



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Human Medicines Division

## Pharmacovigilance Risk Assessment Committee (PRAC)

### Draft agenda for the meeting on 26-29 September 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

26 September 2022, 13:00 – 19:30, room 1C / via teleconference

27 September 2022, 08:30 – 19:30, room 1C / via teleconference

28 September 2022, 08:30 – 19:30, room 1C / via teleconference

29 September 2022, 08:30 – 16:00, room 1C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

13 October 2022, 09:00 – 12:00, via teleconference

#### Health and safety information

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

#### Disclaimers

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

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

#### Note on access to documents

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



## Table of contents

<b>1.</b>	<b>Introduction</b>	<b>12</b>
1.1.	Welcome and declarations of interest of members, alternates and experts.....	12
1.2.	Agenda of the meeting on 26-29 September 2022.....	12
1.3.	Minutes of the previous meeting on 29 August-01 September 2022.....	12
<b>2.</b>	<b>EU referral procedures for safety reasons: urgent EU procedures</b>	<b>12</b>
2.1.	Newly triggered procedures .....	12
2.2.	Ongoing procedures .....	12
2.3.	Procedures for finalisation.....	12
<b>3.</b>	<b>EU referral procedures for safety reasons: other EU referral procedures</b>	<b>12</b>
3.1.	Newly triggered procedures .....	12
3.2.	Ongoing procedures .....	13
3.2.1.	Janus kinase (JAK) inhibitors: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517.....	13
3.3.	Procedures for finalisation.....	13
3.3.1.	Terlipressin (NAP) - EMEA/H/A-31/1514 .....	13
3.4.	Re-examination procedures.....	13
3.5.	Others .....	13
<b>4.</b>	<b>Signals assessment and prioritisation</b>	<b>14</b>
4.1.	New signals detected from EU spontaneous reporting systems.....	14
4.1.1.	Enfortumab vedotin - PADCEV (CAP).....	14
4.1.2.	Nivolumab – OPDIVO (CAP) .....	14
4.2.	New signals detected from other sources.....	14
4.2.1.	Bosutinib – BOSULIF (CAP) .....	14
4.2.2.	Colistimethate sodium (NAP).....	15
4.2.3.	Selpercatinib – RETSEVMO (CAP).....	15
4.3.	Signals follow-up and prioritisation.....	15
4.3.1.	Codeine, ibuprofen (NAP) .....	15
4.3.2.	Gemtuzumab ozogamicin – MYLOTARG (CAP) - EMEA/H/C/004204/SDA/005.1 .....	15
4.3.3.	Rivaroxaban - RIVAROXABAN ACCORD (CAP), RIVAROXABAN MYLAN (CAP), XARELTO (CAP); NAP - EMEA/H/C/000944/SDA/051 .....	16
4.3.1.	Selective serotonin reuptake transporter inhibitors (SSRIs): citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); paroxetine (NAP); sertraline (NAP) serotonin-norepinephrine reuptake inhibitor (SNRIs): desvenlafaxine (NAP); duloxetine – CYMBALTA (CAP) - EMEA/H/C/000572/SDA/050, DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), YENTREVE (CAP) - EMEA/H/C/000545/SDA/046; NAP;	

	milnacipran (NAP); venlafaxine (NAP); mirtazapine (NAP); vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/SDA/008 .....	16
4.3.2.	Temozolomide – TEMODAL (CAP) - EMEA/H/C/000229/SDA/043, TEMOMEDAC (CAP), TEMOZOLOMIDE ACCORD (CAP), TEMOZOLOMIDE HEXAL (CAP), TEMOZOLOMIDE SANDOZ (CAP), TEMOZOLOMIDE SUN (CAP), TEMOZOLOMIDE TEVA (CAP); NAP .....	16
<b>4.4.</b>	<b>Variation procedure(s) resulting from signal evaluation .....</b>	<b>16</b>

## **5. Risk management plans (RMPs) 17**

<b>5.1.</b>	<b>Medicines in the pre-authorisation phase .....</b>	<b>17</b>
5.1.1.	Coronavirus (COVID-19) vaccine (recombinant) - EMEA/H/C/005754 .....	17
5.1.2.	Dimethyl fumarate - EMEA/H/C/005950 .....	17
5.1.3.	Etranacogene dezaparovec - EMEA/H/C/004827, PRIME, Orphan .....	17
5.1.4.	Paclitaxel - EMEA/H/C/005997 .....	17
5.1.5.	Pegfilgrastim - EMEA/H/C/005810 .....	17
5.1.6.	Ruxolitinib - EMEA/H/C/005843 .....	17
5.1.7.	Tolvaptan - EMEA/H/C/005961 .....	17
5.1.8.	Tremelimumab - EMEA/H/C/004650 .....	18
<b>5.2.</b>	<b>Medicines in the post-authorisation phase – PRAC-led procedures.....</b>	<b>18</b>
5.2.1.	Adalimumab - IDACIO (CAP) - EMEA/H/C/004475/II/0017 .....	18
5.2.2.	Aripiprazole - ARIPIPIRAZOLE MYLAN PHARMA (CAP); NAP - EMEA/H/C/003803/WS2306/0020 .....	18
5.2.3.	Caspofungin - CANCIDAS (CAP) - EMEA/H/C/000379/II/0078 .....	18
5.2.4.	Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/WS2320/0120; emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/WS2320/0177 .....	19
5.2.5.	Fentanyl - EFFENTORA (CAP); NAP - EMEA/H/C/000833/WS2212/0060 .....	19
5.2.6.	Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/II/0054 .....	19
<b>5.3.</b>	<b>Medicines in the post-authorisation phase – CHMP-led procedures .....</b>	<b>19</b>
5.3.1.	(1R,2S,5S)-N-((1S)-1-Cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0007 .....	19
5.3.2.	Adalimumab - HEFIYA (CAP) - EMEA/H/C/004865/X/0036/G .....	20
5.3.3.	Adalimumab - HYRIMOZ (CAP) - EMEA/H/C/004320/X/0036/G .....	20
5.3.4.	Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0077/G .....	20
5.3.5.	Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0033 .....	21
5.3.6.	Besilesomab - SCINTIMUN (CAP) - EMEA/H/C/001045/II/0015 .....	21
5.3.7.	Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0060 .....	21
5.3.8.	Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0064 .....	21
5.3.9.	Casirivimab, imdevimab - RONAPREVE (CAP) - EMEA/H/C/005814/II/0002 .....	22
5.3.10.	Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/II/0026 .....	22
5.3.11.	Dalbavancin - XYDALBA (CAP) - EMEA/H/C/002840/II/0043 .....	22

