polysulfate sodium¹³ - ELMIRON (CAP) - PSUSA/00010614/201806

Applicant: bene-Arzneimittel GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Peramivir - ALPIVAB (CAP) - PSUSA/00010687/201806

Applicant: Biocryst UK Limited

PRAC Rapporteur: Ulla Wändel Liminga

¹³ Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Pertuzumab - PERJETA (CAP) - PSUSA/00010125/201806

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Rilpivirine - EDURANT (CAP) - PSUSA/00009282/201805 (with RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Rotavirus vaccine monovalent (live, oral) - ROTARIX (CAP) - PSUSA/00002665/201807

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/201806

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Semaglutide - OZEMPIC (CAP) - PSUSA/00010671/201805

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Sildenafil¹⁴ - REVATIO (CAP) - PSUSA/00002700/201805

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/201806

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201806

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/201807

Applicant: CO.DON AG, ATMP¹⁵

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.58. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/201807

Applicant: Vanda Pharmaceuticals Ltd.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/201806

Applicant: Merck Sharp & Dohme B.V.

¹⁴ Indicated for the treatment of pulmonary arterial hypertension (PAH)

¹⁵ Advanced therapy medicinal product

PRAC Rapporteur: Maria del Pilar Rayon
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.60. [Trametinib - MEKINIST \(CAP\) - PSUSA/00010262/201805](#)

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Patrick Batty
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.61. [Venetoclax - VENCLYXTO \(CAP\) - PSUSA/00010556/201806](#)

Applicant: AbbVie Deutschland GmbH & Co. KG
PRAC Rapporteur: Patrick Batty
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. [Capecitabine - CAPECITABINE ACCORD \(CAP\); CAPECITABINE MEDAC \(CAP\); ECANSYA \(CAP\); XELODA \(CAP\); NAP - PSUSA/00000531/201804](#)

Applicants: Accord Healthcare Limited (Capecitabine Accord), Krka, d.d., Novo mesto (Ecansya), Medac Gesellschaft für klinische Spezialpräparate mbH (Capecitabine medac), Roche Registration GmbH (Xeloda), various
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.2.2. [Imatinib - GLIVEC \(CAP\); NAP - PSUSA/00001725/201805](#)

Applicants: Novartis Europharm Limited, various
PRAC Rapporteur: Eva Segovia
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.2.3. Lutetium (¹⁷⁷Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/201806

Applicants: I.D.B. Holland B.V. (LuMark), ITG Isotope Technologies Garching GmbH (EndolucinBeta), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Measles, mumps, rubella vaccine (live, attenuated) - M-M-RVAXPRO (CAP); NAP - PSUSA/00001937/201805

Applicants: MSD Vaccins, various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Naloxone¹⁶ - NYXOID (CAP); NAP - PSUSA/00010657/201805

Applicants: Mundipharma Corporation (Ireland) Limited (Nyxoid), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Olopatadine - OPATANOL (CAP); NAP - PSUSA/00002211/201804

Applicants: Novartis Europharm Limited (Opatanol), various

PRAC Rapporteur: Ronan Grimes

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. 5 fluorouracil, salicylic acid - PSUSA/00000008/201805

Applicant(s): various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁶ For use in non-medical settings only

6.3.2. Acemetacin - PSUSA/00000026/201805

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Acipimox (NAP) - PSUSA/00000050/201805

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Bismuth subcitrate potassium, metronidazole, tetracycline (NAP) - PSUSA/00010199/201805

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Carmustine¹⁷ (NAP) - PSUSA/00010349/201804

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ceftriaxone (NAP) - PSUSA/00000613/201805

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Cefuroxime sodium¹⁸ (NAP) - PSUSA/00010206/201805

Applicant(s): various

¹⁷ Powder and solvent for solution for infusion only

¹⁸ Intracameral use only

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Chlorphenoxamine hydrochloride (NAP) - PSUSA/00010361/201805

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Cidofovir (NAP) - PSUSA/00010558/201806

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Clevidipine (NAP) - PSUSA/00010288/201805

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Ebastine (NAP) - PSUSA/00001191/201805

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Fentanyl¹⁹ (NAP) - PSUSA/00001370/201804

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁹ Transdermal patches and solution for injection only

6.3.13. Flunarizine (NAP) - PSUSA/00001416/201805

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Human hemin (NAP) - PSUSA/00001629/201805

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Iodine (¹³¹I) iobenguane (NAP) - PSUSA/00001764/201805

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Loperamide (NAP); loperamide, simeticone (NAP) - PSUSA/00010665/201805

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Methoxyflurane (NAP) - PSUSA/00010484/201805

