



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 February 2019
EMA/PRAC/111893/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 11-14 February 2019

Chair: Sabine Straus – Vice-Chair: Martin Huber

11 February 2019, 13:00 – 19:30, room 3/A

12 February 2019, 08:30 – 19:30, room 3/A

13 February 2019, 08:30 – 19:30, room 3/A

14 February 2019, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

28 February 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	12
1.1.	Welcome and declarations of interest of members, alternates and experts.....	12
1.2.	Agenda of the meeting on 11-14 February 2019.....	12
1.3.	Minutes of the previous meeting on 14-17 January 2019	12
2.	EU referral procedures for safety reasons: urgent EU procedures	12
2.1.	Newly triggered procedures	12
2.1.1.	Fenspiride (NAP) - EMEA/H/A-107i/1480	12
2.2.	Ongoing procedures	12
2.3.	Procedures for finalisation.....	12
2.4.	Planned public hearings	12
3.	EU referral procedures for safety reasons: other EU referral procedures	13
3.1.	Newly triggered procedures	13
3.2.	Ongoing procedures	13
3.2.1.	Methotrexate - JYLAMVO (CAP), NORDIMET (CAP); NAP - EMEA/H/A-31/1463	13
3.3.	Procedures for finalisation.....	13
3.4.	Re-examination procedures.....	13
3.5.	Others	13
4.	Signals assessment and prioritisation	13
4.1.	New signals detected from EU spontaneous reporting systems	13
4.1.1.	Bevacizumab - AVASTIN (CAP), MVASI (CAP).....	13
4.1.2.	Secukinumab – COSENTYX (CAP)	14
4.2.	New signals detected from other sources	14
4.2.1.	Angiotensin converting enzyme (ACE) inhibitors: benazepril (NAP), captopril (NAP), cilazapril (NAP), delapril (NAP), enalapril (NAP), fosinopril (NAP), imidapril (NAP), lisinopril (NAP), moexipril (NAP), perindopril (NAP), quinapril (NAP), ramipril (NAP), trandolapril (NAP), zofenopril (NAP)	14
4.2.2.	Armodafinil (NAP), modafinil (NAP)	14
4.2.3.	Olanzapine - OLANZAPINE APOTEX (CAP), OLANZAPINE GLENMARK (CAP), OLANZAPINE GLENMARK EUROPE (CAP), OLANZAPINE MYLAN (CAP), OLANZAPINE TEVA (CAP), OLAZAX (CAP), OLAZAX DISPERZI (CAP), ZALASTA (CAP), ZYPADHERA (CAP), ZYPREXA (CAP), ZYPREXA VELOTAB (CAP); NAP	15
4.2.4.	Propylthiouracil (NAP)	15
4.2.5.	Sulfasalazine (NAP).....	15
4.3.	Signals follow-up and prioritisation	16
4.3.1.	Olanzapine – OLANZAPINE APOTEX (CAP), OLANZAPINE GLENMARK (CAP), OLANZAPINE GLENMARK EUROPE (CAP), OLANZAPINE MYLAN (CAP), OLANZAPINE TEVA (CAP), OLAZAX (CAP), OLAZAX DISPERZI (CAP), ZALASTA (CAP) - EMEA/H/C/000792/SDA/007, ZYPADHERA	

(CAP) - EMEA/H/C/000890/SDA/029, ZYPREXA (CAP) - EMEA/H/C/000115/SDA/050, ZYPREXA VELOTAB (CAP) - EMEA/H/C/000287/SDA/043; NAP 16

4.3.2. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/054 16

5. Risk management plans (RMPs) 16

5.1. Medicines in the pre-authorisation phase 16

5.1.1. Ambrisentan - EMEA/H/C/004985 16

5.1.2. Avatrombopag - EMEA/H/C/004722 16

5.1.3. Cabazitaxel - EMEA/H/C/004951 17

5.1.4. Crisaborole - EMEA/H/C/004863 17

5.1.5. Edaravone - EMEA/H/C/004938, Orphan 17

5.1.6. Ioflupane (¹²³I) - EMEA/H/C/004745 17

5.1.7. Onasemnogene abeparvovec - EMEA/H/C/004750, Orphan 17

5.1.8. Posaconazole - EMEA/H/C/005005 17

5.1.9. Ravulizumab - EMEA/H/C/004954, Orphan 17

5.1.10. Talazoparib - EMEA/H/C/004674 17

5.2. Medicines in the post-authorisation phase – PRAC-led procedures 18

5.2.1. Abacavir - ZIAGEN (CAP) - EMEA/H/C/000252/WS1521/0105; abacavir, lamivudine - KIVEXA (CAP) - EMEA/H/C/000581/WS1521/0079; abacavir, lamivudine, zidovudine - TRIZIVIR (CAP) - EMEA/H/C/000338/WS1521/0112 18

5.2.2. Ambrisentan - VOLIBRIS (CAP) - EMEA/H/C/000839/II/0055 18

5.2.3. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/II/0015 18

5.2.4. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/II/0148 19

5.2.5. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0064 19

5.2.6. Dexamethasone - NEOFORDEX (CAP) - EMEA/H/C/004071/II/0008 19

5.2.7. Fluciclovine (¹⁸F) - AXUMIN (CAP) - EMEA/H/C/004197/II/0010 19

5.2.8. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0011 20

5.2.9. Human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - GARDASIL 9 (CAP) - EMEA/H/C/003852/II/0029 20

5.2.10. Panobinostat - FARYDAK (CAP) - EMEA/H/C/003725/II/0013, Orphan 20

5.2.11. Piperaquine tetraphosphate, arteminol - EURARTESIM (CAP) - EMEA/H/C/001199/II/0032 21

5.2.12. Pramipexole - MIRAPEXIN (CAP) - EMEA/H/C/000134/WS1510/0089; SIFROL (CAP) - EMEA/H/C/000133/WS1510/0080 21

5.2.13. Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/II/0048 21

5.2.14. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/II/0006 22

5.2.15. Tolcapone - TASMAR (CAP) - EMEA/H/C/000132/II/0061 22

5.2.16. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0042/G 22

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

5.3.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0064/G 23

5.3.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0047, Orphan 23

5.3.3.	Beclometasone dipropionate, formoterol fumarate dehydrate, glycopyrronium - RIARIFY (CAP) - EMEA/H/C/004836/WS1554/0002; TRYDONIS (CAP) - EMEA/H/C/004702/WS1554/000223	
5.3.4.	Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/II/0028, Orphan	24
5.3.5.	Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0062	24
5.3.6.	Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0014/G	25
5.3.7.	Ceftaroline fosamil - ZINFORO (CAP) - EMEA/H/C/002252/II/0041	25
5.3.8.	Ciclosporin - IKERVIS (CAP) - EMEA/H/C/002066/WS1490/0014; VERKAZIA (CAP) - EMEA/H/C/004411/WS1490/0001	26
5.3.9.	Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/II/0031	26
5.3.10.	Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0049.....	26
5.3.11.	Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/X/0001.....	26
5.3.12.	Etelcalcetide - PARSABIV (CAP) - EMEA/H/C/003995/II/0010.....	27
5.3.13.	Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/II/0015.....	27
5.3.14.	Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0005	27
5.3.15.	Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0046, Orphan.....	27
5.3.16.	Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0047, Orphan.....	28
5.3.17.	Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/II/0137/G.....	28
5.3.18.	Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/II/0124/G	29
5.3.19.	Interferon beta-1b - EXTAVIA (CAP) - EMEA/H/C/000933/II/0096/G.....	29
5.3.20.	Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/II/0073/G	29
5.3.21.	Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0013.....	30
5.3.22.	Modified vaccinia Ankara virus - IMVANEX (CAP) - EMEA/H/C/002596/II/0036	30
5.3.23.	Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0029/G	30
5.3.24.	Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/II/0046/G.....	31
5.3.25.	Plerixafor - MOZOBIL (CAP) - EMEA/H/C/001030/II/0034, Orphan.....	31
5.3.26.	Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0023	31
5.3.27.	Palbociclib - IBRANCE (CAP) - EMEA/H/C/003853/II/0017/G	32
5.3.28.	Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0052/G	32
5.3.29.	Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58) - EMEA/H/W/002300/II/0036	33
5.3.30.	Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - EMEA/H/C/002094/II/0044/G	33
5.3.31.	Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0076	33
5.3.32.	Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0152	34
5.3.33.	Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0022.....	34
5.3.34.	Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0029.....	34
5.3.35.	Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0191	34
5.3.36.	Thalidomide - THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/II/0056, Orphan	35
5.3.37.	Trastuzumab - ONTRUZANT (CAP) - EMEA/H/C/004323/II/0016.....	35

5.3.38.	Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/II/0028	35
5.3.39.	Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0020, Orphan	36

6. Periodic safety update reports (PSURs) 36

6.1.	PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only	36
6.1.1.	Acidinium bromide - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/201807	36
6.1.2.	Aflibercept - ZALTRAP (CAP) - PSUSA/00010019/201808	36
6.1.3.	Albutrepenonacog alfa - IDELVION (CAP) - PSUSA/00010497/201807.....	36
6.1.4.	Alirocumab - PRALUENT (CAP) - PSUSA/00010423/201807.....	37
6.1.5.	Antithrombin alfa - ATRYN (CAP) - PSUSA/00000224/201807	37
6.1.6.	Asparaginase - SPECTRILA (CAP) - PSUSA/00010445/201807.....	37
6.1.7.	Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/201807	37
6.1.8.	Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/201807.....	37
6.1.9.	Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/201807	38
6.1.10.	Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - PSUSA/00010695/201808	38
6.1.11.	Birch bark extract - EPISALVAN (CAP) - PSUSA/00010446/201807	38
6.1.12.	Brivaracetam - BRIVIACT (CAP) - PSUSA/00010447/201807.....	38
6.1.13.	Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/201807	38
6.1.14.	Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201807	38
6.1.15.	Catridecacog - NOVOTHIRTEEN (CAP) - PSUSA/00010034/201807	39
6.1.16.	Efavirenz, emtricitabine, tenofovir - ATRIPLA (CAP) - PSUSA/00001201/201807	39
6.1.17.	Elbasvir, grazoprevir - ZEPATIER (CAP) - PSUSA/00010519/201807	39
6.1.18.	Etanercept - BENEPALI (CAP); ERELZI (CAP) - PSUSA/00010452/201807.....	39
6.1.19.	Evolocumab - REPATHA (CAP) - PSUSA/00010405/201807	39
6.1.20.	Gefitinib - IRESSA (CAP) - PSUSA/00001518/201807.....	40
6.1.21.	Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/201807.....	40
6.1.22.	Guselkumab - TREMFYA (CAP) - PSUSA/00010652/201807.....	40
6.1.23.	Hydrocortisone - ALKINDI (CAP) - PSUSA/00010674/201808.....	40
6.1.24.	Ibandronic acid – BONDRONAT (CAP); BONVIVA (CAP) - PSUSA/00001702/201806	40
6.1.25.	Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/201807	40
6.1.26.	Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/201807	41
6.1.27.	Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201807 (with RMP)	41
6.1.28.	Lipegfilgrastim - LONQUEX (CAP) - PSUSA/00010111/201807.....	41
6.1.29.	Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/201807	41
6.1.30.	Mercaptamine - CYSTADROPS (CAP) - PSUSA/00010574/201807	41
6.1.31.	Modified vaccinia Ankara virus - IMVANEX (CAP) - PSUSA/00010119/201807	42
6.1.32.	Natalizumab - TYSABRI (CAP) - PSUSA/00002127/201808 (with RMP)	42