5.3.12.	Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS2318/0056/G; FORXIGA (CAP) - EMEA/H/C/002322/WS2318/0077/G; dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS2318/0058/G; XIGDUO (CAP) - EMEA/H/C/002672/WS2318/0068/G; saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/WS2318/0036/G .....	22
5.3.13.	Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/X/0101/G .....	23
5.3.14.	Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0065.....	23
5.3.15.	Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0060 .....	24
5.3.16.	Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0041 .....	24
5.3.17.	Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0046 .....	24
5.3.18.	Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0067 .....	25
5.3.19.	Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0027 .....	25
5.3.20.	Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0012, Orphan .....	25
5.3.21.	Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0015, Orphan .....	25
5.3.22.	Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/II/0018 .....	26
5.3.23.	Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0011/G, Orphan .....	26
5.3.24.	Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0013/G, Orphan .....	26
5.3.25.	Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0073 .....	27
5.3.26.	Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0075 .....	27
5.3.27.	Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0052 .....	27
5.3.28.	Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/X/0078/G .....	28
5.3.29.	Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0053 .....	28
5.3.30.	Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0112 .....	28
5.3.31.	Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0121 .....	29
5.3.32.	Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/II/0074.....	29
5.3.33.	Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/II/0018, Orphan.....	29
5.3.34.	Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/X/0027/G.....	29
5.3.35.	Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/II/0005/G, Orphan.....	30
5.3.36.	Tadalafil - ADCIRCA (CAP) - EMEA/H/C/001021/X/0035/G.....	30
5.3.37.	Tixagevimab, cilgavimab - EVUSHELD (CAP) - EMEA/H/C/005788/II/0003.....	30
5.3.38.	Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/X/138.....	31
5.3.39.	Treosulfan - TRECONDI (CAP) - EMEA/H/C/004751/II/0013, Orphan.....	31
5.3.40.	Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0003.....	31

## **6. Periodic safety update reports (PSURs) 32**

<b>6.1.</b>	<b>PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) only .....</b>	<b>32</b>
6.1.1.	Abrocitinib - CIBINQO (CAP) - PSUSA/00010976/202203 .....	32
6.1.2.	Apalutamide - ERLEADA (CAP) - PSUSA/00010745/202202 .....	32
6.1.3.	Axitinib - INLYTA (CAP) - PSUSA/00010022/202201 .....	32
6.1.4.	Baloxavir marboxil - XOFLUZA (CAP) - PSUSA/00010895/202202.....	32
6.1.5.	Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/202202 .....	32

6.1.6.	Bempedoic acid - NILEMDO (CAP); bempedoic acid, ezetimibe - NUSTENDI (CAP) - PSUSA/00010841/202202 .....	33
6.1.7.	Bevacizumab - ABEVMI (CAP); ALYMSYS (CAP); AVASTIN (CAP); AYBINTIO (CAP); MVASI (CAP); ONBEVZI (CAP); OYAVAS (CAP); ZIRABEV (CAP) - PSUSA/00000403/202202 .....	33
6.1.8.	Bimekizumab - BIMZELX (CAP) - PSUSA/00010953/202202.....	33
6.1.9.	Burosumab - CRYSVITA (CAP) - PSUSA/00010669/202202.....	33
6.1.10.	Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/202202 .....	33
6.1.11.	Coronavirus (COVID-19) vaccine (Ad26.COVS-S, recombinant) - JCOVDEN (CAP) - PSUSA/00010916/202202 .....	34
6.1.12.	Degarelix - FIRMAGON (CAP) - PSUSA/00000944/202202 .....	34
6.1.13.	Dexamethasone - OZURDEX (CAP) - PSUSA/00000985/202201 .....	34
6.1.14.	Eptinezumab - VYEPTI (CAP) - PSUSA/00010966/202202.....	34
6.1.15.	Eravacycline - XERAVA (CAP) - PSUSA/00010718/202202 .....	34
6.1.16.	Esketamine - SPRAVATO (CAP) - PSUSA/00010825/202203.....	34
6.1.17.	Evinacumab - EVKEEZA (CAP) - PSUSA/00010945/202202 .....	35
6.1.18.	Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202202 .....	35
6.1.19.	Fedratinib - INREBIC (CAP) - PSUSA/00010909/202202 .....	35
6.1.20.	Fenofibrate, simvastatin - CHOLIB (CAP) - PSUSA/00010096/202202 .....	35
6.1.21.	Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/202202 .....	35
6.1.22.	Hepatitis B (rDNA) vaccine (adjuvanted, adsorbed) - FENDRIX (CAP) - PSUSA/00001598/202202 .....	36
6.1.23.	Ibalizumab - TROGARZO (CAP) - PSUSA/00010797/202203.....	36
6.1.24.	Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202202 .....	36
6.1.25.	Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - FLUCELVAX TETRA (CAP) - PSUSA/00010737/202203 .....	36
6.1.26.	Isatuximab - SARCLISA (CAP) - PSUSA/00010851/202203 .....	36
6.1.27.	Lefamulin - XENLETA (CAP) - PSUSA/00010872/202202.....	36
6.1.28.	Lonapegsomatropin - SKYTROFA (CAP) - PSUSA/00010969/202202 (with RMP) .....	37
6.1.29.	Nitisinone - ORFADIN (CAP) - PSUSA/00002169/202202 .....	37
6.1.30.	Pegfilgrastim - CEGFILA (CAP); FULPHILA (CAP); GRASUSTEK (CAP); NEULASTA (CAP); NYVEPRIA (CAP); PELGRAZ (CAP); PELMEG (CAP); ZIEXTENZO (CAP) - PSUSA/00002326/202201 .....	37
6.1.31.	Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58) - EMEA/H/W/002300/PSUV/0062 .....	37
6.1.32.	Pralsetinib - GAVRETO (CAP) - PSUSA/00010961/202203.....	38
6.1.33.	Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202202 .....	38
6.1.34.	Ribociclib - KISQALI (CAP) - PSUSA/00010633/202203 .....	38
6.1.35.	Ropeginterferon alfa-2b - BESREMI (CAP) - PSUSA/00010756/202202.....	38
6.1.36.	Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/202202 .....	38
6.1.37.	Somapacitan - SOGROYA (CAP) - PSUSA/00010920/202202.....	38
6.1.38.	Sotrovimab - XEVUDY (CAP) - PSUSA/00010973/202202 .....	39