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Milnacipran (NAP) - PSUSA/00002063/201804

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Misoprostol²⁰ (NAP) - PSUSA/00010353/201805

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Nalbuphine (NAP) - PSUSA/00002110/201805

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Nitrous oxide (NAP); nitrous oxide, oxygen (NAP) - PSUSA/00010572/201806

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Olodaterol, tiotropium (NAP) - PSUSA/00010489/201805

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Ozenoxacin (NAP) - PSUSA/00010651/201805

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Pamidronate (NAP) - PSUSA/00002269/201805

Applicant(s): various

²⁰ Gynaecological indication - labour induction only

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. [Patent blue V sodium \(NAP\) - PSUSA/00002320/201804](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. [Pelargonium sidoides DC and/or pelargonium reniforme Curt., radix \(NAP\) - PSUSA/00002329/201806](#)

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. [Pholcodine \(NAP\) - PSUSA/00002396/201805](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. [Pholcodine, bictotymol, chlorphenamine maleate \(NAP\) - PSUSA/00010437/201804](#)

Applicant(s): various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. [Praziquantel \(NAP\) - PSUSA/00002503/201804](#)

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Ranitidine (NAP) - PSUSA/00002610/201805

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Tafluprost (NAP) - PSUSA/00002843/201804

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Terlipressin (NAP) - PSUSA/00002905/201804

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Thiamphenicol (NAP) - PSUSA/00002925/201805

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Treprostinil (NAP) - PSUSA/00003013/201805

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/LEG 018

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Detailed review of the signal of hepatic failure in patients with Child-Pugh A (compensated) as requested in the conclusions of PSUSA/00010363/201801 adopted in September 2018

Action: For adoption of advice to CHMP

6.4.2. [Dibotermin alfa - INDUCTOS \(CAP\) - EMEA/H/C/000408/LEG 074](#)

Applicant: Medtronic BioPharma B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Detailed evaluation of the effectiveness of the current educational materials as requested in the conclusions of PSUSA/00001034/201709 adopted in April 2018

Action: For adoption of advice to CHMP

6.4.3. [Fingolimod - GILENYA \(CAP\) - EMEA/H/C/002202/LEG 037](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Review of the potential benefit of Gilenya (fingolimod) use in pregnant women and women of child-bearing potential (WCBP) not using effective contraception, as well as up-to-date information on reproductive toxicity, as requested in the conclusions of PSUSA/00001393/201802 adopted in September 2018

Action: For adoption of a list of questions (LoQ) for a Scientific Advisory Group on Neurology (SAG-N) meeting

6.4.4. [Ibrutinib - IMBRUVICA \(CAP\) - EMEA/H/C/003791/MEA 027](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Feasibility assessment report for a study (listed as category 3 study in the RMP) designed to further understand the effect of ibrutinib on various component functions of the innate and adaptive immune systems as requested in the conclusions of procedure PSUSA/00010301/201611 adopted in June 2017

Action: For adoption of advice to CHMP

6.4.5. [Natalizumab - TYSABRI \(CAP\) - EMEA/H/C/000603/LEG 066.1](#)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to LEG 066 [detailed study report of the retrospective analysis of extended interval dosing (EID) versus standard interval dosing (SID), a proposal for further investigation of efficacy and safety in terms of progressive multifocal leukoencephalopathy (PML) risk reduction with EID relative to SID, and updated pharmacokinetic/pharmacodynamic (PK/PD) modelling taking into account body weight and

extended dosing intervals, as requested in the conclusions of PSUSA/00002127/201708 adopted by PRAC in March 2018] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

6.4.6. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/LEG 020

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Detailed review of the signal of hepatic failure in patients with Child-Pugh A (compensated) as requested in the conclusions of PSUSA/00010367/201801 adopted in September 2018

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

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

7.1.1. Acitretin (NAP), alitretinoin (NAP), isotretinoin (NAP) - EMEA/H/N/PSP/J/0069

Applicant: F. Hoffmann-La Roche Ltd.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Protocol for a joint drug utilisation study (DUS) to describe the prescribing practices before and after the update of the pregnancy prevention programme (PPP) for the following oral retinoids: acitretin, alitretinoin and isotretinoin in order to assess the effectiveness of the updated risk minimisation measures (RMMs) in women of childbearing potential, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC for retinoids for oral use completed in 2018 (EMEA/H/A-31/1446)

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

7.1.2. Dexketoprofen, tramadol (NAP) - EMEA/H/N/PSP/S/0062.1

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

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to PSP/S/0062 [PASS protocol for a drug utilisation study (DUS) 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] as per the request for supplementary information (RSI) adopted in June 2018