6.1.33.	Palbociclib - IBRANCE (CAP) - PSUSA/00010544/201808.....	42
6.1.34.	Paliperidone - INVEGA (CAP); paliperidone palmitate - TREVICTA (CAP); XEPLION (CAP) - PSUSA/00002266/201806	42
6.1.35.	Pegaptanib - MACUGEN (CAP) - PSUSA/00002324/201806	42
6.1.36.	Pegaspargase - ONCASPAR (CAP) - PSUSA/00010457/201807 (with RMP).....	42
6.1.37.	Peginterferon beta-1A - PLEGRIDY (CAP) - PSUSA/00010275/201807	43
6.1.38.	Perampanel - FYCOMPA (CAP) - PSUSA/00009255/201807	43
6.1.39.	Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/201807	43
6.1.40.	Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/201807	43
6.1.41.	Sarilumab - KEVZARA (CAP) - PSUSA/00010609/201807	43
6.1.42.	Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/201807	44
6.1.43.	Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/201807.....	44
6.1.44.	Stavudine - ZERIT (CAP) - PSUSA/00002787/201806	44
6.1.45.	Telithromycin - KETEK (CAP) - PSUSA/00002881/201807.....	44
6.1.46.	Tobramycin - TOBI PODHALER (CAP) - PSUSA/00009315/201806	44
6.1.47.	Tocofersolan - VEDROP (CAP) - PSUSA/00002981/201807.....	44
6.2.	PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)	45
6.2.1.	5-aminolevulinic acid - AMELUZ (CAP); NAP - PSUSA/00010006/201806.....	45
6.2.2.	Aripiprazole - ABILIFY (CAP); ABILIFY MAINTENA (CAP); ARIPIPRAZOLE SANDOZ (CAP); NAP - PSUSA/00000234/201807	45
6.3.	PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only	45
6.3.1.	Aciclovir (NAP) – PSUSA/00000048/201806.....	45
6.3.2.	Calcitonin salmon (NAP); synthetic analogue of eel calcitonin (NAP) - PSUSA/00000494/201806	45
6.3.3.	Cefepime (NAP) - PSUSA/00000593/201806.....	46
6.3.4.	Daunorubicin (NAP) - PSUSA/00000936/201806	46
6.3.5.	Dexchlorpheniramine (NAP) - PSUSA/00000989/201806	46
6.3.6.	Dihydroergocryptine (NAP) - PSUSA/00001074/201807	46
6.3.7.	Fosinopril (NAP); fosinopril, hydrochlorothiazide (NAP) - PSUSA/00010463/201807	46
6.3.8.	Glibenclamide, metformin hydrochloride (NAP) - PSUSA/00002002/201806.....	46
6.3.9.	Human fibrinogen (NAP) - PSUSA/00001624/201806.....	47
6.3.10.	Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/201807	47
6.3.11.	Levonorgestrel, ethinylestradiol; ethinylestradiol (NAP) - PSUSA/00010442/201807	47
6.3.12.	Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/201807	47
6.3.13.	Manidipine (NAP) - PSUSA/00001932/201806	47
6.3.14.	Metyrapone (NAP) - PSUSA/00002046/201806	48
6.3.15.	Misoprostol (NAP) - PSUSA/00010291/201806	48
6.3.16.	Nilutamide (NAP) - PSUSA/00002163/201807	48

6.3.17.	Nimesulide (NAP) - PSUSA/00009236/201806.....	48
6.3.18.	Nimesulide (NAP) - PSUSA/00002165/201806.....	48
6.3.19.	Paracetamol, pseudoephedrine (NAP) - PSUSA/00002307/201806.....	48
6.3.20.	Phenylpropanolamine (NAP) - PSUSA/00010483/201806.....	49
6.3.21.	Pipobroman (NAP) - PSUSA/00002427/201806.....	49
6.3.22.	Pitavastatin (NAP) - PSUSA/00010502/201807.....	49
6.3.23.	Pseudoephedrine (CAP); acetylsalicylic acid, pseudoephedrine (NAP) - PSUSA/00010667/201806.....	49
6.3.24.	Rabbit anti-human T-lymphocyte immunoglobulin (NAP) - PSUSA/00010252/201806.....	49
6.3.25.	Rizatriptan (NAP) - PSUSA/00002655/201806.....	50
6.3.26.	Solifenacin, tamsolusin (NAP) - PSUSA/00010285/201807.....	50
6.3.27.	Thiocolchicoside (CAP); paracetamol, thiocolchicoside (NAP) - PSUSA/00010464/201807.....	50
6.3.28.	Tiagabine (NAP) - PSUSA/00002942/201806.....	50
6.3.29.	Tianeptine (NAP) - PSUSA/00002943/201806.....	50
6.3.30.	Urapidil (NAP) - PSUSA/00003078/201807.....	50
6.4.	Follow-up to PSUR/PSUSA procedures.....	51
6.4.1.	Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/LEG 037.....	51
6.4.2.	Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/LEG 024.....	51

7. Post-authorisation safety studies (PASS) 51

7.1.	Protocols of PASS imposed in the marketing authorisation(s).....	51
7.1.1.	Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSP/S/0071.....	51
7.1.2.	Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/PSP/S/0070.....	51
7.1.3.	Valproate (NAP) - EMEA/H/N/PSP/J/0072.....	52
7.1.4.	Valproate (NAP) - EMEA/H/N/PSP/J/0073.....	52
7.1.5.	Valproate (NAP) - EMEA/H/N/PSP/J/0074.....	52
7.1.6.	Valproate (NAP) - EMEA/H/N/PSP/J/0075.....	53
7.1.7.	Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/PSP/S/0060.2.....	53
7.2.	Protocols of PASS non-imposed in the marketing authorisation(s).....	53
7.2.1.	Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/MEA 016.1.....	53
7.2.2.	Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/MEA 002.1.....	53
7.2.3.	Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.1.....	54
7.2.4.	Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/MEA 001.....	54
7.2.5.	Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/MEA 004.1.....	54
7.2.6.	Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.6.....	54
7.2.7.	Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/MEA 007.1.....	55
7.2.8.	Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 002.....	55
7.2.9.	Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/MEA 002.....	55
7.2.10.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.1.....	55

7.2.11.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.1	56
7.2.12.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.1	56
7.2.13.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.1	56
7.2.14.	Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/MEA 004.4	57
7.3.	Results of PASS imposed in the marketing authorisation(s).....	57
7.4.	Results of PASS non-imposed in the marketing authorisation(s).....	57
7.4.1.	Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0050/G	57
7.4.2.	Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/II/0039	57
7.4.3.	Collagenase clostridium histolyticum - XIAPEX (CAP) - EMEA/H/C/002048/II/0106	58
7.4.4.	Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0159.....	58
7.4.5.	Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/II/0042/G	58
7.4.6.	Propranolol - HEMANGIOL (CAP) - EMEA/H/C/002621/II/0019	59
7.4.7.	Teriparatide - FORSTEO (CAP) - EMEA/H/C/000425/II/0050/G.....	59
7.5.	Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation.....	59
7.5.1.	Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.4	59
7.5.2.	Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.10.....	60
7.5.3.	Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.3	60
7.5.4.	Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 027.6.....	60
7.5.5.	Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/ANX 191.7	60
7.5.6.	Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/MEA 007.4	61
7.5.7.	Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/MEA 010.4	61
7.5.8.	Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 007.4.....	61
7.5.9.	Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 010.4.....	61
7.5.10.	Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/MEA 015.3.....	62
7.5.11.	Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.2	62
7.5.12.	Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 002.4	62
7.5.13.	Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.7	62
7.5.14.	Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/MEA 005.....	62
7.5.15.	Rituximab - RIXIMYO (CAP) - EMEA/H/C/004729/MEA 005	63
7.5.16.	Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/ANX 001.2.....	63
7.5.17.	Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004.4.....	63
7.5.18.	Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/MEA 004.3	63
7.5.19.	Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005	64
7.5.20.	Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 006	64
7.6.	Others	64
7.6.1.	Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.10..	64
7.6.2.	Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.4	64
7.7.	New Scientific Advice	65

7.8.	Ongoing Scientific Advice	65
7.9.	Final Scientific Advice (Reports and Scientific Advice letters)	65

8. Renewals of the marketing authorisation, conditional renewal and annual reassessments 65

8.1.	Annual reassessments of the marketing authorisation	65
8.1.1.	Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0073 (without RMP)	65
8.1.2.	Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0012 (without RMP)	65
8.1.3.	Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0055 (with RMP)	65
8.1.4.	Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0023 (without RMP)	66
8.1.5.	Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0031 (without RMP).....	66
8.2.	Conditional renewals of the marketing authorisation	66
8.3.	Renewals of the marketing authorisation	66
8.3.1.	Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/R/0063 (with RMP)	66
8.3.2.	Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/R/0043 (with RMP).....	66
8.3.3.	Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - EMEA/H/C/003963/R/0019 (with RMP)	66
8.3.4.	Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/R/0027 (without RMP).....	67

9. Product related pharmacovigilance inspections 67

9.1.	List of planned pharmacovigilance inspections	67
9.2.	Ongoing or concluded pharmacovigilance inspections	67
9.3.	Others	67