6.1.39.	Telotristat - XERMELO (CAP) - PSUSA/00010639/202202 .....	39
6.1.40.	Tezacaftor, ivacaftor - SYMKEVI (CAP) - PSUSA/00010730/202202 .....	39
6.1.41.	Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/202202 .....	39
6.1.42.	Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/202202 .....	39
6.1.43.	Ulipristal acetate - ESMYA (CAP) - PSUSA/00009325/202202 .....	40
6.1.44.	Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202202 .....	40
6.1.45.	Vosoritide - VOXZOGO (CAP) - PSUSA/00010952/202202 .....	40
<b>6.2.</b>	<b>PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs) .....</b>	<b>40</b>
6.2.1.	Anidulafungin - ECALTA (CAP); NAP - PSUSA/00000215/202201 .....	40
6.2.2.	Dexrazoxane - SAVENE (CAP); NAP - PSUSA/00001001/202202 .....	40
6.2.3.	Influenza vaccine (surface antigen, inactivated, adjuvanted) - FLUAD TETRA (CAP); NAP - PSUSA/00010300/202203 .....	41
6.2.4.	Orlistat - ALLI (CAP); XENICAL (CAP); NAP - PSUSA/00002220/202202 .....	41
<b>6.3.</b>	<b>PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only .....</b>	<b>41</b>
6.3.1.	Acetylsalicylic acid (NAP) - PSUSA/00000039/202202 .....	41
6.3.2.	Alverine (NAP) - PSUSA/00000124/202202 .....	41
6.3.3.	Alverine, simeticone (NAP) - PSUSA/00000125/202202 .....	41
6.3.4.	Amlodipine, atorvastatin (NAP) - PSUSA/00000177/202201 .....	42
6.3.5.	Carbomers (NAP) - PSUSA/00000557/202201 .....	42
6.3.6.	Carboplatin (NAP) - PSUSA/00000559/202201 .....	42
6.3.7.	Cromoglicic acid (NAP) - PSUSA/00000883/202202 .....	42
6.3.8.	Dorzolamide (NAP) - PSUSA/00003168/202202 .....	42
6.3.9.	Gabapentin (NAP) - PSUSA/00001499/202202 .....	42
6.3.10.	Glipizide (NAP) - PSUSA/00001535/202201 .....	43
6.3.11.	Hydroxyethyl starch (HES) (NAP) - PSUSA/00001694/202203 .....	43
6.3.12.	Influenza vaccine (split virion, inactivated) (NAP) - PSUSA/00010298/202203 .....	43
6.3.13.	Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/202203 .....	43
6.3.14.	Interferon gamma (NAP) - PSUSA/00001760/202201 .....	43
6.3.15.	Ketoprofen (NAP) - PSUSA/00001809/202201 .....	44
6.3.16.	Ketoprofen (NAP) - PSUSA/00009205/202201 .....	44
6.3.17.	Levothyroxine (NAP) - PSUSA/00001860/202201 .....	44
6.3.18.	Lisdexamfetamine (NAP) - PSUSA/00010289/202202 .....	44
6.3.19.	Loratadine (NAP) - PSUSA/00001907/202202 .....	44
6.3.20.	Loratadine, pseudoephedrine (NAP) - PSUSA/00001908/202202 .....	44
6.3.21.	Lorazepam (NAP) - PSUSA/00001909/202201 .....	45
6.3.22.	Mesalazine (NAP) - PSUSA/00001990/202202 .....	45
6.3.23.	Mesterolone (NAP) - PSUSA/00010551/202201 .....	45
6.3.24.	Moxonidine (NAP) - PSUSA/00002095/202201 .....	45

6.3.25.	Zanamivir (NAP) - PSUSA/00003141/202201 .....	45
<b>6.4.</b>	<b>Follow-up to PSUR/PSUSA procedures .....</b>	<b>46</b>
6.4.1.	Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/LEG 008.1 .....	46
<b>6.5.</b>	<b>Variation procedure(s) resulting from PSUSA evaluation .....</b>	<b>46</b>
6.5.1.	Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0022 .....	46
6.5.2.	Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0077 .....	46
<b>6.6.</b>	<b>Expedited summary safety reviews .....</b>	<b>47</b>
6.6.1.	Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 009 .....	47
6.6.2.	Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 009.1 .....	47
6.6.3.	Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.6 .....	47

## **7. Post-authorisation safety studies (PASS) 48**

<b>7.1.</b>	<b>Protocols of PASS imposed in the marketing authorisation(s).....</b>	<b>48</b>
7.1.1.	Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSA/S/0089 .....	48
7.1.2.	Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/PSP/S/0100.....	48
7.1.3.	Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/PSP/S/0101 .....	48
7.1.4.	Pomalidomide – IMNOVID (CAP) - EMEA/H/C/PSA/S/0090 .....	48
7.1.5.	Teduglutide – REVESTIVE (CAP) - EMEA/H/C/PSA/S/0086 .....	49
7.1.6.	Valproate (NAP) - EMEA/H/N/PSP/J/0075.8.....	49
7.1.7.	Valproate (NAP) - EMEA/H/N/PSA/J/0091 .....	49
<b>7.2.</b>	<b>Protocols of PASS non-imposed in the marketing authorisation(s) .....</b>	<b>50</b>
7.2.1.	Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/MEA 035.4.....	50
7.2.2.	Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 002.3.....	50
7.2.3.	Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 006 .....	50
7.2.4.	Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092.4.....	50
7.2.5.	Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 002.1 .....	51
7.2.6.	Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 006.4 .....	51
7.2.7.	Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 004.6 .....	51
7.2.8.	Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 006.8 .....	51
7.2.9.	Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.8 .....	52
7.2.10.	Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 016.1.....	52
7.2.11.	Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/MEA 005 .....	52
7.2.12.	Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/MEA 035.....	52
7.2.13.	Insulin lispro - LYUMJEV (CAP) - EMEA/H/C/005037/MEA 004 .....	53
7.2.14.	Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 003.1 .....	53
7.2.15.	Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 002.2 .....	53

7.2.16.	Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 004 .....	53
7.2.17.	Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.4 .....	54
7.2.18.	Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 003 .....	54
7.2.19.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 018.1 .....	54
7.2.20.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 019.1 .....	54
7.2.21.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 020.1 .....	55
7.2.22.	Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.5 .....	55
7.2.23.	Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037.2 .....	55
7.2.24.	Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 053.1 .....	55
7.2.25.	Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 054.1 .....	56
<b>7.3.</b>	<b>Results of PASS imposed in the marketing authorisation(s).....</b>	<b>56</b>
7.3.1.	Aprotinin (NAP) - EMEA/H/N/PSR/S/0030 .....	56
7.3.2.	Lumacaftor, ivacaftor – ORKAMBI (CAP) - EMEA/H/C/PSR/S/0039 .....	56
<b>7.4.</b>	<b>Results of PASS non-imposed in the marketing authorisation(s).....</b>	<b>56</b>
7.4.1.	Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0090.....	56
7.4.2.	Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0072 .....	57
7.4.3.	Hepatitis B surface antigen - HEPLISAV B (CAP) - EMEA/H/C/005063/II/0015.....	57
7.4.4.	Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0041, Orphan .....	57
7.4.5.	Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0054.....	57
7.4.6.	Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/II/0049 .....	58
7.4.7.	Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0073 .....	58
<b>7.5.</b>	<b>Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation.....</b>	<b>58</b>
7.5.1.	Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/MEA 001.6 .....	58
7.5.2.	Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.7 .....	58
7.5.3.	Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 002 .....	59
7.5.4.	Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 002.1.....	59
7.5.5.	Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/MEA 009 .....	59
7.5.6.	Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.5.....	59
7.5.7.	Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 024 .....	60
7.5.8.	Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.4 .....	60
7.5.9.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 026.4 .....	60
7.5.10.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 027.4 .....	60
<b>7.6.</b>	<b>Others .....</b>	<b>61</b>
7.6.1.	Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 003.2 .....	61
7.6.2.	Azathioprine - JAYEMPI (CAP) - EMEA/H/C/005055/MEA 001.....	61
7.6.3.	Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 008 .....	61
7.6.4.	Radium (Ra <sup>223</sup> ) - XOFIGO (CAP) - EMEA/H/C/002653/ANX 013.2.....	61