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

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

7.1.3. Hydroxyethyl starch (NAP) - EMEA/H/N/PSP/J/0067

Applicant(s): Fresenius Kabi Deutschland GmbH, B. Braun Melsungen AG

PRAC Rapporteur: Adrien Inoubli

Scope: Protocol for a joint retrospective, multinational, drug utilisation study (DUS) to assess the non-adherence of physicians in hydroxyethyl starch (HES) accredited hospitals to the approved European product information regarding indication for use, contraindications and posology (dosage) for HES 130-containing medicinal products in clinical routine after implementation of a set of risk minimisation measures, as required in the outcome of the referral procedure under Article 107i of Directive 2001/83/EC for HES completed in 2018 (EMEA/H/A-107i/1457)

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

7.1.4. Hydroxyethyl starch (NAP) - EMEA/H/N/PSP/S/0068

Applicant: Serumwerk Bernburg AG

PRAC Rapporteur: Adrien Inoubli

Scope: Protocol for a retrospective, multinational, drug utilisation study (DUS) to assess the non-adherence of physicians in hydroxyethyl starch (HES) accredited hospitals to the approved European product information regarding indication for use, contraindications and posology (dosage) for HES 130-containing medicinal products in clinical routine after implementation of a set of risk minimisation measures, as required in the outcome of the referral procedure under Article 107i of Directive 2001/83/EC for HES completed in 2018 (EMEA/H/A-107i/1457)

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

7.1.5. Lesinurad – ZURAMPIC (CAP) - EMEA/H/C/PSA/S/0036

Applicant: Grünenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Amendment to a previously agreed protocol in June 2017 (PSP/S/0050.2) for a study to further characterise the cardiovascular safety of lesinurad in combination with a xanthine oxidase inhibitor (XOI) (lesinurad + XOI cohort) in patients aged 18 years and older who have a diagnosis of gout compared with similar patients who are continuing treatment with XOI monotherapy (XOI mono cohort)

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

7.1.6. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSP/S/0064.1

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG (Medikinet)

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0064 [protocol for a multicentre, observational,

prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice] as per the request for supplementary information (RSI) adopted in July 2018

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

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

7.2.1. Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/MEA 019.3

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 019.2 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.2. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/MEA 007.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 007.2 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.3. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/MEA 003.1

Applicant: Sanofi-aventis groupe

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

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to MEA 003 [protocol for study R668-AD-1639 pregnancy registry: a safety study to monitor pregnancy and infant outcomes following administration of dupilumab during planned or unexpected pregnancy in North America] as per the request for supplementary information (RSI) adopted in April 2018

Action: For adoption of advice to CHMP

7.2.4. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/REC 001.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to REC 001 [protocol for study R668-AD-1225: a non-imposed, interventional PASS: an open-label study of dupilumab in patients with atopic dermatitis who participated in previous dupilumab clinical trials, five year open label extension study] as per the request for supplementary information (RSI) adopted at the November 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.2.5. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/MEA 004.3

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 004.2 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.6. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Protocol for study BO40853: a PASS based on healthcare professional (HCP) and patient/carer survey to evaluate the awareness, knowledge and compliance of HCPs and patients/carers to the additional risk minimisation measures (guide for HCPs, patient/carer guide, patient alert card), in relation to the safety concerns of thromboembolic events, thrombotic microangiopathy as well as life-threatening bleeding due to misinterpretation of the standard coagulation tests [final study report due date: 30/04/2021] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.7. Glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/MEA 006.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 006.1 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.8. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001

Applicant: Akcea Therapeutics UK Ltd.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for a retrospective chart review for evaluating adherence to and effectiveness of the proposed platelet monitoring schedule, proposed cut-off points, dose adaptation, and initiation of corticosteroids on thrombocyte recovery (from opinion/MA)

Action: For adoption of advice to CHMP

7.2.9. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 002

Applicant: Akcea Therapeutics UK Ltd.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for a study to evaluate and further characterize the events of thrombocytopenia, glomerulonephritis and retinal toxicity/eye disease related to vitamin A deficiency when Tegsedi (inotersen) is prescribed in normal clinical practice (from opinion/MA)

Action: For adoption of advice to CHMP

7.2.10. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002.3

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 002.2 [protocol for a study/survey (listed as a category 3 study in the RMP): a cross-sectional multinational, multichannel survey conducted among healthcare professionals and patients to measure the effectiveness of Suliqua (insulin glargine/lixisenatide) educational materials set up to evaluate the knowledge and

understanding of the key safety messages in the healthcare professional guide and the patient guide] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.11. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/MEA 017.3