10. Other safety issues for discussion requested by the CHMP or the EMA 67

10.1.	Safety related variations of the marketing authorisation.....	67
10.1.1.	Cobicistat - TYBOST (CAP) - EMEA/H/C/002572/WS1401/0044; cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/WS1401/0047; STRIBILD (CAP) - EMEA/H/C/002574/WS1401/0094	67
10.2.	Timing and message content in relation to Member States' safety announcements	68
10.3.	Other requests.....	68
10.4.	Scientific Advice	68

11. Other safety issues for discussion requested by the Member States 68

11.1.	Safety related variations of the marketing authorisation.....	68
11.1.1.	Leuprorelin (NAP) - DE/H/0580/001-003/II/077, DE/H/0580/001-003/II/078	68
11.2.	Other requests.....	68
11.2.1.	Atorvastatin (NAP) - DE/H/PSUFU/00010347/201710/B	68

12. Organisational, regulatory and methodological matters 69

12.1.	Mandate and organisation of the PRAC.....	69
--------------	--	-----------

12.1.1.	PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals	69
12.2.	Coordination with EMA Scientific Committees or CMDh-v	69
12.3.	Coordination with EMA Working Parties/Working Groups/Drafting Groups	69
12.4.	Cooperation within the EU regulatory network	69
12.4.1.	European Network Training Centre (EU NTC) - Pharmacovigilance - Training curriculum (TC) – Strategy for 2019	69
12.5.	Cooperation with International Regulators.....	69
12.6.	Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee	69
12.7.	PRAC work plan	69
12.8.	Planning and reporting	70
12.8.1.	PRAC workload statistics – Q4 2018	70
12.9.	Pharmacovigilance audits and inspections	70
12.9.1.	Pharmacovigilance systems and their quality systems	70
12.9.2.	Pharmacovigilance inspections	70
12.9.3.	Pharmacovigilance audits.....	70
12.10.	Periodic safety update reports (PSURs) & Union reference date (EURD) list	70
12.10.1.	Periodic safety update reports	70
12.10.2.	Granularity and Periodicity Advisory Group (GPAG)	70
12.10.3.	PSURs repository	70
12.10.4.	Union reference date list – consultation on the draft list	70
12.11.	Signal management	71
12.11.1.	Signal management – feedback from Signal Management Review Technical (SMART) Working Group	71
12.12.	Adverse drug reactions reporting and additional monitoring.....	71
12.12.1.	Management and reporting of adverse reactions to medicinal products.....	71
12.12.2.	Additional monitoring	71
12.12.3.	List of products under additional monitoring – consultation on the draft list	71
12.13.	EudraVigilance database	71
12.13.1.	Activities related full functionality	71
12.13.2.	EudraVigilance – annual report 2018.....	71
12.14.	Risk management plans and effectiveness of risk minimisations.....	71
12.14.1.	Risk management systems	71
12.14.2.	Tools, educational materials and effectiveness measurement of risk minimisations	71
12.15.	Post-authorisation safety studies (PASS)	72
12.15.1.	Post-authorisation Safety Studies – imposed PASS	72
12.15.2.	Post-authorisation Safety Studies – non-imposed PASS	72
12.16.	Community procedures.....	72
12.16.1.	Referral procedures for safety reasons	72

12.17.	Renewals, conditional renewals, annual reassessments	72
12.18.	Risk communication and transparency	72
12.18.1.	Public participation in pharmacovigilance	72
12.18.2.	Safety communication	72
12.19.	Continuous pharmacovigilance	72
12.19.1.	Incident management	72
12.20.	Others	72
12.20.1.	Guideline on good pharmacovigilance practices (GVP) Product- or Population- Specific considerations III: risk management in pregnant and breastfeeding women	72
12.20.2.	EMA relocation to Amsterdam, the Netherlands – Questions & Answers (Q&As)	73
13.	Any other business	73
14.	Explanatory notes	74

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 11-14 February 2019. See February 2019 PRAC minutes (to be published post March 2019 PRAC meeting).

1.2. Agenda of the meeting on 11-14 February 2019

Action: For adoption

1.3. Minutes of the previous meeting on 14-17 January 2019

Action: For adoption

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

2.1. Newly triggered procedures

2.1.1. Fenspiride (NAP) - EMEA/H/A-107i/1480

Applicant(s): various

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

Scope: Review of the benefit-risk balance following notification by France of a referral under Article 107i of Directive 2001/83/EC, based on pharmacovigilance data

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

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

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

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

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

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

3.3. Procedures for finalisation

None

3.4. Re-examination procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation²

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Bevacizumab - AVASTIN (CAP), MVASI (CAP)

Applicant(s): Roche Registration GmbH (Avastin), Amgen Europe B.V. (Mvasi)

PRAC Rapporteur: Doris Stenver

Scope: Signal of splenic infarction

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

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

Action: For adoption of PRAC recommendation

EPITT 19344 – New signal

Lead Member State(s): DK

4.1.2. Secukinumab – COSENTYX (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Signal of dermatitis exfoliative generalised

Action: For adoption of PRAC recommendation

EPITT 19354 – New signal

Lead Member State(s): ES

4.2. New signals detected from other sources

4.2.1. Angiotensin converting enzyme (ACE) inhibitors: benazepril (NAP), captopril (NAP), cilazapril (NAP), delapril (NAP), enalapril (NAP), fosinopril (NAP), imidapril (NAP), lisinopril (NAP), moexipril (NAP), perindopril (NAP), quinapril (NAP), ramipril (NAP), trandolapril (NAP), zofenopril (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Evaluation of data on risk of lung cancer from a population based cohort study

Action: For adoption of PRAC recommendation

EPITT 19346 – New signal

Lead Member State(s): DE, DK, ES, IE, IT, NL, PT, SE, SK, UK

4.2.2. Armodafinil (NAP), modafinil (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Evaluation of data on foetal outcomes including congenital anomalies from a single observational study in the US

Action: For adoption of PRAC recommendation

EPITT 19367 – New signal

Lead Member State(s): DE

4.2.3. Olanzapine - OLANZAPINE APOTEX (CAP), OLANZAPINE GLENMARK (CAP), OLANZAPINE GLENMARK EUROPE (CAP), OLANZAPINE MYLAN (CAP), OLANZAPINE TEVA (CAP), OLAZAX (CAP), OLAZAX DISPERZI (CAP), ZALASTA (CAP), ZYPADHERA (CAP), ZYPREXA (CAP), ZYPREXA VELOTAB (CAP); NAP

Applicant(s): Apotex Europe BV (Olanzapine Apotex), Eli Lilly Nederland B.V. (Zypadhera, Zyprexa, Zyprexa Velotab), Glenmark Arzneimittel GmbH (Olanzapine Glenmark, Olanzapine Glenmark Europe), Glenmark Pharmaceuticals (Olazax, Olazax Disperzi), Krka, d.d. (Zalasta), Mylan S.A.S (Olanzapine Mylan), Teva B.V. (Olanzapine Teva), various

PRAC Rapporteur: To be appointed

Scope: Signal of salivary hypersecretion

Action: For adoption of PRAC recommendation

EPITT 19357 – New signal

Lead Member State(s): FI

4.2.4. Propylthiouracil (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of risk of congenital anomalies

Action: For adoption of PRAC recommendation

EPITT 19358 – New signal

Lead Member State(s): EE

4.2.5. Sulfasalazine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of interference with dihydronicotinamide-adenine dinucleotide / dihydronicotinamide-adenine dinucleotide phosphate (NADH/NADP) reaction assays

Action: For adoption of PRAC recommendation

EPITT 19351 – New signal

Lead Member State(s): DK

4.3. Signals follow-up and prioritisation

4.3.1. Olanzapine – OLANZAPINE APOTEX (CAP), OLANZAPINE GLENMARK (CAP), OLANZAPINE GLENMARK EUROPE (CAP), OLANZAPINE MYLAN (CAP), OLANZAPINE TEVA (CAP), OLAZAX (CAP), OLAZAX DISPERZI (CAP), ZALASTA (CAP) - EMEA/H/C/000792/SDA/007, ZYPADHERA (CAP) - EMEA/H/C/000890/SDA/029, ZYPREXA (CAP) - EMEA/H/C/000115/SDA/050, ZYPREXA VELOTAB (CAP) - EMEA/H/C/000287/SDA/043; NAP

Applicant(s): Apotex Europe BV (Olanzapine Apotex), Eli Lilly Nederland B.V. (Zypadhera, Zyprexa, Zyprexa Velotab), Glenmark Arzneimittel GmbH (Olanzapine Glenmark, Olanzapine Glenmark Europe), Glenmark Pharmaceuticals (Olazax, Olazax Disperzi), Krka, d.d. (Zalasta), Mylan S.A.S (Olanzapine Mylan), Teva B.V. (Olanzapine Teva), various

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of gestational diabetes

Action: For adoption of PRAC recommendation

EPITT 19306 – Follow up to October 2018

4.3.2. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/054

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of facial paralysis

Action: For adoption of PRAC recommendation

EPITT 19295 – Follow up to October 2018

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Ambrisentan - EMEA/H/C/004985

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. Avatrombopag - EMEA/H/C/004722

Scope: Treatment of thrombocytopenia

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

5.1.3. Cabazitaxel - EMEA/H/C/004951

Scope: Treatment of prostate cancer

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

5.1.4. Crisaborole - EMEA/H/C/004863

Scope: Treatment of mild to moderate atopic dermatitis

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

5.1.5. Edaravone - EMEA/H/C/004938, Orphan

Applicant: Mitsubishi Tanabe Pharma Europe Ltd

Scope: Treatment of amyotrophic lateral sclerosis (ALS)

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

5.1.6. Ioflupane (¹²³I) - EMEA/H/C/004745

Scope: Detection of loss of functional dopaminergic neuron terminals in the striatum

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

5.1.7. Onasemnogene abeparvovec - EMEA/H/C/004750, Orphan

Applicant: AveXis Netherlands B.V., ATMP³

Scope (accelerated assessment): Treatment of spinal muscular atrophy (SMA)