7.6.5.	Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 002.5 .....	62
7.6.6.	Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 032.2 .....	62
7.6.7.	Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 024.2 .....	62
7.6.8.	Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 024.4 .....	62
<b>7.7.</b>	<b>New Scientific Advice .....</b>	<b>63</b>
<b>7.8.</b>	<b>Ongoing Scientific Advice .....</b>	<b>63</b>
<b>7.9.</b>	<b>Final Scientific Advice (Reports and Scientific Advice letters) .....</b>	<b>63</b>

## **8. Renewals of the marketing authorisation, conditional renewal and annual reassessments 63**

<b>8.1.</b>	<b>Annual reassessments of the marketing authorisation .....</b>	<b>63</b>
8.1.1.	Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/S/0046 (without RMP) .....	63
8.1.2.	Ebola vaccine (rDNA, replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/S/0015 (without RMP) .....	63
8.1.3.	Ebola vaccine (rDNA, replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/S/0012 (without RMP) .....	63
8.1.4.	Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/S/0008 (without RMP) .....	64
<b>8.2.</b>	<b>Conditional renewals of the marketing authorisation .....</b>	<b>64</b>
8.2.1.	(1R,2S,5S)-N-((1S)-1-Cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/R/0023 (without RMP).....	64
8.2.2.	Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/R/0031 (without RMP) .....	64
8.2.3.	Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/R/0079 (without RMP) .....	64
8.2.4.	Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/R/0018 (without RMP) .....	64
<b>8.3.</b>	<b>Renewals of the marketing authorisation .....</b>	<b>65</b>
8.3.1.	Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - RIARIFY (CAP) - EMEA/H/C/004836/R/0022 (with RMP) .....	65
8.3.2.	Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRYDONIS (CAP) - EMEA/H/C/004702/R/0025 (with RMP).....	65
8.3.3.	Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/R/0057 (without RMP) .....	65
8.3.4.	Infliximab - ZESSLY (CAP) - EMEA/H/C/004647/R/0025 (without RMP) .....	65
8.3.5.	Insulin glargine - SEMGLEE (CAP) - EMEA/H/C/004280/R/0040 (without RMP) .....	65
8.3.6.	Sodium zirconium cyclosilicate - LOKELMA (CAP) - EMEA/H/C/004029/R/0027 (without RMP).....	66
8.3.7.	Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/R/0029 (without RMP) .....	66

## **9. Product related pharmacovigilance inspections 66**

<b>9.1.</b>	<b>List of planned pharmacovigilance inspections.....</b>	<b>66</b>
<b>9.2.</b>	<b>Ongoing or concluded pharmacovigilance inspections.....</b>	<b>66</b>
<b>9.3.</b>	<b>Others .....</b>	<b>66</b>

<b>10.</b>	<b>Other safety issues for discussion requested by the CHMP or the EMA</b>	<b>66</b>
10.1.	Safety related variations of the marketing authorisation.....	66
10.2.	Timing and message content in relation to Member States' safety announcements	66
10.3.	Other requests.....	67
10.4.	Scientific Advice .....	67
<b>11.</b>	<b>Other safety issues for discussion requested by the Member States</b>	<b>67</b>
11.1.	Safety related variations of the marketing authorisation.....	67
11.1.1.	Bismuth subcitrate potassium, metronidazole, tetracycline (NAP) - DE/H/2467/001/II/05267	
11.2.	Other requests.....	67
<b>12.</b>	<b>Organisational, regulatory and methodological matters</b>	<b>67</b>
12.1.	Mandate and organisation of the PRAC.....	67
12.1.1.	PRAC membership .....	67
12.1.2.	Vote by proxy .....	67
12.2.	Coordination with EMA Scientific Committees or CMDh-v .....	67
12.3.	Coordination with EMA Working Parties/Working Groups/Drafting Groups .....	68
12.4.	Cooperation within the EU regulatory network.....	68
12.4.1.	Coronavirus (COVID-19) pandemic - update .....	68
12.4.2.	PRAC and CMDh strategic review and learning meeting (SRLM) under the Czech Presidency of the European Union (EU) Council – Prague, 17 – 19 October 2022 - agenda .....	68
12.5.	Cooperation with International Regulators.....	68
12.6.	Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee.....	68
12.7.	PRAC work plan .....	68
12.8.	Planning and reporting .....	68
12.8.1.	Marketing authorisation applications (MAA) forecast for 2022 – planning update dated Q3 2022 .....	68
12.9.	Pharmacovigilance audits and inspections .....	68
12.9.1.	Pharmacovigilance systems and their quality systems .....	68
12.9.2.	Pharmacovigilance inspections .....	69
12.9.3.	Pharmacovigilance audits.....	69
12.10.	Periodic safety update reports (PSURs) & Union reference date (EURD) list .....	69
12.10.1.	Periodic safety update reports .....	69
12.10.2.	Granularity and Periodicity Advisory Group (GPAG) .....	69
12.10.3.	PSURs repository .....	69
12.10.4.	Union reference date list – consultation on the draft list .....	69
12.11.	Signal management .....	69
12.11.1.	Signal management – feedback from Signal Management Review Technical (SMART) Working Group .....	69

<b>12.12.</b>	<b>Adverse drug reactions reporting and additional reporting .....</b>	<b>69</b>
12.12.1.	Management and reporting of adverse reactions to medicinal products.....	69
12.12.2.	Additional monitoring .....	70
12.12.3.	List of products under additional monitoring – consultation on the draft list .....	70
<b>12.13.</b>	<b>EudraVigilance database .....</b>	<b>70</b>
12.13.1.	Activities related to the confirmation of full functionality .....	70
<b>12.14.</b>	<b>Risk management plans and effectiveness of risk minimisations .....</b>	<b>70</b>
12.14.1.	Risk management systems .....	70
12.14.2.	Tools, educational materials and effectiveness measurement of risk minimisations .....	70
<b>12.15.</b>	<b>Post-authorisation safety studies (PASS) .....</b>	<b>70</b>
12.15.1.	Post-authorisation Safety Studies – imposed PASS .....	70
12.15.2.	Post-authorisation Safety Studies – non-imposed PASS .....	70
12.15.3.	International Conference on Harmonisation (ICH) E19 - A selective approach to safety data collection in specific late-stage pre-approval or post-approval clinical trials.....	70
<b>12.16.</b>	<b>Community procedures.....</b>	<b>71</b>
12.16.1.	Referral procedures for safety reasons .....	71
<b>12.17.</b>	<b>Renewals, conditional renewals, annual reassessments.....</b>	<b>71</b>
<b>12.18.</b>	<b>Risk communication and transparency .....</b>	<b>71</b>
12.18.1.	Public participation in pharmacovigilance.....	71
12.18.2.	Safety communication.....	71
<b>12.19.</b>	<b>Continuous pharmacovigilance .....</b>	<b>71</b>
12.19.1.	Incident management .....	71
<b>12.20.</b>	<b>Impact of pharmacovigilance activities .....</b>	<b>71</b>
12.20.1.	Impact of EU label changes on post-referral prescribing trends and risk of long-term/persistent symptoms associated with gadolinium based contrast agents (GBCA) exposure.....	71
<b>12.21.</b>	<b>Others .....</b>	<b>71</b>
12.21.1.	Data analysis and real world interrogation network (DARWIN EU) – introduction of the coordination centre and next steps for real-world evidence (RWE) .....	71
12.21.2.	Launch of EMA coordinated CHMP/PRAC requested GVP inspections in IRIS.....	71
<b>13.</b>	<b>Any other business</b>	<b>72</b>
<b>14.</b>	<b>Explanatory notes</b>	<b>73</b>

## **1. Introduction**

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 26 -29 September 2022. See October 2022 PRAC minutes (to be published post November 2022 PRAC meeting).