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 017.2 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.12. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Annika Folin

Scope: Protocol for an observational study to characterise hepatic related toxicity and overall safety profile in real-life conditions in the EU (Western population) in hepatocellular carcinoma (HCC) patients, including patients with Child-Pugh B

Action: For adoption of advice to CHMP

7.2.13. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/MEA 003.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 003 [protocol for study B1971060: a phase 4, open-label, single-arm trial, to describe the safety, tolerability and immunogenicity of Trumenba (bivalent rLP2086 vaccine) when administered in immunocompromised subjects \geq 10 years of age] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.14. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 004.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 004 [protocol for study BA39730 (listed as a category 3 study in the RMP): a long term surveillance study to assess and characterize the long-term safety data from the use of ocrelizumab in treated patients with multiple sclerosis (MS) [final report due date expected in 12/2028] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.15. [Ombitasvir, paritaprevir, ritonavir - VIEKIRAX \(CAP\) - EMEA/H/C/003839/MEA 007.3](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 007.2 including a revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.16. [Sirolimus - RAPAMUNE \(CAP\) - EMEA/H/C/000273/MEA 054](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study B1741224: a non-interventional observational PASS to present additional long-term safety and effectiveness data on patients with sporadically lymphangiioleiomyomatosis (S-LAM) treated with sirolimus, as requested in the conclusion of variation II/164 finalised in June 2018

Action: For adoption of advice to CHMP

7.2.17. [Sofosbuvir - SOVALDI \(CAP\) - EMEA/H/C/002798/MEA 024.3](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 024.2 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.18. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/MEA 008.3

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 008.2 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.19. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/MEA 002.2

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 002.1 including revised protocol version 2 [feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) using the Veterans Health Administration Cohort (listed as category 3 study in RMP) as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.2.20. Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/MEA 021.3

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to 021.3 [amendment to the previously agreed protocol in July 2016 for study CLDE225A2404: a non-interventional, multi-national, multicentre PASS to assess the long-term safety and tolerability of Odomzo (sonidegib) administered in patients with locally advanced basal cell carcinoma (laBCC), in order to execute and update the milestones, sample size and execution methods] as per the request for supplementary information (RSI) adopted in October 2018

Action: For adoption of advice to CHMP

7.2.21. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 007.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 007.1 [protocol for a non-interventional PASS study A3921298 (listed as a category 3 study in the RMP) evaluating the effectiveness of additional risk minimisation measures (aRMM) for Xeljanz (tofacitinib) in the European Union via a survey of healthcare professionals (HCPs) considered as an additional pharmacovigilance activity in the RMP] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.22. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 024

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Protocol for study PGL18-002: a retrospective, multi-national, comparative, non-interventional cohort study to investigate the risk of liver injury possibly associated with Esmya (ulipristal acetate) use based on data from various national electronic health record based databases in Europe [final study report expected by Q4 2019] as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.2.23. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 028

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Protocol for study PGL18-001: a retrospective drug utilisation study (DUS) through a chart review across four major EU countries [final study report expected by Q2 2020], as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.2.24. Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/MEA 001

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study VON (BAX0111) VWF-500 COL (listed as category 3 study in the RMP): a real world safety and effectiveness study of factor replacement for clinically severe von Willebrand disease (VWD) [interim report due date: 30/06/2019; final report due date: 30/06/2022] (as requested in initial opinion/MA)

Action: For adoption of advice to CHMP

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

7.3.1. Domperidone (NAP) - EMEA/H/N/PSR/J/0015

Applicant: Janssen Pharmaceutical Companies of Johnson & Johnson

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to PSR/S/0015 [results of a drug utilisation study (DUS) of domperidone in Europe using databases to investigate the effectiveness of risk minimisation measures and to describe the prescribing patterns before and after the changes to the domperidone label in routine clinical practice in selected European countries, as required in the conclusions of the referral procedure under Article 31 of Directive 2001/83/EC concluded in 2013] as per the request for supplementary information (RSI) adopted in September 2018

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

7.3.2. Mannitol – BRONCHITOL (CAP) - EMEA/H/C/PSR/S/0020

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Results of an observational 5 year safety study to assess the identified and potential risks of Bronchitol (mannitol) in cystic fibrosis (CF) through a comparison between Bronchitol-exposed patients and unexposed patients matched for key characteristics

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

7.3.3. Piperaquine tetraphosphate, arteminol – EURARTESIM (CAP) - EMEA/H/C/PSR/S/0018

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Julie Williams

Scope: MAH's response to PSR/S/0018 [results of a safety registry study in the EU assessing the association between the QTc prolongation induced by Eurartesim (piperaquine tetraphosphate/arteminol) and various factors, co-morbidities and concomitant medications, as well as at monitoring patterns of drug utilisation] as per the request for supplementary information (RSI) adopted in September 2018