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

5.1.8. Posaconazole - EMEA/H/C/005005

Scope: Treatment of fungal infections

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

5.1.9. Ravulizumab - EMEA/H/C/004954, Orphan

Applicant: Alexion Europe SAS

Scope: Treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH)

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

5.1.10. Talazoparib - EMEA/H/C/004674

Scope: Treatment of adult patients with germline breast cancer susceptibility gene (BRCA)

³ Advanced therapy medicinal product

mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

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

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

5.2.1. Abacavir - ZIAGEN (CAP) - EMEA/H/C/000252/WS1521/0105; abacavir, lamivudine - KIVEXA (CAP) - EMEA/H/C/000581/WS1521/0079; abacavir, lamivudine, zidovudine - TRIZIVIR (CAP) - EMEA/H/C/000338/WS1521/0112

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an RMP (version 1.0) combining the RMPs for Ziagen (abacavir), Kivexa (abacavir/lamivudine) and Trizivir (abacavir/lamivudine/zidovudine) into one RMP specific to abacavir-active substance

Action: For adoption of PRAC Assessment Report

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

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Eva Segovia

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

Action: For adoption of PRAC Assessment Report

5.2.3. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/II/0015

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of the RMP (version 2.0) in order to update the requirements for a planned study (listed as a category 3 in the RMP): a multicentre, observational, non-interventional European study of patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelor. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC Assessment Report

5.2.5. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0064

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Update of the RMP (version 16.0) to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template) and consequential removal of the food interaction and drug-drug interactions (DDI) from the list of important identified risks. In addition, 'drug reaction with eosinophilia and systemic symptoms (DRESS)' is reclassified from important potential risk to important identified risk as requested in the conclusions of PSUSA/00000939/201710 procedure adopted in May 2018. Furthermore, the healthcare professional (HCP) guide is also updated. The MAH took the opportunity to include minor changes throughout the RMP

Action: For adoption of PRAC Assessment Report

5.2.6. Dexamethasone - NEOFORDEX (CAP) - EMEA/H/C/004071/II/0008

Applicant: Laboratoires CTRS

PRAC Rapporteur: Ghania Chamouni

Scope: Update of the RMP (version 4.0) in order to propose the 'removal of the score line for subdivision of the 40mg tablet and consequent deletion of the 20mg posology' as a category 3 activity. In addition, the MAH updated the other category 3 activity 'development of a 20mg oral dosage form'. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.7. Fluciclovine (¹⁸F) - AXUMIN (CAP) - EMEA/H/C/004197/II/0010

Applicant: Blue Earth Diagnostics Ltd

PRAC Rapporteur: Rugile Pilviniene

Scope: Update of the RMP (version 2.0) in order to bring it 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). In addition, the MAH updated the RMP to include new exposure details from clinical trials and exposure from US and EU in real-world setting and corrected the effectiveness measurement of the image interpretation training from a review of self-assessments scores to standard pharmacovigilance activities

Action: For adoption of PRAC Assessment Report

5.2.8. [Herpes zoster vaccine \(recombinant, adjuvanted\) - SHINGRIX \(CAP\) - EMEA/H/C/004336/II/0011](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Daniela Philadelphia

Scope: Update of the RMP (version 2) in order to extend the due dates of four category 3 studies, namely: study ZOSTER-002: an observer-blind study to evaluate efficacy, safety, and immunogenicity of Shingrix (herpes zoster vaccine) in adult autologous haematopoietic stem cell transplant (HCT) recipients; study ZOSTER-039: an observer blind study to evaluate safety and immunogenicity of Shingrix (herpes zoster vaccine) in adults aged 18 years and older with haematologic malignancies, study ZOSTER-041: an observer-blind study to evaluate immunogenicity and safety of Shingrix (herpes zoster vaccine) in adults aged 18 years and older with renal transplant; study ZOSTER-028: an observer-blind study to evaluate immunogenicity and safety of Shingrix (herpes zoster vaccine) in adults aged 18 years and older with solid tumours receiving chemotherapy. In addition, the RMP is updated to change the study design and due dates of category 3 study EPI-ZOSTER-030 VS: a targeted safety study (TSS) to evaluate the safety of Shingrix (herpes zoster vaccine) in adults 50 years of age and older. Furthermore, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.9. [Human papillomavirus vaccine \[types 6, 11, 16, 18, 31, 33, 45, 52, 58\] \(recombinant, adsorbed\) - GARDASIL 9 \(CAP\) - EMEA/H/C/003852/II/0029](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of the RMP (version 3.1) in order to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template). As a result, the safety concerns are updated

Action: For adoption of PRAC Assessment Report

5.2.10. [Panobinostat - FARYDAK \(CAP\) - EMEA/H/C/003725/II/0013, Orphan](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Patrick Batty

Scope: Update of the RMP (version 5.0) in order to remove the commitment to conduct study LBH589D2408 (listed as a category 3 study in the RMP): a non-interventional PASS of panobinostat use in relapsed or relapsed/refractory multiple myeloma patients who have received at least two prior regimens including bortezomib and an immunomodulatory agent

in a real-world setting according to the current EU prescribing information and document adherence to dosing regimen (including the dosing card, blister pack) by describing clinical characteristics, frequency and severity of medication error events

Action: For adoption of PRAC Assessment Report

5.2.11. [Piperaquine tetraphosphate, arteminol - EURARTESIM \(CAP\) - EMEA/H/C/001199/II/0032](#)

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 15.2) to close the pregnancy registry 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 include the 'distribution of a new version of the educational material', to add 'delayed haemolytic anaemia' and 'severe cutaneous adverse reactions (SCARs)' such as Stevens-Johnson syndrome and toxic epidermal necrolysis as important potential risks, to limit the reproductive risk to the first trimester of pregnancy; to update on several studies, to include Eurartesim (piperaquine tetraphosphate/arteminol) into the WHO⁴ list of essential medicines and to update the details of the MAH

Action: For adoption of PRAC Assessment Report

5.2.12. [Pramipexole - MIRAPEXIN \(CAP\) - EMEA/H/C/000134/WS1510/0089; SIFROL \(CAP\) - EMEA/H/C/000133/WS1510/0080](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of the RMP (version 9) to implement changes as requested in the conclusions of PSUSA/00002491/201604 procedure and in connection with a PRAC signal assessment procedure. In addition, the RMP is in order to bring it in line with revision 2 of the guidance on the format of RMP in the EU (template). Furthermore, the MAH took the opportunity to adapt the medical search strategies and data retrieval approach without any impact on the overall safety conclusion

Action: For adoption of PRAC Assessment Report

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

⁴ World Health Organization

5.2.14. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/II/0006

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Update of the RMP (version 3.0) in order to reflect that the first milestones (i.e. final protocol submissions) are fulfilled for study NN9535-4447: a cohort study based on Nordic registry data to assess the risk of pancreatic cancer associated with the use of Ozempic (semaglutide) in patients with type 2 diabetes mellitus (T2DM) and study NN9535-4352: a randomised, double-masked parallel-group, placebo-controlled trial assessing the long-term effects of Ozempic (semaglutide) on diabetic retinopathy in subjects with T2DM. In addition, the RMP is updated in line with revision 2 of the guidance on the format of RMP in the EU (template) and in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.15. Tolcapone - TASMAR (CAP) - EMEA/H/C/000132/II/0061

Applicant: Meda AB

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of the RMP (version 7) in order to reflect currently available data from post-marketing experience and patient exposure data, to align the RMP with revision 2 of GVP module V on 'Risk management systems' as well as to remove 'dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)' as an important identified risk and 'drug interactions with significant clinical consequence including sudden sleep onset' as a potential risk

Action: For adoption of PRAC Assessment Report

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

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

completion of the renewal procedure of the marketing authorisation in July 2018

Action: For adoption of PRAC Assessment Report

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

5.3.1. [Anakinra - KINERET \(CAP\) - EMEA/H/C/000363/II/0064/G](#)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of section 4.4 of the SmPC in order to add a warning on pulmonary events based on post-marketing data. The package leaflet is updated accordingly. Consequently, the important potential risks and the list of target medical events in the RMP (version 4.6) are updated to include pulmonary events and a specific follow-up questionnaire is introduced. The RMP is also revised in line with revision 2 of the guidance on the format of RMP in the EU (template). In addition, the due date for submission of the final study report for study Sobi ANAKIN-302 (listed as a category 3 in the RMP): 'a non-interventional study to follow-up long term safety including macrophage activation syndrome MAS in paediatric patients with Still's disease (PRINTO/Pharmachild registry)' is proposed to be extended. Furthermore, the MAH took the opportunity to move the text about MAS and malignancies from section 4.8 to section 4.4 of the SmPC

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

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

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

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

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

5.3.3. [Beclometasone dipropionate, formoterol fumarate dehydrate, glycopyrronium - RIARIFY \(CAP\) - EMEA/H/C/004836/WS1554/0002; TRYDONIS \(CAP\) - EMEA/H/C/004702/WS1554/0002](#)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication based on results from two Phase 3 studies, namely Triple 7 (CCD-05993AA1-07): 'a multinational, multicentre, randomised, open-label, active-controlled, 26-week, 2-arm, parallel group study to evaluate the non-inferiority of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium

bromide (Riarify/Trydonis (CHF 5993)) administered via pressurized metered-dose inhaler (pMDI) versus fixed combination of fluticasone furoate plus vilanterol administered via dry powder inhaler (DPI) (Relvar) plus tiotropium bromide (Spiriva) for the treatment of patients with chronic obstructive pulmonary disease' and Triple 8 (CCD-05993AA1-08): '52-week, double blind, randomized, 2 active parallel arms study of fixed combination CHF 5993 administered vs glycopyrronium bromide/indacaterol maleate (Ultibro) in chronic obstructive pulmonary disease (COPD) patients' in order to include maintenance treatment in adult patients with moderate to severe COPD who are not adequately treated by combination of a long-acting beta2-agonist and a long-acting muscarinic antagonist. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.4. [Bedaquiline - SIRTURO \(CAP\) - EMEA/H/C/002614/II/0028, Orphan](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to update the safety information with inclusion of a statement on bedaquiline resistance in line with the outcome of the PSUSA procedure (PSUSA/00010074/201709) finalised in April 2018. The RMP (version 3.0) is updated based on the data triggering the SmPC update and to reflect completion of studies which were assessed in previous procedures. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.5. [Belimumab - BENLYSTA \(CAP\) - EMEA/H/C/002015/II/0062](#)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include patients aged 5 years and older in the current approved indication for the powder for solution for infusion 120 mg/mL and 400 mg/mL based on the results of study BEL114055: a multicentre, randomized parallel group, placebo-controlled double-blind trial to evaluate the safety, efficacy, and pharmacokinetics of belimumab, a human monoclonal anti-BLyS antibody, plus standard therapy in paediatric patients with systemic lupus erythematosus (SLE). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information. In addition, sections 4.2, 5.1 and 5.2 of the SmPC for the solution for injection in pre-filled pen and pre-filled syringe, 200 mg are updated to reflect the paediatric data available for the intravenous formulation. The package leaflet is updated accordingly. Furthermore, the RMP (version 28.0) is updated accordingly and with revision 2 of the guidance on the format of RMP in the EU (template). Finally, the MAH took the opportunity to introduce some editorial changes in the product information and bring it in line with the latest QRD template (version 10.0)