### **1.2. Agenda of the meeting on 26-29 September 2022**

**Action:** For adoption

### **1.3. Minutes of the previous meeting on 29 August-01 September 2022**

**Action:** For adoption

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

### **2.1. Newly triggered procedures**

None

### **2.2. Ongoing procedures**

None

### **2.3. Procedures for finalisation**

None

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

### **3.1. Newly triggered procedures**

None

## 3.2. Ongoing procedures

### 3.2.1. Janus kinase (JAK) inhibitors<sup>1</sup>: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517

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Applicant(s): AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur(s): Liana Gross-Martirosyan (Olumiant, Xeljanz), Nikica Mirošević Skvrce (Cibinqo, Jyseleca, Rinvoq)

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

**Action:** For discussion (Ad-hoc expert group (AHEG) meeting feedback)

## 3.3. Procedures for finalisation

### 3.3.1. Terlipressin (NAP) - EMEA/H/A-31/1514

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Applicant(s): various

PRAC Rapporteur: Krööt Aab; PRAC Co-rapporteur: Anette Kirstine Stark

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

**Action:** For adoption of a recommendation to CMDh

## 3.4. Re-examination procedures<sup>2</sup>

None

## 3.5. Others

None

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<sup>1</sup> Indicated for the treatment of inflammatory disorders

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

## 4. Signals assessment and prioritisation<sup>3</sup>

### 4.1. New signals detected from EU spontaneous reporting systems

#### 4.1.1. Enfortumab vedotin - PADCEV (CAP)

---

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Signal of interstitial lung disease (ILD)

**Action:** For adoption of PRAC recommendation

EPITT 19842 – New signal

Lead Member State(s): CZ

#### 4.1.2. Nivolumab – OPDIVO (CAP)

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of morphea

**Action:** For adoption of PRAC recommendation

EPITT 19839 – New signal

Lead Member State(s): DE

### 4.2. New signals detected from other sources

#### 4.2.1. Bosutinib – BOSULIF (CAP)

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Signal of interstitial lung disease (ILD)

**Action:** For adoption of PRAC recommendation

EPITT 19843 – New signal

Lead Member State(s): DE

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

#### 4.2.2. Colistimethate sodium<sup>4</sup> (NAP)

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Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of pseudo-bartter syndrome

**Action:** For adoption of PRAC recommendation

EPITT 19845 – New signal

Lead Member State(s): PL

#### 4.2.3. Selpercatinib – RETSEVMO (CAP)

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Signal of hypothyroidism

**Action:** For adoption of PRAC recommendation

EPITT 19847 – New signal

Lead Member State(s): NL

### 4.3. Signals follow-up and prioritisation

#### 4.3.1. Codeine, ibuprofen (NAP)

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Applicant(s): various

PRAC Rapporteur: Rhea Fitzgerald

Scope: Signal of renal tubular acidosis and hypokalaemia

**Action:** For adoption of PRAC recommendation

EPITT 19820 – Follow-up to June 2022

#### 4.3.2. Gemtuzumab ozogamicin – MYLOTARG (CAP) - EMEA/H/C/004204/SDA/005.1

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Applicant(s): Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of atypical haemolytic reactions

**Action:** For adoption of PRAC recommendation

EPITT 19788 – Follow-up to June 2022

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<sup>4</sup> For intravenous use only

4.3.3. Rivaroxaban - RIVAROXABAN ACCORD (CAP), RIVAROXABAN MYLAN (CAP), XARELTO (CAP); NAP - EMEA/H/C/000944/SDA/051

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Applicant(s): Accord Healthcare S.L.U. (Rivaroxaban Accord), Bayer AG (Xarelto), Mylan Ireland Limited (Rivaroxaban Mylan)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pemphigoid

**Action:** For adoption of PRAC recommendation

EPITT 19785 – Follow-up to April 2022

4.3.1. Selective serotonin reuptake transporter inhibitors (SSRIs): citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); paroxetine (NAP); sertraline (NAP)  
serotonin-norepinephrine reuptake inhibitor (SNRIs): desvenlafaxine (NAP); duloxetine – CYMBALTA (CAP) - EMEA/H/C/000572/SDA/050, DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), YENTREVE (CAP) - EMEA/H/C/000545/SDA/046; NAP; milnacipran (NAP); venlafaxine (NAP); mirtazapine (NAP); vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/SDA/008

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Applicant(s): Eli Lilly Nederland B.V. (Cymbalta, Duloxetine Lilly, Yentreve), H. Lundbeck A/S (Brintellix), Mylan Pharmaceuticals Limited (Duloxetine Mylan), Zentiva k.s. (Duloxetine Zentiva), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of pulmonary hypertension

**Action:** For adoption of PRAC recommendation

EPITT 19772 – Follow-up to March 2022

4.3.2. Temozolomide – TEMODAL (CAP) - EMEA/H/C/000229/SDA/043, TEMOMEDAC (CAP), TEMOZOLOMIDE ACCORD (CAP), TEMOZOLOMIDE HEXAL (CAP), TEMOZOLOMIDE SANDOZ (CAP), TEMOZOLOMIDE SUN (CAP), TEMOZOLOMIDE TEVA (CAP); NAP

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Applicant(s): Accord Healthcare S.L.U. (Temozolomide Accord), Hexal AG (Temozolomide Hexal), medac Gesellschaft für klinische Spezialpräparate mbH (Temomedac), Merck Sharp & Dohme B.V. (Temodal), Sandoz GmbH (Temozolomide Sandoz), Sun Pharmaceutical Industries Europe B.V. (Temozolomide Sun), Teva B.V. (Temozolomide Teva)

PRAC Rapporteur: Martin Huber

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

**Action:** For adoption of PRAC recommendation

EPITT 19814 – Follow-up to June 2022

#### 4.4. Variation procedure(s) resulting from signal evaluation

None



## 5. Risk management plans (RMPs)

### 5.1. Medicines in the pre-authorisation phase

#### 5.1.1. Coronavirus (COVID-19) vaccine (recombinant) - EMEA/H/C/005754

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Scope: Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus), in individuals 18 years of age and older

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

#### 5.1.2. Dimethyl fumarate - EMEA/H/C/005950

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Scope: Treatment of multiple sclerosis

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

#### 5.1.3. Etranacogene dezaparvovec - EMEA/H/C/004827, PRIME, Orphan

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Applicant: CSL Behring GmbH, ATMP<sup>5</sup>

Scope: Treatment of adults with Haemophilia B

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

#### 5.1.4. Paclitaxel - EMEA/H/C/005997

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Scope: Treatment of metastatic breast cancer