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

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

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

7.4.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0185

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from the Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) registry (listed as a category 3 study in the RMP): an ongoing long-term observational cohort study initiated in Germany in 2001 by the German Society of Rheumatology to investigate the long-term safety, effectiveness, and costs of biologic therapies for rheumatoid arthritis

Action: For adoption of PRAC Assessment Report

7.4.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0040

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for study RRA-21651: a retrospective, observational, new-user cohort study using 4 administrative claims databases in the US, undertaken to investigate the incidence of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with sodium-glucose cotransporter 2 (SGLT2) inhibitors or other antihyperglycemic agents

Action: For adoption of PRAC Assessment Report

7.4.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0041

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final clinical study report (CSR) for study RRA-21651: a retrospective, observational, new-user cohort study using 4 administrative claims databases in the US, undertaken to investigate the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus (T2DM) treated with sodium-glucose cotransporter 2 (SGLT2) inhibitors or other antihyperglycemic agents

Action: For adoption of PRAC Assessment Report

7.4.4. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0074/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) submission of the final report from study RA0021 (Anti-Rheumatic Therapies in Sweden (ARTIS) registry) (listed as a category 3

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

studies in the RMP): registry to gather short- and long-term safety data from the use of certolizumab pegol (CZP) in Sweden for rheumatoid arthritis (RA) patients.; 2) submission of the final report from study RA005 (NBD registry) (listed as a category 3 studies in the RMP): registry to gather safety and outcome data in RA patients receiving CZP and other RA treatments. In addition, the MAH submitted interim results for two ongoing registries studies, namely: study RA0020/Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT): a German long-term observation of biologics/disease-modifying antirheumatic drugs (DMARD) in RA; and study RA0022/British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR): a longitudinal observational study of patients with RA treated with biologic agents, and prospective surveillance study for adverse events

Action: For adoption of PRAC Assessment Report

7.4.5. [Etanercept - ENBREL \(CAP\) - EMEA/H/C/000262/WS1270/0216; LIFMIOR \(CAP\) - EMEA/H/C/004167/WS1270/0013](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final report from study B1801396 (listed as a category 3 study in the RMP): a non-interventional, population-based, multi-country, observational cohort register study to evaluate the risk of adverse pregnancy outcomes in patients with rheumatoid arthritis and related inflammatory diseases, who were treated with etanercept compared to patients with the same diseases of interest who were treated with non-biologic systemic drugs (i.e. without etanercept or other biologics during pregnancy), using merged data from Sweden, Denmark and Finland

Action: For adoption of PRAC Assessment Report

7.4.6. [Exenatide - BYDUREON \(CAP\) - EMEA/H/C/002020/II/0054](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Submission of the final study report, as requested by PRAC in the conclusions of MEA 11.5 adopted at the October 2016 meeting, from study H80-MC-B015 extension/D5550R00003: 'incidence of pancreatic malignancy and thyroid neoplasm in type 2 diabetes mellitus (T2DM) patients who initiate exenatide compared to other antihyperglycemic drugs' as well as the feasibility study on 'incidence of pancreatic cancer and thyroid neoplasm among T2DM who initiated Bydureon (exenatide) as compared with those who initiated other glucose lowering drugs'. The RMP (version 32) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. [Golimumab - SIMPONI \(CAP\) - EMEA/H/C/000992/II/0085](#)

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study CNTO148ART4002 (listed as a category 3

study in the RMP): an observational phase 4 study using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi (golimumab) treatment and/or other types of biologic and non-biologic treatments. The RMP (version 19.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems' in order to reflect changes in the categorisation of safety concerns

Action: For adoption of PRAC Assessment Report

7.4.8. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0218

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final study report from the Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) cohort 2 portion of the registry: a German rheumatoid arthritis (RA) registry established as a prospective observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs (DMARDs) in patients with RA. The RMP (version 19) is updated accordingly. The MAH also revised the RMP list of safety concerns as requested in the conclusions of procedure LEG 156 adopted in October 2017

Action: For adoption of PRAC Assessment Report

7.4.9. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/II/0030

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report for study 178-PV-002: a drug utilisation study (DUS) of mirabegron using real-world healthcare databases from Finland, the Netherlands (NL) and the United Kingdom (UK) (in fulfilment of post-approval commitment MEA 009.2)