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

5.3.6. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0014/G

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Grouped variation consisting of: 1) addition of an auto-injector delivery device, Fasentra 30 mg solution for injection in pre-filled pen, 2) update of sections 4.2, 6.4, 6.5 and 6.6 of the SmPC in order to update the information for self-administration for Fasentra 30 mg solution for injection in pre-filled syringe. The labelling and the package leaflet are updated accordingly. In addition, the RMP (version 2.0) is updated to reflect the information about the new presentation, to include additional information on completed studies, namely: study ALIZE: 'a multicentre, randomized, double-blind, parallel group, placebo-controlled, phase 3b study to evaluate the potential effect of benralizumab on the humoral immune response to the seasonal influenza vaccination in adolescent and young adult patients with severe asthma'; study GREGALE: a multicentre, open-label, functionality, reliability, and performance study of an accessorized pre-filled syringe with home-administered subcutaneous benralizumab in adult patients with severe asthma; study AMES: a multicentre, randomised, open-label, parallel group, phase 1 study designed to compare benralizumab pharmacokinetics exposure in healthy subjects following single subcutaneous administration of a fixed 30 mg dose of benralizumab when using an autoinjector and accessorised pre-filled syringe; study GRECO: a multicentre, open-label, functionality, reliability and performance study of a single-use auto-injector with home-administered subcutaneous benralizumab in adult patients with severe asthma. The RMP is also updated with exposure data post marketing authorisation (MA) approval, and additional details on the following post-authorisation safety studies: study D3250R00026 (pregnancy registry): benralizumab pregnancy exposure study: a Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) post marketing surveillance study, and study D3250R00042 (malignancy PASS): a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other biologic therapy. Furthermore, the RMP is updated in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.7. Ceftaroline fosamil - ZINFORO (CAP) - EMEA/H/C/002252/II/0041

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Extension of indication to include paediatric patients from birth to less than 2 months old based on results from study D3720C00009 (C2661002) an open-label, multicentre study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of ceftaroline in neonates and young infants with late-onset sepsis. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, 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

5.3.8. [Ciclosporin - IKERVIS \(CAP\) - EMEA/H/C/002066/WS1490/0014; VERKAZIA \(CAP\) - EMEA/H/C/004411/WS1490/0001](#)

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Update of the RMP (version 7.0) in order to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template). The milestones for the Verkazia (ciclosporin) PASS on: quantification of the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin) for vernal keratoconjunctivitis (VKC), have also been updated. In addition, the MAH proposed to align Ikervis (ciclosporin) SmPC section 4.4 on concomitant therapy and effects on immune system with Verkazia (ciclosporin) SmPC in order to harmonise the routine risk minimisation measures for both medicinal products. The MAH took this opportunity to implement the latest QRD template and the safety features for Ikervis (ciclosporin)

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

5.3.9. [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

5.3.10. [Eltrombopag - REVOLADE \(CAP\) - EMEA/H/C/001110/II/0049](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include first line treatment of adult and paediatric patients aged 2 years and older with severe aplastic anaemia. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 50.0) are updated accordingly

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

5.3.11. [Erenumab - AIMOVIG \(CAP\) - EMEA/H/C/004447/X/0001](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

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

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

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

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

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

5.3.13. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/II/0015

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit organic cation transporter 1 (OCT1) based on final results from study V8953M-SPD503: a non-clinical study to investigate the rate limiting step (hepatic uptake or hepatic metabolism) in the elimination of guanfacine. The RMP (version 3.0) is updated accordingly

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

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

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

5.3.15. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0046, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include treatment of adult patients with Waldenström's macroglobulinaemia (WM) in combination with rituximab, based on the results of the final clinical study report of study PCYC-1127-CA: a randomized, double-blind, placebo-controlled, phase 3 study of ibrutinib or placebo in combination with rituximab in subjects with WM (iNNOVATE study). As a consequence, sections 4.1 and 4.8 of the SmPC are updated accordingly. The RMP (version 12) is updated accordingly. In addition, the MAH took the opportunity to update the SmPC and package leaflet with minor editorial/administrative changes

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

5.3.16. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0047, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to extend the existing indication on chronic lymphocytic leukaemia (CLL) to include the combination use with obinutuzumab for the treatment of adult patients with previously untreated CLL, based on the data from study PCYC-1130-CA: a randomized, multicentre, open-label, phase 3 study of the Bruton's tyrosine kinase inhibitor ibrutinib in combination with obinutuzumab versus chlorambucil in combination with obinutuzumab in subjects with treatment-naïve CLL or small lymphocytic lymphoma. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly. The RMP (version 12) is updated accordingly. In addition, the MAH took the opportunity to update the SmPC and package leaflet with minor editorial/administrative changes

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

5.3.17. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/II/0137/G

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.3, 4.6 and 5.3 of the SmPC in order to add information about pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries (EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries); 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The package leaflet is updated accordingly (fulfilment of MEA 43.2 and 39). The RMP (version 10.0) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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

5.3.18. Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/II/0124/G

Applicant: Bayer AG

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries (EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries); 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The package leaflet has been updated accordingly (fulfilment of MEA 024.2 and 21). The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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. Interferon beta-1b - EXTAVIA (CAP) - EMEA/H/C/000933/II/0096/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries (EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries); 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The package leaflet is updated accordingly (fulfilment of MEA 022.2 and 019). The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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

5.3.20. Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/II/0073/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR); 2) update of section 4.8 of the SmPC to update the frequency of some adverse events (AEs) based on data obtained from the updated safety pool analysis (Pool DBC-1) which consists of the combined data from SP667, SP754, SP755, and EP0008. All of these studies were randomized, double-blind, placebo-controlled, parallel-group,

adjunctive therapy studies in subjects with epilepsy. The package leaflet and the RMP (version 13.0) are updated accordingly

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

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

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

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

5.3.22. [Modified vaccinia Ankara virus - IMVANEX \(CAP\) - EMEA/H/C/002596/II/0036](#)

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 provide confirmation in terms of immunogenicity based on the results from study POX-MVA-006 (listed as an obligation in Annex II (ANX 004)): a randomized, open-label phase 3 non-inferiority trial to compare indicators of efficacy for smallpox vaccine to the US licensed replicating smallpox vaccine in 18-42 year old healthy vaccinia-naïve subjects. The package leaflet and the RMP (version 7.2) are updated accordingly

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

5.3.23. [Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA \(CAP\) - EMEA/H/C/003687/II/0029/G](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.8 to adjust the list of adverse drug reactions and their corresponding frequencies in line with the outcome of the PSUSA procedure (PSUSA/00010366/201709) finalised in April 2018 ; 2) update of sections 4.2, 4.4 and 5.2 of the SmPC to add results from a phase 1 open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning is updated accordingly. The warning related to contraindications is aligned to section 4.3 to add end-stage renal failure patients. As a consequence, the RMP is updated accordingly (version 11). In addition, the MAH took the opportunity to update the warning on lactose in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

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

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

5.3.25. Plerixafor - MOZOBIL (CAP) - EMEA/H/C/001030/II/0034, Orphan

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

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

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

5.3.26. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0023

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

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

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

5.3.27. [Palbociclib - IBRANCE \(CAP\) - EMEA/H/C/003853/II/0017/G](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of an update of section 5.3 of the SmPC in order to include information from two completed non-clinical studies: a 6-month carcinogenicity study in mice (20084764), and a 2-year carcinogenicity study in rats (20066483). Furthermore, the MAH submitted the final report from the non-clinical study 20084675: a pre- and postnatal developmental toxicity study in rats. The RMP (version 1.5) is updated accordingly. The MAH took the opportunity to introduce minor editorial changes throughout the product information

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

5.3.28. [Peginterferon beta-1a - PLEGRIDY \(CAP\) - EMEA/H/C/002827/II/0052/G](#)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries (EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries); 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The package leaflet has been updated accordingly (fulfilment of MEA 8.2 and 002). The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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 International Federation of Gynaecology and Obstetrics

5.3.29. [Plasmodium falciparum and hepatitis B vaccine \(recombinant, adjuvanted\) - MOSQUIRIX \(Art 58⁶\) - EMEA/H/W/002300/II/0036](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.4 of the SmPC in order to modify the warning on 'protection against *Plasmodium falciparum* malaria' over time. This update is based on the final results from study MALARIA-076 (listed as a category 3 study in the RMP): an open extension to phase 3, multicentre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of Mosquirix (plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)) malaria vaccine in infants and children. The RMP (version 4.1) is updated accordingly

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

5.3.30. [Prepandemic influenza vaccine \(H5N1\) \(surface antigen, inactivated, adjuvanted\) - AFLUNOV \(CAP\) - EMEA/H/C/002094/II/0044/G](#)

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Grouped variations consisting of an update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following the completion of clinical study reports for 1) study V87_25: a phase 3, prospective, controlled, observer-blind, multicentre study to evaluate the safety, tolerability and immunogenicity of two doses of a monovalent A/H5N1 influenza vaccine adjuvanted with MF59 when administered to subjects with and without underlying medical conditions; 2) study V87_26: a phase 3, prospective, controlled, observer-blind, multicentre study to evaluate the safety, tolerability and immunogenicity of two doses of a monovalent A/H5N1 influenza vaccine adjuvanted with MF59 when administered to adults and elderly subjects with immunosuppressive disorders. The package leaflet, labelling and RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to implement some amendments to the product information and introduce some additional minor editorial corrections