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

#### 5.1.5. Pegfilgrastim - EMEA/H/C/005810

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Scope: Treatment of neutropenia

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

#### 5.1.6. Ruxolitinib - EMEA/H/C/005843

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Scope: Treatment of non-segmental vitiligo

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

#### 5.1.7. Tolvaptan - EMEA/H/C/005961

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Scope: Treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic

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<sup>5</sup> Advanced therapy medicinal product

hormone secretion (SIADH)

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

#### 5.1.8. Tremelimumab - EMEA/H/C/004650

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Scope: Treatment of adults with metastatic non-small cell lung cancer (NSCLC) with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations

**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. Adalimumab - IDACIO (CAP) - EMEA/H/C/004475/II/0017

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Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP version 6 in order to propose a continuation of the observational registry (RABBIT) Study #1 (Study Identifier: FKS0-000-RAB) and the cancellation of the observational registry (IBD UK) (Study Identifier: FKS0-000-IBD). In addition, the MAH took the opportunity to align the RMP with the current approved RMP of the reference product

**Action:** For adoption of PRAC Assessment Report

#### 5.2.2. Aripiprazole - ARIPIPRAZOLE MYLAN PHARMA (CAP); NAP - EMEA/H/C/003803/WS2306/0020

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Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 6.0) to align the safety concerns in the RMP with the reference product. In addition nationally authorised product have been included in the RMP for the company

**Action:** For adoption of PRAC Assessment Report

#### 5.2.3. Caspofungin - CANCIDAS (CAP) - EMEA/H/C/000379/II/0078

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jo Robays

Scope: Submission of an updated RMP version 4.2 in order to remove safety concerns and align it with the EU GVP Module V (Revision 2)

**Action:** For adoption of PRAC Assessment Report

5.2.4. [Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD \(CAP\) - EMEA/H/C/002574/WS2320/0120; emtricitabine, tenofovir disoproxil - TRUVADA \(CAP\) - EMEA/H/C/000594/WS2320/0177](#)

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: To update Annex II and the RMP for Truvada and Stribild to version 18.1 and 14.1 to remove of the paediatric additional Risk Minimisation Measures (aRMMs) for HIV indication. In addition, the MAH took the opportunity to introduce changes to the PI

**Action:** For adoption of PRAC Assessment Report

5.2.5. [Fentanyl - EFFENTORA \(CAP\); NAP - EMEA/H/C/000833/WS2212/0060](#)

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Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 5.1) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to implement PRAC requests arising from previous assessments as follows: 1) revision of the list of safety concerns; 2) update of the key messages of the educational materials in line with another centrally authorised product containing fentanyl (Instanyl (fentanyl)). As a result, Annex II on additional risk minimisation measures is updated accordingly

**Action:** For adoption of PRAC Assessment Report

5.2.6. [Fentanyl - PECFENT \(CAP\) - EMEA/H/C/001164/II/0054](#)

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Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 8.0) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with Instanyl (fentanyl). As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2)

**Action:** For adoption of PRAC Assessment Report

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

5.3.1. [\(1R,2S,5S\)-N-\(\(1S\)-1-Cyano-2-\(\(3s\)-2-oxopyrrolidin-3-yl\)ethyl\)-3-\(\(2S\)-3,3-dimethyl-2-\(2,2,2-trifluoroacetamido\) butanoyl\)-6,6-dimethyl-3-azabicyclo\[3.1.0\]hexane-2-carboxamide, ritonavir - PAXLOVID \(CAP\) - EMEA/H/C/005973/II/0007](#)

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study C4671010 (listed as a category 3 study in the RMP): a phase 1, non-randomised, open label study to assess the pharmacokinetics, safety and tolerability of PF-07321332 boosted with ritonavir (Paxlovid) in adults with moderate hepatic impairment and individuals with normal hepatic function. The RMP (version 2.0) has also been submitted

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

### 5.3.2. Adalimumab - HEFIYA (CAP) - EMEA/H/C/004865/X/0036/G

Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with the following quality variations. The package leaflet and labelling are updated in accordance. The RMP (version 9.0) has also been submitted. Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in Annex A to differentiate packs of pre-filled syringes with or without needle safety device; 2) other quality variations

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

### 5.3.3. Adalimumab - HYRIMOZ (CAP) - EMEA/H/C/004320/X/0036/G

Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with the following quality variations. The package leaflet and labelling are updated in accordance. The RMP (version 9.0) has also been submitted. Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device; 2) other quality variations

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

### 5.3.4. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0077/G

Applicant: Bayer AG

PRAC Rapporteur: Nathalie Gault

Scope: Grouped application consisting of: 1) extension of indication to include as a paediatric indication retinopathy of prematurity (ROP). As a consequence, sections 2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 32.1) are updated in accordance. Separate package leaflet is proposed for the guardians of preterm babies; 2) addition of a stand-alone paediatric dosing device, which will be CE marked and cross-labelled to the EU product information

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

#### 5.3.5. [Andexanet alfa - ONDEXXYA \(CAP\) - EMEA/H/C/004108/II/0033](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 5.1 of the SmPC based on interim results from pharmacokinetic (PK)/pharmacodynamic(PD) study (listed as a specific obligation in the Annex II in order to fulfil SOB 1 and SOB 3): a PK and PK/PD analysis of intravenously administered andexanet after dosing to steady state with a factor Xa inhibitor, rivaroxaban or Apixaban, in healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity implement editorial changes in Annex II of the SmPC. The RMP version 3.0 has also been submitted

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

#### 5.3.6. [Besilesomab - SCINTIMUN \(CAP\) - EMEA/H/C/001045/II/0015](#)

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Applicant: CIS BIO International

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study AG-2012 (listed as a category 3 study in the RMP): a non-interventional controlled survey on the impact of Scintimun (besilesomab) administered for scintigraphic imaging on diagnostic thinking and management of patient with suspicion of peripheral osteomyelitis (in fulfilment of MEA 08.4). The RMP (version 15) is updated accordingly

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

#### 5.3.7. [Canagliflozin - INVOKANA \(CAP\) - EMEA/H/C/002649/II/0060](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from non-clinical studies 1 and 2, listed as category 3 studies in the RMP, in order to fulfil MEA/007.2. Nonclinical study 1 was designed to evaluate the effects of canagliflozin on ketone clearance and production; nonclinical study 2 objective is to evaluate the effects of canagliflozin on ketone clearance and production during prolonged fast. The RMP version 9.1 has also been submitted

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

#### 5.3.8. [Canagliflozin, metformin - VOKANAMET \(CAP\) - EMEA/H/C/002656/II/0064](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from non-clinical studies 1 and 2, listed as category 3 studies in the RMP in order to fulfil MEA/006.2. Nonclinical study 1 was designed to evaluate the effects of canagliflozin on ketone clearance and production; nonclinical study 2 objective

is to evaluate the effects of canagliflozin on ketone clearance and production during prolonged fast. The RMP version 9.1 has also been submitted