Action: For adoption of PRAC Assessment Report

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

Applicant: Oxurion NV

PRAC Rapporteur: Julie Williams

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

patients treated with Jetrea (ocriplasmin) in order to evaluate safety, clinical effectiveness, and health-related quality of life (HRQoL) outcomes in a real world setting among a large population of patients exposed to ocriplasmin across different countries according to country's approved indications. The RMP (version 7.2) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

7.4.11. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0041

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Submission of the final report from the pregnancy registry H4621g study (MoTHER) (listed as a category 3 study in the RMP): an observational study of pregnancy and pregnancy outcome in women with breast cancer treated with trastuzumab, pertuzumab in combination with trastuzumab, or ado-trastuzumab emtansine during pregnancy or within 7 months prior to conception. The RMP (version 11) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.12. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0082

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final study report (listed as a category 3 study in the RMP): 'safety report on hypersensitivity in patients who switched between tocilizumab intravenous and subcutaneous routes of administration' based on safety data from the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR), study WA22479: a prospective observational cohort study for safety data collection (BSRBR) and study ML22928: a prospective, non-interventional multicentre observational study to evaluate the long-term effectiveness and safety of tocilizumab in patients with active rheumatoid arthritis in daily practice

Action: For adoption of PRAC Assessment Report

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

7.5.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 046.8

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Ninth annual interim report for study P10-262, a registry study in juvenile idiopathic arthritis (JIA) patients: a long term, multicentre, longitudinal post-marketing, observational study to assess long term safety and effectiveness of Humira (adalimumab) in children with moderately to severely active polyarticular or polyarticular-course JIA – STRIVE [final study report due date: 31 December 2024]

Action: For adoption of advice to CHMP

7.5.2. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.7

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 007.6 [third annual report for study OBS13434: a prospective, multicentre, observational PASS to evaluate the long term safety profile of Lemtrada (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis (MS) and to determine the incidence of adverse events of special interest (AESIs)] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.3. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 006.4

Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Interim results for year 3 for the UK clinical practice research datalink (CPRD) database data analysis for psoriatic arthritis (PsA) and psoriasis [due date: CPRD data analysis at years 1, 3 and 5 starting from the date of first commercial availability in the UK. Final study report due for submission within 6 months after the 5 year-data analysis cut-off date]

Action: For adoption of advice to CHMP

7.5.4. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/MEA 024.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

Scope: Third interim report for study A8081062 (listed as category 3 study in the RMP): a PASS descriptive study evaluating the frequency of risk factors for and sequelae of potential sight threatening event and severe visual loss among patients following exposure to Xalkori (crizotinib) and measuring the effectiveness of the crizotinib therapeutic management guide in communicating risks, and recommended actions to minimize risks, among physicians prescribing crizotinib in Europe

Action: For adoption of advice to CHMP

7.5.5. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/MEA 010.4

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth interim report for study TMC207TBC4002 (listed as a category 3 study in the RMP): a multi-country prospective multidrug resistant tuberculosis (MDRTB) patient registry to monitor bedaquiline safety, utilisation, and emergence of resistance

Action: For adoption of advice to CHMP

7.5.6. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 008.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 008 [annual progress report (version 2.0) for study 109MS402: Biogen multiple sclerosis pregnancy exposure registry [final clinical study report (CSR) expected due date: Q4 2021] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.7. Human rotavirus, live attenuated - ROTARIX (CAP) - EMEA/H/C/000639/MEA 094

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual report for study EPI-ROTA-052 BOD EU SUPP (201433) (EuroRotaNet): observational community-based strain surveillance study

Action: For adoption of advice to CHMP

7.5.8. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/MEA 114.10

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim results for 2017 for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): a multicentre, open study of patients with plaque psoriasis who are candidates for systemic therapy including biologics [final clinical study report (CSR) for PSOLAR expected in June 2023]

Action: For adoption of advice to CHMP

7.5.9. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.5

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Interim results for a prospective, multi-country, observational registry study to collect clinical information on patients with endogenous Cushing's syndrome exposed to ketoconazole using the existing European registry on Cushing's syndrome (ERCUSYN) to assess drug utilisation pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of ketoconazole

Action: For adoption of advice to CHMP

7.5.10. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.6

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Third annual interim report for a PASS (ENCEPP/SDPP/8585) (listed as a category 1 study): an observational retrospective cohort study of ospemifene utilising existing databases in Germany, Italy, Spain, and the United States to evaluate the incidence of venous thromboembolism and other adverse events in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective oestrogen receptor modulators (SERM) for oestrogen-deficiency conditions or breast cancer prevention and; 2) the incidence in untreated VVA patients [final report expected in February 2021]