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

5.3.31. [Ranibizumab - LUCENTIS \(CAP\) - EMEA/H/C/000715/II/0076](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of moderately severe to severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated with. The package leaflet and the RMP (version 19.0) are updated accordingly

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

⁶ 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)

5.3.32. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0152

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

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

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

5.3.33. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0022

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Update of Sections 4.2, 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study AC-065-117 (listed as a category 3 study in the RMP): clinical pharmacology drug-drug interaction (DDI) study evaluating the effect of clopidogrel a moderate inhibitor of CYP2C8⁷, on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet and the RMP (version 6.1) are updated accordingly. In addition, the MAH took the opportunity to correct minor discrepancies in the SmPC

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

5.3.34. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0029

Applicant: Amgen Europe B.V., ATMP⁸

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.2 of the SmPC in order to amend the pharmacokinetic properties information based on the final results from study 20120324: a phase 2, multicentre, single-arm trial to evaluate the biodistribution and shedding of talimogene laherparepvec in subjects with unresected, stage IIIB to stage IVM1c melanoma. This submission fulfils MEA 006.1. In addition, the MAH took the opportunity to update Annex II as per the outcome of the assessment of ANX 001 procedure concluded in October 2018

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

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

Applicant: Gilead Sciences Ireland UC

⁷ Cytochrome P450 2C8

⁸ Advanced therapy medicinal product

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication to include as a new indication treatment of chronic hepatitis B (CHB) in paediatric patients aged 6 to < 12 years (film coated tablets 123 mg; 163 mg; 204 mg) and to extend the existing CHB indication to include treatment of CHB in paediatric patients aged 2 to < 12 years (granules 33 mg/g), based on results from interim week 48 clinical study report (CSR) for study GS-US-174-0144: a randomized, double-blind evaluation of the antiviral efficacy, safety and tolerability of tenofovir disoproxil fumarate versus placebo in paediatric patients with CHB infection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated for Viread (tenofovir disoproxil) 123 mg, 163 mg and 204 mg; sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Viread (tenofovir disoproxil) 245 mg; and sections 4.1, 4.2, 4.4, 5.1 and 5.2 for Viread (tenofovir disoproxil) granules 33 mg/g. The package leaflet and the RMP (version 22.1) are updated accordingly

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

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

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

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

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

5.3.37. Trastuzumab - ONTRUZANT (CAP) - EMEA/H/C/004323/II/0016

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Addition of a new presentation with a new fill weight (420 mg) of a sterile single dose partial use parenteral medicinal product for Ontruzant (trastuzumab). The RMP (version 3.0) is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes in the product information in line with the originator product

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

5.3.38. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/II/0028

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding rearranged during transfection (RET) mutation. The application fulfils SOB 001 and includes a proposal to revert from conditional marketing authorisation to standard

marketing authorisation. Annex II, the package leaflet and the RMP (version 12.2) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

5.3.39. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0020, Orphan

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsova

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to include that a 50% dose reduction of venetoclax is recommended in patients with severe hepatic impairment, based on the final results from study M15-342 (listed as a category 3 study in the RMP): a study to evaluate the safety and pharmacokinetics of a single dose of ventoclax in female subjects with mild, moderate, or severe hepatic impairment. The package leaflet and the RMP (version 3.4) are 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. Aclidinium bromide - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/201807

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aflibercept⁹ - ZALTRAP (CAP) - PSUSA/00010019/201808

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Albutrepenonacog alfa - IDELVION (CAP) - PSUSA/00010497/201807

Applicant: CSL Behring GmbH

⁹ Oncology indication(s) only

PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.4. [Alirocumab - PRALUENT \(CAP\) - PSUSA/00010423/201807](#)

Applicant: Sanofi-aventis groupe
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.5. [Antithrombin alfa - ATRYN \(CAP\) - PSUSA/00000224/201807](#)

Applicant: Laboratoire Francais du Fractionnement et des Biotechnologies
PRAC Rapporteur: Ghania Chamouni
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.6. [Asparaginase¹⁰ - SPECTRILA \(CAP\) - PSUSA/00010445/201807](#)

Applicant: Medac Gesellschaft fur klinische Spezialpreparate mbH
PRAC Rapporteur: Patrick Batty
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.7. [Ataluren - TRANSLARNA \(CAP\) - PSUSA/00010274/201807](#)

Applicant: PTC Therapeutics International Limited
PRAC Rapporteur: Liana Gross-Martirosyan
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.8. [Atazanavir, cobicistat - EVOTAZ \(CAP\) - PSUSA/00010404/201807](#)

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

¹⁰ Centrally authorised product(s) only

6.1.9. **Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/201807**

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. **Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - PSUSA/00010695/201808**

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. **Birch bark extract¹¹ - EPISALVAN (CAP) - PSUSA/00010446/201807**

Applicant: Amryt AG

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. **Brivaracetam - BRIVIACT (CAP) - PSUSA/00010447/201807**

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. **Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/201807**

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. **Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201807**

Applicant: Amgen Europe B.V.

¹¹ Centrally authorised product(s) only

PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.15. [Catridecacog - NOVOTHIRTEEN \(CAP\) - PSUSA/00010034/201807](#)

Applicant: Novo Nordisk A/S
PRAC Rapporteur: Ghania Chamouni
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.16. [Efavirenz, emtricitabine, tenofovir - ATRIPLA \(CAP\) - PSUSA/00001201/201807](#)

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.17. [Elbasvir, grazoprevir - ZEPATIER \(CAP\) - PSUSA/00010519/201807](#)

Applicant: Merck Sharp & Dohme B.V.
PRAC Rapporteur: Ana Sofia Diniz Martins
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.18. [Etanercept¹² - BENEPALI \(CAP\); ERELZI \(CAP\) - PSUSA/00010452/201807](#)

Applicant: Samsung Bioepis NL B.V. (Benepali), Sandoz GmbH (Erelzi)
PRAC Rapporteur: Patrick Batty
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.19. [Evolocumab - REPATHA \(CAP\) - PSUSA/00010405/201807](#)

Applicant: Amgen Europe B.V.
PRAC Rapporteur: Kimmo Jaakkola
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹² Biosimilar products only

6.1.20. Gefitinib - IRESSA (CAP) - PSUSA/00001518/201807

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/201807

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/201807

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Hydrocortisone¹³ - ALKINDI (CAP) - PSUSA/00010674/201808

Applicant: Diurnal Europe BV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ibandronic acid – BONDRONAT (CAP); BONVIVA (CAP) - PSUSA/00001702/201806

Applicant: Atnahs Pharma UK Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/201807

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Patrick Batty

¹³ Centrally authorised product(s) for adrenal insufficiency, paediatric use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. [Idursulfase - ELAPRASE \(CAP\) - PSUSA/00001722/201807](#)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. [Ingenol mebutate - PICATO \(CAP\) - PSUSA/00010035/201807 \(with RMP\)](#)

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. [Lipegfilgrastim - LONQUEX \(CAP\) - PSUSA/00010111/201807](#)

Applicant: Teva B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. [Lomitapide - LOJUXTA \(CAP\) - PSUSA/00010112/201807](#)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. [Mercaptamine¹⁴ - CYSTADROPS \(CAP\) - PSUSA/00010574/201807](#)

Applicant: Orphan Europe SARL

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁴ For treatment of corneal cystine crystal deposits only

6.1.31. Modified vaccinia Ankara virus - IMVANEX (CAP) - PSUSA/00010119/201807

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Natalizumab - TYSABRI (CAP) - PSUSA/00002127/201808 (with RMP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/201808

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Paliperidone - INVEGA (CAP); paliperidone palmitate - TREVICTA (CAP); XEPLION (CAP) - PSUSA/00002266/201806

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Pegaptanib - MACUGEN (CAP) - PSUSA/00002324/201806

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pegaspargase¹⁵ - ONCASPAR (CAP) - PSUSA/00010457/201807 (with RMP)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Patrick Batty

¹⁵ Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Peginterferon beta-1A - PLEGRIDY (CAP) - PSUSA/00010275/201807

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/201807

Applicant: Eisai GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/201807

Applicant: Omeros London Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/201807

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Sarilumab - KEVZARA (CAP) - PSUSA/00010609/201807

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/201807

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - PSUSA/00010619/201807

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Stavudine - ZERIT (CAP) - PSUSA/00002787/201806

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Telithromycin - KETEK (CAP) - PSUSA/00002881/201807

Applicant: Aventis Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Tobramycin¹⁶ - TOBI PODHALER (CAP) - PSUSA/00009315/201806

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/201807

Applicant: Orphan Europe SARL

PRAC Rapporteur: Patrick Batty

¹⁶ Inhalation powder, capsules only

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. 5-aminolevulinic acid¹⁷ - AMELUZ (CAP); NAP - PSUSA/00010006/201806

Applicants: Biofrontera Bioscience GmbH (Ameluz), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Aripiprazole - ABILIFY (CAP); ABILIFY MAINTENA (CAP); ARIPIPRAZOLE SANDOZ (CAP); NAP - PSUSA/00000234/201807

Applicants: Otsuka Pharmaceutical Netherlands B.V. (Abilify, Abilify Maintena), Sandoz GmbH (Aripiprazole Sandoz), various

PRAC Rapporteur: Ana Sofia Diniz Martins

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. Aciclovir (NAP) – PSUSA/00000048/201806

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Calcitonin salmon (NAP); synthetic analogue of eel calcitonin (NAP) - PSUSA/00000494/201806

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁷ For treatment of keratosis only

6.3.3. Cefepime (NAP) - PSUSA/00000593/201806

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Daunorubicin (NAP) - PSUSA/00000936/201806

Applicant(s): various

PRAC Lead: Daniela Philadelphy

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Dexchlorpheniramine (NAP) - PSUSA/00000989/201806

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Dihydroergocryptine (NAP) - PSUSA/00001074/201807

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Fosinopril (NAP); fosinopril, hydrochlorothiazide (NAP) - PSUSA/00010463/201807

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Glibenclamide, metformin hydrochloride (NAP) - PSUSA/00002002/201806