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

#### 5.3.9. [Casirivimab, imdevimab - RONAPREVE \(CAP\) - EMEA/H/C/005814/II/0002](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of coronavirus (COVID-19) in hospitalised patients in adults and adolescents aged 12 years and older weighing at least 40 kg. As a consequence, sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The package leaflet, the labelling and the RMP (version 1.1) are updated in accordance

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

#### 5.3.10. [Cemiplimab - LIBTAYO \(CAP\) - EMEA/H/C/004844/II/0026](#)

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Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include monotherapy treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated in accordance

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

#### 5.3.11. [Dalbavancin - XYDALBA \(CAP\) - EMEA/H/C/002840/II/0043](#)

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to the paediatric population (aged 3 months to < 18 years) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) based on the interim results from the study DUR001-306: a phase 3, multicentre, open-label, randomized, comparator controlled trial of the safety and efficacy of dalbavancin versus active comparator in paediatric subjects with ABSSSI, together with data from three phase 1 pharmacokinetic studies (A8841004, DUR001-106, and DAL-PK-02). Consequently, the sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC were updated. The package leaflet is updated accordingly. In addition, the applicant took the opportunity to make minor editorial amendments and to bring the product information in line with the latest quality review of documents (QRD) (version 10.2). The RMP (version 7.0) has also been submitted

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

#### 5.3.12. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS2318/0056/G; FORXIGA \(CAP\) - EMEA/H/C/002322/WS2318/0077/G; dapagliflozin, metformin - EBYMECT \(CAP\) - EMEA/H/C/004162/WS2318/0058/G; XIGDUO \(CAP\) -](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Grouped application consisting of: 1) Update of section 4.4 of the SmPC in order to remove the potential risk of lower limb amputation (LLA) based on studies D1690C00018, D1690C00019, DECLARE, DAPA-HF, DAPA-CKD, and DELIVER. The package leaflets are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and to align it with the latest QRD template. In addition, the MAH took the opportunity to update the list of local representatives in the Qtern (saxagliptin/dapagliflozin) package leaflet; 2) Submission of an updated RMP in order to align the EU RMPs for the FDCs Xigduo, Ebymect and Qtern, to recently approved updates to the Forxiga (dapagliflozin) EU RMP; 3) Update of section 4.5 of the SmPC to include a further product information harmonization to address the consideration raised during the ongoing dapagliflozin procedure PSUSA/00010029/202110. The Forxiga (dapagliflozin) RMP and Edistride (dapagliflozin) RMP version 28 has been submitted. The Qtern (saxagliptin/dapagliflozin) RMP version 7 has been submitted. The Xigduo (dapagliflozin/metformin) RMP and Ebymect (dapagliflozin/metformin) RMP version 13 has been submitted

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

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#### 5.3.13. [Dolutegravir, abacavir, lamivudine - TRIUMEQ \(CAP\) - EMA/H/C/002754/X/0101/G](#)

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Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form associated with a new strength (5 mg/60 mg/30 mg dispersible tablet). The new presentation is indicated for the treatment of human immunodeficiency virus (HIV) infected children weighing at least 14 kg to less than 25 kg; 2) extension of indication to include treatment of human immunodeficiency virus (HIV) infected children weighing at least 25kg for the already approved film-coated tablets. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 19) is updated in accordance

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

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#### 5.3.14. [Dulaglutide - TRULICITY \(CAP\) - EMA/H/C/002825/II/0065](#)

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety. As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The package

leaflet is updated in accordance. Version 7.1 of the RMP has also been submitted

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

#### 5.3.15. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0060

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of atopic dermatitis in paediatric patients from 6 months to <6 years of age based on final results from study R668-AD-1539: a phase 2/3 study investigating the pharmacokinetics, safety, and efficacy of dupilumab in patients aged ≥6 months to <6 years with moderate-to-severe atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0) are updated in accordance

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

#### 5.3.16. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0041

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include first-line treatment, with durvalumab in combination with tremelimumab and platinum-based chemotherapy, of adults with metastatic non-small-cell lung carcinoma (NSCLC) with no sensitizing epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations, based on final results from study D419MC00004 (POSEIDON): a phase 3, randomised, multicentre, open-label, comparative global study to determine the efficacy and safety of tremelimumab and durvalumab or durvalumab in combination with platinum based chemotherapy for first-line treatment in patients with metastatic NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2). The RMP (version 5.1) is updated accordingly

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

#### 5.3.17. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0046

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include Imfinzi in combination with chemotherapy for the treatment of adults with locally advanced or metastatic biliary tract cancer (BTC), based on the second interim analysis from the ongoing pivotal study D933AC00001 (TOPAZ-1): a phase III randomized, double-blind, placebo-controlled, multi-regional, international study conducted to assess the efficacy and safety of durvalumab in combination with the current standard of care Gemcitabine/Cisplatin for the first-line treatment of patients with locally advanced or metastatic BTC. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of



the SmPC have been updated and the Package leaflet has been updated accordingly. Version 7.1 of the RMP has also been submitted

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

#### 5.3.18. Elasoameran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0067

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include immunisation of paediatric individuals from 6 months through 5 years of age based on results from the study P204 (KidCove); this is a phase 2/3, two-part, open-label, dose-escalation, age de-escalation and randomised, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 SARS-CoV-2 vaccine in healthy children 6 months to less than 12 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the package leaflet is updated in accordance. The MAH also took the opportunity to implement minor editorial changes in the product information. The submission includes a revised RMP version 4.1

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

#### 5.3.19. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0027

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adult and paediatric patients with haemophilia A without factor VIII (FVIII) inhibitors who have mild or moderate disease for whom prophylaxis is clinically indicated. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, section 4.2 of the SmPC is updated to make clearer that the maintenance dose for Hemlibra (emicizumab) applies from week 5 of dosing. The package leaflet and the RMP (version 4.0) are updated accordingly

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

#### 5.3.20. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0012, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of seizures associated with Lennox-Gastaut syndrome as an add on therapy to other anti-epileptic medicines for patients 2 years of age and older. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 2.3) are updated accordingly

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

#### 5.3.21. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0015, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.2 and 5.2 of the SmPC to update the safety information based on final results from study ZX008-1903 listed as a category 3 study in the RMP: a phase 1, open-label, single-dose study to evaluate the safety, tolerability, and pharmacokinetics of ZX008 (fenfluramine hydrochloride) in subjects with varying degrees of hepatic impairment. The primary objective of this study was to compare the pharmacokinetics (PK) of a single dose of ZX008 (fenfluramine hydrochloride) in subjects with varying degrees of hepatic impairment with that of healthy matched control subjects. The RMP (version 2.7) was updated accordingly

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

#### 5.3.22. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/II/0018

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4, 4.6 and 5.1 of the SmPC in order to update information on fertility based on interim results from studies GLPG0634-CL-227 (MANTA Ray) and GS-US-418-4279 (MANTA) listed as a category 3 study in the RMP. The package leaflet and Annex II are updated accordingly. The RMP version 4.1 has also been submitted