Action: For adoption of advice to CHMP

7.5.11. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/ANX 001.1

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Interim results for study P15-11: a multicentre, observational PASS to document the drug utilisation of Wakix (pitolisant) and to collect information on the safety of Wakix when used in routine medical practice [final results planned in 2023] (from opinion/MA)

Action: For adoption of advice to CHMP

7.5.12. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/MEA 003.6

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Ninth annual report for a post-marketing surveillance study 20070797: a population based prospective study evaluating the short and long term safety of romiplostim treatment in real-life clinical practice in adult patients with chronic idiopathic (immune) thrombocytopenic purpura (ITP) based on national health registry systems in Denmark, Sweden, and Norway over a period of 11 years

Action: For adoption of advice to CHMP

7.5.13. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.15

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 022.14 [annual report for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.14. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Patrick Batty

Scope: Interim analysis for study P16-562: a prospective observational study to assess the long term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients [final clinical study report (CSR) planned in December 2025]

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/LEG 031

Applicant: Servier (Ireland) Industries Ltd.

PRAC Rapporteur: Karen Pernille Harg

Scope: Comprehensive review of the results of study CLE-20098-096 (listed as a category 3 study in the RMP): agomelatine drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess effectiveness of risk-minimisation measures, together with a review of post-marketing observational studies and available pharmacovigilance data in relation to hepatotoxicity and consideration on the need for continuing and improving the current additional risk minimisation measures (RMM) including a discussion on whether liver function testing prior to and during treatment with agomelatine is regarded as a standard of care in the EU Member States, as requested in the conclusions of variation II/38 adopted in September 2018

Action: For adoption of advice to CHMP

7.6.2. Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/LEG 031

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Karen Pernille Harg

Scope: Comprehensive review of the results of study CLE-20098-096 (listed as a category 3 study in the RMP): agomelatine drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess effectiveness of risk-minimisation measures, together with a review of post-marketing observational studies and available pharmacovigilance data in relation to hepatotoxicity and consideration on the need for continuing and improving the current additional risk minimisation measures (RMM) including a discussion on whether liver function testing prior to and during treatment with agomelatine is regarded as a standard of care in the EU Member States, as requested in the conclusions of variation II/39 adopted in September 2018

Action: For adoption of advice to CHMP

7.6.3. Desloratadine - AERIUS (CAP) - EMEA/H/C/000313/MEA 065.4

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 065.3 [status update and study milestones for a Nordic register-based study exploring the association between the use of desloratadine and the risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.6.4. Desloratadine - AZOMYR (CAP) - EMEA/H/C/000310/MEA 065.4

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 065.3 [status update and study milestones for a Nordic register-based study exploring the association between the use of desloratadine and the risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.6.5. Desloratadine - NEOCLARITYN (CAP) - EMEA/H/C/000314/MEA 065.4

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 065.3 [status update and study milestones for a Nordic register-based study exploring the association between the use of desloratadine and the risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

7.6.6. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 047.6

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 047.45 on sensitivity analysis [revised statistical analysis plan (SAP) amendment 5 for the HUBIN registry: a European observational cohort of patients with type 1 diabetes mellitus (T1DM) treated via intraperitoneal route with Insuman Implantable 400 IU/mL in MedtronicMiniMed implantable pump] as per the request for supplementary information (RSI) adopted in May 2018

Action: For adoption of advice to CHMP

7.6.7. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 023

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Feasibility assessment for study 3083-S03-000: a physiologically based

pharmacokinetic (PBPK) modelling of ulipristal acetate under conditions of impaired bile secretion, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.6.8. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 025

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Feasibility report for a retrospective case control study utilising medical records of transplantation centres in at least five EU Member States as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.6.9. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 026

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Feasibility report for an observational study using EU registries with biomarker data, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.6.10. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 027

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Feasibility report for a genetic analysis (human leukocyte antigen (HLA)) study using data from EU registries with biomarker data in patients with severe drug-induced liver injury (DILI), as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.6.11. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 029

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Feasibility report for a study using EU registries and the drug-induced liver injury (DILI) registry databases to measure the effectiveness of the risk minimisation measures to mitigate the risk of DILI, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0012 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0032 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/R/0029 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - EMEA/H/C/003963/R/0019 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Daniela Philadelphly

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0016 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Pixantrone - PIXUVRI (CAP) - EMEA/H/C/002055/R/0046 (with RMP)

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.6. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/R/0008 (without RMP)

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Budesonide, formoterol - BIRESP SPIROMAX (CAP) - EMEA/H/C/003890/R/0027 (without RMP)

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Budesonide, formoterol - DUORESP SPIROMAX (CAP) - EMEA/H/C/002348/R/0027 (without RMP)