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Human fibrinogen (NAP) - PSUSA/00001624/201806

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/201807

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Levonorgestrel, ethinylestradiol; ethinylestradiol (NAP)¹⁸ - PSUSA/00010442/201807

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/201807

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Manidipine (NAP) - PSUSA/00001932/201806

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁸ Combination pack only

6.3.14. Metyrapone (NAP) - PSUSA/00002046/201806

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Misoprostol¹⁹ (NAP) - PSUSA/00010291/201806

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Nilutamide (NAP) - PSUSA/00002163/201807

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Nimesulide²⁰ (NAP) - PSUSA/00009236/201806

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Nimesulide²¹ (NAP) - PSUSA/00002165/201806

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Paracetamol, pseudoephedrine (NAP) - PSUSA/00002307/201806

Applicant(s): various

PRAC Lead: Laurence de Fays

¹⁹ For gastrointestinal indication(s) only

²⁰ Systemic formulations only

²¹ Topical formulations only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Phenylpropanolamine (NAP) - PSUSA/00010483/201806

Applicant(s): various

PRAC Lead: Eva Jirsova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Pipobroman (NAP) - PSUSA/00002427/201806

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Pitavastatin (NAP) - PSUSA/00010502/201807

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Pseudoephedrine (CAP); acetylsalicylic acid, pseudoephedrine (NAP) - PSUSA/00010667/201806

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Rabbit anti-human T-lymphocyte immunoglobulin (NAP) - PSUSA/00010252/201806

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Rizatriptan (NAP) - PSUSA/00002655/201806

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Solifenacin, tamsolusin (NAP) - PSUSA/00010285/201807

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Thiocolchicoside (CAP); paracetamol, thiocolchicoside (NAP) - PSUSA/00010464/201807

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Tiagabine (NAP) - PSUSA/00002942/201806

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Tianeptine (NAP) - PSUSA/00002943/201806

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Urapidil (NAP) - PSUSA/00003078/201807

Applicant(s): various

PRAC Lead: Eva Jirsova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. 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 advice to CHMP

6.4.2. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/LEG 024

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Review on the risk of interaction between morphine and Brilique (ticagrelor) as requested in the conclusions of PSUSA/00002499/201802 for prasugrel adopted in September 2018 for other P2Y₁₂ inhibitors, agents of the same class as prasugrel

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²²

7.1.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSP/S/0071

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Protocol for an observational PASS to describe the long-term safety profile of first-relapse B-precursor acute lymphoblastic leukaemia (ALL) paediatric patients who have been treated with blinatumomab or chemotherapy prior to undergoing haematopoietic stem cell transplant

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

7.1.2. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/PSP/S/0070

Applicant: Bayer AG

²² In accordance with Article 107n of Directive 2001/83/EC

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for an observational study to assess the effectiveness and long term safety of prophylaxis with damoctocog alfa pegol in real-world settings through the collection of total bleeding events and analysis of the annualised bleeding rate (ABR) in the different prophylaxis regimens (following approved local label or any other regimen prescribed by the physician as part of normal clinical practice) in patients with haemophilia A

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

7.1.3. Valproate (NAP) - EMEA/H/N/PSP/J/0072

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for a retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in March 2018 (EMEA/H/A-31/1454)

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

7.1.4. Valproate (NAP) - EMEA/H/N/PSP/J/0073

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for a survey among healthcare professionals (HCP) to assess the knowledge of HCP and behaviour with regard to the pregnancy prevention programme (PPP), the receipt/use of direct healthcare professional communication (DHPC) and educational materials as well as for a survey among patients to assess the knowledge of patients with regards to PPP and receipt/use of educational materials, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in March 2018 (EMEA/H/A-31/1454)

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

7.1.5. Valproate (NAP) - EMEA/H/N/PSP/J/0074

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: Protocol for an observational study to evaluate and identify the best practices for switching of valproate in clinical practice, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in March 2018 (EMEA/H/A-31/1454)

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

7.1.6. Valproate (NAP) - EMEA/H/N/PSP/J/0075

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for a drug utilisation study (DUS) to assess the effectiveness of the new risk minimisation measures and to further characterise the prescribing patterns for valproate as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in March 2018 (EMEA/H/A-31/1454)

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

7.1.7. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/PSP/S/0060.2

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to PSP/S/060.1 [protocol for the alfa-mannosidosis registry: a multicentre, multi-country, non-interventional, prospective cohort, in alfa-mannosidosis patients to evaluate the long-term effectiveness and safety profile of treatment with Lamzede (velmanase alfa) under conditions of routine clinical care and to characterize the entire alfa-mannosidosis population, including variability of clinical manifestation, progression and natural history] as per the request for supplementary information (RSI) adopted in October 2018

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²³

7.2.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/MEA 016.1

Applicant: Bayer AG

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 016 [Protocol for a follow-up survey measuring the effectiveness of the updated educational material for healthcare professionals (HCPs): a survey to investigate whether physicians have received the revised educational materials, measuring physician knowledge and understanding of the key information in the revised educational materials, and whether physicians have provided the patient booklet to their patients [result due date expected within 6 months after completion of the survey] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.2. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/MEA 002.1

Applicant: Roche Registration GmbH

²³ 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: Patrick Batty

Scope: MAH's response to MEA 002 [protocol for study BO40643: a survey measuring the effectiveness of the risk minimisation activities to prescribers: correct implementation of Alecensa (alectinib) label guidance by prescribers of the following important identified risks: interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, photosensitivity, bradycardia, severe myalgia and creatine phosphokinase (CPK) elevations] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.3. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.1

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: MAH's response to MEA 004 [protocol for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.4. Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/MEA 001

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Protocol and feasibility study for a case-control study linked to existing cancer registries to understand the data sources and analytic methods available to quantify the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.5. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/MEA 004.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 004 [Protocol for study CSIMM000265: a retrospective cohort study using health administrative claims databases to assess adverse pregnancy and infant outcomes in women with psoriasis who were exposed to guselkumab versus other biologic therapies during pregnancy] as per the request for supplementary information (RSI) adopted in November 2018

Action: For adoption of advice to CHMP

7.2.6. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.6

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.5 [protocol for study NB-451: a protocol synopsis for an observational retrospective database study based on secondary data analysis using existing databases, as suitable] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.7. [Obinutuzumab - GAZYVARO \(CAP\) - EMEA/H/C/002799/MEA 007.1](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Protocol for study BO41031: a survey to prescribers, with the objective to evaluate the effectiveness of Gazyvaro (obinutuzumab) routine risk minimisation activities of important identified risks in the SmPC by investigating healthcare professionals' (HCPs) awareness and knowledge of the important identified risks of infusion related reactions (IRR), tumour lysis syndrome (TLS), thrombocytopenia, worsening of pre-existing cardiac conditions, progressive multifocal leukoencephalopathy (PML), hepatitis B virus (HBV) reactivation, neutropenia and infection

Action: For adoption of advice to CHMP

7.2.8. [Patisiran - ONPATTRO \(CAP\) - EMEA/H/C/004699/MEA 002](#)

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study ALN-TTR02-0009: a prospective observational study to monitor and assess the safety of Onpattro (patisiran) in a real-world cohort of hereditary transthyretin amyloidosis (hATTR) patients

Action: For adoption of advice to CHMP

7.2.9. [Tezacaftor, ivacaftor - SYMKEVI \(CAP\) - EMEA/H/C/004682/MEA 002](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study VX17-661-117 (listed as a category 3 study in the RMP): an observational cohort study on utilisation patterns and real-world effects of tezacaftor and ivacaftor combination therapy (TEZ/IVA) in patients with cystic fibrosis (CF) [final report expected: December 2023]

Action: For adoption of advice to CHMP

7.2.10. [Tofacitinib - XELJANZ \(CAP\) - EMEA/H/C/004214/MEA 008.1](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 008 [protocol for study A3921312 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.11. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 009 [protocol for study A3921314 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Swedish (ARTIS) register] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.12. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 010 [protocol for study A3921316 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Spanish registry of adverse events of biological therapies and biosimilars in rheumatoid diseases (BIOBADASER)] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.13. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 008 [Protocol for study A3921317 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.2.14. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/MEA 004.4

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Additional Interim Report for study NN7008-3553: a multicentre non-interventional study of safety and efficacy of turoctocog alfa (recombinant factor VIII (rFVIII)) during long-term treatment of severe and moderately severe haemophilia A (FVIII \leq 2%) [final clinical study report (CSR): Q4 2021]

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²⁴

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)²⁵

7.4.1. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0050/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from studies (listed as category 3 studies in the RMP), namely: 1) study IM103074: an observational study designed to assess the pattern of use of belatacept in US transplant recipients in routine clinical practice; 2) study IM103077: an observational study designed to assess the patterns of use of belatacept in renal transplantation using the collaborative transplant study. The RMP is updated accordingly (version 16.0). In addition, the MAH took the opportunity to update the RMP in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template) and also to reflect minor editorial changes and the earlier completion dates for two remaining studies (listed as category 3 studies in the RMP), namely study IM103075: a study to assess the association between the use of belatacept and the risk of post-transplant lymphoproliferative disease (PTLD) in US renal transplant recipients; and study IM103076: evaluation of Nulojix (belatacept) long term safety in transplant (ENLIST) registry in order to estimate the incidence rates (IRs) of confirmed PTLD and central nervous system (CNS) PTLD in adult renal transplant recipients treated with belatacept in the US

Action: For adoption of PRAC Assessment Report

7.4.2. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/II/0039

Applicant: Teva B.V.

²⁴ In accordance with Article 107p-q of Directive 2001/83/EC

²⁵ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report from study CLB-MD-08 (listed as a category 3 study in the RMP): a non-interventional PASS cross-sectional survey study to evaluate the effectiveness of Colobreathe (colistimethate sodium) risk minimisation educational programme among healthcare professionals and patients. This submission fulfils MEA 012.1

Action: For adoption of PRAC Assessment Report

7.4.3. Collagenase clostridium histolyticum - XIAPEX (CAP) - EMEA/H/C/002048/II/0106

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from a non-interventional PASS (listed as a category 3 study in the RMP): effectiveness of the educational material for healthcare professionals of Xiapex (collagenase clostridium histolyticum) in the treatment of Peyronie's disease

Action: For adoption of PRAC Assessment Report

7.4.4. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0159

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final study report for the non-interventional study GS-EU-276-4027 (listed as a category 3 study in the RMP): a cross-sectional post-authorisation safety study to assess healthcare providers' level of awareness of risk minimisation materials for Truvada (emtricitabine/tenofovir disoproxil) for pre-exposure prophylaxis (PrEP) in the European Union. This submission fulfils MEA 045.7

Action: For adoption of PRAC Assessment Report

7.4.5. 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

7.4.6. Propranolol - HEMANGIOL (CAP) - EMEA/H/C/002621/II/0019

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: Submission of the results of a drug utilisation study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of risk minimisation measures (RMM) in a real-life clinical setting (MEA 002). As a consequence, the package leaflet is updated to strengthen the warning on hypoglycemia and bronchospasm. The RMP (version 3.1) is updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes in section 4.4 of the SmPC as well as changes in the package leaflet in accordance with the QRD template (version 10.0)

Action: For adoption of PRAC Assessment Report

7.4.7. Teriparatide - FORSTEO (CAP) - EMEA/H/C/000425/II/0050/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped variations consisting of the submission of the final study reports of the European Union (EU) components of two PASS; namely study B3DMC-GHBX (2.2) and study B3D-MC-GHBX (2.3b) both US population-based comparative cohort studies undertaken to evaluate a potential association between teriparatide and adult osteosarcoma. The RMP (version 7.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.4

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.3 [three year interim report for study PTC124-GD-025o-DMD (listed as a category 3 study in the RMP): a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting [final clinical study report (CSR) expected in: April 2023]] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.2. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.10

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Fifth annual interim report for study C1CL670E2422: an observational, multicentre cohort study to evaluate the long term exposure and safety of deferasirox in the treatment of paediatric non-transfusion dependent thalassaemia patients over 10 years old for whom deferoxamine is contraindicated or inadequate

Action: For adoption of advice to CHMP

7.5.3. Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Second annual report for study ZOB-NIV-1513 (C1121008): a multinational, multicentre, prospective, non-interventional PASS in healthy donors (HDs) exposed to Nivestim (biosimilar filgrastim) for haematopoietic stem cell (HSC) mobilisation (NEST) [final clinical study report (CSR) due date: March 2023]

Action: For adoption of advice to CHMP

7.5.4. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 027.6

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual progress report of the ENEIDA registry (study MK-8259-042): a long-term, non-interventional observational study of patients with inflammatory bowel disease (IBD) in Spain to evaluate whether the use of golimumab is associated with a risk of colectomy for intractable disease, advanced neoplasia (colorectal cancer or high grade dysplasia), and hepatosplenic T-cell lymphoma (HSTCL) in patients with ulcerative colitis (UC) as compared with alternative therapies for similar severity of disease [final clinical study report (CSR) expected: March 2023]

Action: For adoption of advice to CHMP

7.5.5. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/ANX 191.7

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Fifth progress report for study CSTI571I2201: a European observational registry collecting efficacy and safety data in newly diagnosed paediatric Philadelphia positive (Ph+) acute lymphoblastic leukaemia (ALL) patients treated with chemotherapy + imatinib ± haematopoietic stem cell treatment (±HSCT)

Action: For adoption of advice to CHMP

7.5.6. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 007.4](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 007.3 [annual interim safety and efficacy report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra (infliximab) in patients with rheumatoid arthritis (EU and Korea) [final report expected: May 2026]] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.7. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 010.4](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 010.3 [annual interim safety and efficacy report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) [final report expected: May 2026]] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.8. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 007.4](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 007.3 [annual interim safety and efficacy report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra (infliximab) in patients with rheumatoid arthritis (EU and Korea) [final clinical study report (CSR) expected: May 2026]] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.9. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 010.4](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 010.3 [annual interim safety and efficacy report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) [final report expected: May 2026]] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.10. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/MEA 015.3

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 015.2 [interim results for study NN8022-4246: a drug utilisation study (DUS) in the UK using UK clinical practice research datalink (CPRD) database evaluating if liraglutide (Saxenda) is used according to approved indication and posology and if liraglutide (Victoza) is used for weight management] as per the request for supplementary information (RSI) adopted in September 2018

Action: For adoption of advice to CHMP

7.5.11. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.2

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

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

Action: For adoption of advice to CHMP

7.5.12. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 002.4

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Annual progress report for PASS D3820R00006: a post-marketing observational drug utilisation study (DUS) of Moventig (naloxegol) conducted in selected European populations in order to describe demographic, clinical, and treatment characteristics in the baseline of patients treated with naloxegol as well as to describe treatment pattern characteristics of naloxegol utilisation at initiation and follow-up

Action: For adoption of advice to CHMP

7.5.13. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.7

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

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

Action: For adoption of advice to CHMP

7.5.14. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/MEA 005

Applicant: Sandoz GmbH

PRAC Rapporteur: Doris Stenver

Scope: First interim report for a category 3 study in the RMP from the British Society for Rheumatology Biologicals Register (BSRBR), Register for Antirheumatic Therapies in Sweden (ARTIS) and German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (from initial opinion/MA) [final report expected: December 2022]

Action: For adoption of advice to CHMP

7.5.15. Rituximab - RIXIMYO (CAP) - EMEA/H/C/004729/MEA 005

Applicant: Sandoz GmbH

PRAC Rapporteur: Doris Stenver

Scope: First interim report for a category 3 study in the RMP from the British Society for Rheumatology Biologicals Register (BSRBR), Register for Antirheumatic Therapies in Sweden (ARTIS) and German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (from initial opinion/MA) [final report expected: December 2022]

Action: For adoption of advice to CHMP

7.5.16. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/ANX 001.2

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Third interim report for study ALX-LALD-501: a non-interventional, multicentre, prospective disease and clinical outcome registry of patients with lysosomal acid lipase deficiency (LAL-D) to further understand the disease, its progression and any associated complication, and to evaluate the long-term efficacy and safety of Kanuma (sebelipase alfa)

Action: For adoption of advice to CHMP

7.5.17. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004.4

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Study progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date expected: 2020]

Action: For adoption of advice to CHMP

7.5.18. Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/MEA 004.3

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Study progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical

practice [final report due date expected: 2020]

Action: For adoption of advice to CHMP

7.5.19. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Annual progress report 2018 for study OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project and study OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide)

Action: For adoption of advice to CHMP

7.5.20. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 006

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Annual progress report 2018 for study OBS12753: a prospective cohort study of long-term safety of Aubagio (teriflunomide) in multiple sclerosis (MS) patients in Europe

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.10

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's feasibility analyses to add a second/third US healthcare claim data sources to the ongoing US non-interventional PASS (B2311060 study, listed as category 3 study in the RMP): an active surveillance of conjugated oestrogens (CE)/bazedoxifene acetate (BZA) using US healthcare data

Action: For adoption of advice to CHMP

7.6.2. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.4

Applicant: Teva B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 005.3 [feasibility assessment conducted in US healthcare databases as per the agreed protocol (final version dated 25 May 2017) for study C38072-AS-50027 (listed as category 3 study in the RMP): a long-term non-interventional cohort study comparing the risk of malignancy in severe asthma patients treated with reslizumab

and patients not treated with reslizumab using secondary administrative healthcare data [final clinical study report (CSR) expected: January 2020]]

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)

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0073 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Patrick Batty

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. 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

8.1.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0055 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0023 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0031 (without RMP)

Applicant: Orphan Europe SARL

PRAC Rapporteur: Melinda Palfi

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

None

8.3. Renewals of the marketing authorisation

8.3.1. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/R/0063 (with RMP)

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/R/0043 (with RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. 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 Philadelphia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. 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

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. Cobicistat - TYBOST (CAP) - EMEA/H/C/002572/WS1401/0044; cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/WS1401/0047; STRIBILD (CAP) - EMEA/H/C/002574/WS1401/0094

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Consultation on a type II variation to update section 4.6 the SmPC for Tybost (cobicistat), Stribild and Genvoya (cobicistat/elvitegravir/emtricitabine/tenofovir alafenamide) based on pharmacokinetics data in pregnancy from study P1026s (NCT00042289 or IMPAACT): an ongoing, non-randomized, open-label, parallel-group, multicentre phase 4 prospective study of antiretroviral (ARV) pharmacokinetics (PK) and safety in human immunodeficiency virus-1 (HIV-1) infected pregnant women that includes

an arm for elvitegravir/cobicistat (EVG/COBI). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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. Leuprorelin (NAP) - DE/H/0580/001-003/II/077, DE/H/0580/001-003/II/078

Applicant: Astellas Pharma (Eligard)

PRAC Lead: Martin Huber

Scope: PRAC consultation on national variations on RMP updates proposing the removal of additional risk minimisation measure (aRMM) on the development of a new product presentation, the addition of new risk minimisation measures and pharmacovigilance activities updating the product information with monitoring the response to Eligard (leuprorelin) by measuring the serum concentrations of testosterone, on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

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

Applicant: Pfizer Ltd (Ator, Ator Pfizer, Atorvasa, Atorvastatin Pfizer, Liprimar, Sortis)

PRAC Lead: Martin Huber

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

safety concern of 'muscle rupture/torn muscle' and causal association of atorvastatin as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure on atorvastatin (PSUSA/00010347/201710) concluded in June 2018

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

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

PRAC lead: Martin Huber, Ulla Wändel Liminga, Menno van der Elst, Tatiana Magálová, Ghania Chamouni, Albert van der Zeijden, Jan Neuhauser

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. European Network Training Centre (EU NTC) - Pharmacovigilance - Training curriculum (TC) – Strategy for 2019

Action: For adoption

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

None

12.8. Planning and reporting

12.8.1. PRAC workload statistics – Q4 2018

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. 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 full functionality

None

12.13.2. EudraVigilance – annual report 2018

Action: For information

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. Guideline on good pharmacovigilance practices (GVP) Product- or Population-Specific considerations III: risk management in pregnant and breastfeeding women

Action: For discussion

12.20.2. EMA relocation to Amsterdam, the Netherlands – Questions & Answers (Q&As)

Action: For discussion

13. Any other business

14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:

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

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

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

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

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

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

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

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

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

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

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