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Capsaicin - QUTENZA (CAP) - EMEA/H/C/000909/R/0047 (with RMP)

Applicant: Grunenthal GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Everolimus - AFINITOR (CAP) - EMEA/H/C/001038/R/0060 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/R/0049 (with RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - EMEA/H/C/002705/R/0018 (without RMP)

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/R/0031 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/R/0051 (without RMP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/R/0027 (without RMP)

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Tacrolimus - ENVARUSUS (CAP) - EMEA/H/C/002655/R/0014 (with RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Ronan Grimes

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

10.1.1. Dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/II/0032

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Consultation on a type II variation to update section 4.4 of the SmPC following a cumulative review of acute kidney injury (AKI) events requested by PRAC in May 2018 (EPITT 19204) in order to add information on the potential for dulaglutide to contribute to volume depletion events which could indirectly contribute to the occurrence of AKI. The package leaflet is updated accordingly

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Methylphenidate hydrochloride (NAP) - DE/H/XXXX/WS/547

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG (Medikinet)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a national worksharing variation on RMP safety concerns for methylphenidate-containing products considering the additional risk minimisation measures (aRMM) currently in place and the outcome of the referral procedure for methylphenidate-containing products under Article 31 of Directive 2001/83/EC (EMEA/658285/2008) completed in 2009, in light of revision 2 of GVP module V on 'Risk management systems', on request of Germany

Action: For adoption of advice to Member States

11.1.2. Valproate (NAP) - NL/H/xxxx/WS/0312

Applicant(s): Sanofi (Depakine)

PRAC Lead: Liana Gross-Martirosyan

Scope: PRAC consultation on a national worksharing variation on the RMP for Depakine (valproate) relating to scientific aspects relevant to the condition requesting 'MAHs to conduct a PASS preferably based on existing registries to further characterise the foetal anticonvulsant syndrome in children with valproate in utero exposure as compared to other anti-epileptic drugs' imposed in the outcome of the referral procedure for valproate-containing products under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1454) completed in 2018, on request of the Netherlands

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Phenylephrine hydrochloride, tropicamide (NAP) - DK/H/PSUFU/00010430/201711

Applicant(s): Thea Laboratoires (Mydriaserit), Visufarma SpA (Visumidriatic Fenilefrina)

PRAC Lead: Anette Kirstine Stark

Scope: PRAC consultation on a worksharing PSUR follow-up (PSU FU) procedure on a

cumulative review and characterisation of the risk of 'systemic adverse reactions' associated with ophthalmic use of medicinal products containing phenylephrine/tropicamide in the paediatric population, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on phenylephrine/tropicamide (PSUSA/00010430/201711) concluded in July 2018, on request of Denmark

Action: For adoption of advice to Member States

11.2.2. Rosuvastatin (NAP) - NL/H/PSUFU/00002664/201711

Applicant: AstraZeneca (Crestor, Provisacor)

PRAC Lead: Menno van der Elst

Scope: PRAC consultation on a worksharing PSUR follow-up (PSU FU) procedure on the safety concern of 'systemic lupus erythematosus/lupus erythematosus/lupus-like syndrome' and causal association with rosuvastatin as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on rosuvastatin (PSUSA/00002664/201711) concluded in July 2018, on request of the Netherlands

Action: For adoption of advice to Member States

11.2.3. Ulipristal acetate - AT/H/0862/001/DC, AT/H/0863/001/DC

PRAC Lead: Jan Neuhauser

Scope: PRAC consultation on the evaluation of initial marketing authorisation application(s) under the decentralised procedure for generic ulipristal-containing medicinal products on request of Austria

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Working Party with Patients' and Consumers' Organisations (PCWP) – revised mandate and composition

Action: For adoption

12.3.2. Working Party with Healthcare Professionals' Organisations (HCPWP) - revised mandate and composition

Action: For adoption

12.3.3. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP) - revised rules of procedure

Action: For adoption

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2019

PRAC lead: Sabine Straus, Martin Huber

Action: For adoption

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q4 2018 and predictions

Action: For discussion

12.8.2. Marketing authorisation applications (MAA) forecast for 2019 – planning update dated Q4 2018

Action: For information

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to 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. Others

12.20.1. Drug induced hepatotoxicity – PRAC review status update

PRAC lead: Amelia Cupelli, Liana Gross-Martirosyan, Jolanta Gulbinovic, Martin Huber, Zane Neikena, Sabine Straus, Menno van der Elst, Stefan Weiler

Action: For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance - PRAC interest group (IG) Impact work plan 2019

Action: For adoption

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/