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

#### 5.3.23. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0011/G, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP: a 104-week subcutaneous injection carcinogenicity study in rats; 2) Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004: a 26-week subcutaneous injection carcinogenicity study in mice. The RMP version 2.1 has also been submitted. 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

#### 5.3.24. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0013/G, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final reports from studies ALN-AS1-003 (Study 003) and ALN-AS1-002 (Study 002) listed as a category 3 studies in the RMP. Study 003 is a phase 3 randomised, double-blind, placebo-controlled multicenter study with an open-label extension to evaluate the efficacy and safety of givosiran in patients with acute hepatic porphyrias, while Study 002 is a multicenter, open-label extension study to evaluate the long-term safety and clinical activity of subcutaneously administered ALN AS1 in patients with acute intermittent porphyria who have completed a previous clinical study with ALN-

AS1. The RMP version 2.2 has also been submitted

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

#### 5.3.25. [Ibrutinib - IMBRUVICA \(CAP\) - EMEA/H/C/003791/II/0073](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include treatment with Imbruvica (ibrutinib) in combination with bendamustine and rituximab (BR) of adult patients with previously untreated mantle cell lymphoma (MCL) who are unsuitable for autologous stem cell transplantation, based on final results from study PCI-32765MCL3002 (SHINE) (listed as a category 3 study in the RMP): a randomized, double-blind, placebo-controlled phase 3 study of ibrutinib in combination with BR in subjects with newly diagnosed MCL. 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 19.1) are updated in accordance

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

#### 5.3.26. [Ibrutinib - IMBRUVICA \(CAP\) - EMEA/H/C/003791/II/0075](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.2 of the SmPC to incorporate information specific for dose modifications for non-cardiac events and events of cardiac failure or cardiac arrhythmias events based on data pool from clinical studies which included 4 Phase II (PCYC-1102-CA, PCYC-1104-CA, PCYC-1118E, PCYC-1142-CA) and 8 Phase III studies (PCYC-1112-CA, PCYC-1115-CA, CLL3001, PCYC-1130-CA, MCL3001, PCYC-1127-CA, CLL3011, and MCL3002). The RMP (version 20.2) is updated accordingly

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

#### 5.3.27. [Lenvatinib - KISPLYX \(CAP\) - EMEA/H/C/004224/II/0052](#)

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Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Update of section 4.8 of the SmPC based on pooled safety data including results of Study 307, an ongoing, multicenter, randomised, open-label study that is being conducted to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib as first-line (1L) treatment in adults with advanced renal cell carcinoma (RCC). The provision of the clinical study report (CSR) addresses the post-authorisation measure MEA/FSR 009.3. The package leaflet is updated accordingly. An updated RMP version 15.0 has been submitted

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

### 5.3.28. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/X/0078/G

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Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped application consisting of: 1) Extension application to add a new strength of 75 mg of lumacaftor and 94 mg of ivacaftor fixed dose combination granules; 2) Extension of indication to include treatment of cystic fibrosis for children aged 1 to less than 2 years old of age who are homozygous for the F508del mutation in the CFTR gene, based on final results from study 122, a 2-part study of CF subjects 1 to <2 years of age homozygous for F508del. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 11.2 of the RMP has also been submitted

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

### 5.3.29. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0053

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Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adults with metastatic castration resistant prostate cancer (mCRPC) with olaparib in combination with abiraterone and prednisone or prednisolone, based on the results of the pivotal study D081SC00001 (PROpel study): a phase 3, randomised, double-blind, placebo-controlled, multicentre study evaluating olaparib vs placebo in combination with abiraterone as first line treatment for men with mCRPC, and supportive evidence from study D081DC00008 (study 8): a randomised, double-blind, placebo-controlled, multicentre phase 2 study to compare the efficacy, safety and tolerability of olaparib versus placebo when given in addition to abiraterone treatment in patients with mCRPC who have received prior chemotherapy containing docetaxel. Consequently, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC for Lynparza (olaparib) tablets are updated. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on the updated safety data analysis. The package leaflet and the RMP (version 24) are updated accordingly

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

### 5.3.30. Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0112

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Applicant: Zr Pharma& GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC in order to include information on post-treatment recovery in growth based on final results from study YV25718 listed as a category 3 study in the RMP; this is a Phase IIIb parallel group, open label study of pegylated interferon alfa-2a monotherapy (PEG-IFN, RO0258310) compared to untreated control in children with HBeAg-Positive Chronic Hepatitis B in the immune active phase. The RMP version 9.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the Package Leaflet

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

### 5.3.31. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0121

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include Keytruda as monotherapy for the adjuvant treatment of adults with Stage IB (T2a  $\geq$  4 cm), II or IIIA non-small cell lung carcinoma (NSCLC) who have undergone complete resection, based on study KEYNOTE-091: an ongoing Phase 3, randomized, triple-blinded, placebo-controlled, multicenter study of pembrolizumab versus placebo in patients with early-stage NSCLC after resection and completion of standard adjuvant therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the Package Leaflet is updated in accordance. An updated RMP version 39.1 was also submitted

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

### 5.3.32. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/II/0074

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of 'advanced' idiopathic pulmonary fibrosis (IPF) by the deletion of the current qualifier 'mild to moderate', based on the results from study MA29957: a 52-week phase 2b, multicentre, randomised, double-blind, placebo-controlled clinical trial in IPF-patients with advanced lung function impairment (carbon monoxide diffusion capacity (DLco) < 40% of predicted) and at high risk of grade 3 pulmonary hypertension, and additional analyses performed on the original pivotal trials for pirfenidone in IPF. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. In addition, the MAH took the opportunity to include information in section 4.4 of the SmPC related to the content of sodium. The package leaflet and the RMP (version 12.0) are updated accordingly

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

### 5.3.33. Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/II/0018, Orphan

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study GO29365 listed as a category 3 study in the RMP in order to address MEA/002. This is a phase Ib/II, multicenter, open-label study evaluating the safety, tolerability, and anti-tumor activity of polatuzumab vedotin in combination with rituximab or obinutuzumab plus bendamustine in patients with relapsed/refractory follicular lymphoma or relapsed/refractory diffuse large B-cell lymphoma. The RMP version 3.0 has also been submitted

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

### 5.3.34. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/X/0027/G

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use); 2) type II variation (C.I.4) to align the Summary of product characteristics and Labelling of Ultomiris intravenous formulation (IV) with the proposed Ultomiris subcutaneous formulation (SC). The RMP (version 5.0) is updated in accordance.

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

### 5.3.35. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/II/0005/G, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of patients below 2 months of age based on interim results from pivotal study BN40703 (RAINBOWFISH): an ongoing phase 2 multicentre, open-label, and single-arm study designed to evaluate the efficacy, safety, tolerability, and pharmacokinetic/pharmacodynamic (PK/PD) of risdiplam in pre-symptomatic infants below 2 months of age who were genetically diagnosed with spinal muscular atrophy (SMA). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, the MAH took the opportunity to make some editorial improvements in the product information; 2) update of Evrydsi (risdiplam) pack configuration. As a consequence, section 6.5 of the SmPC and the labelling are updated; 3) removal of a device. As a consequence, section 6.5 of the SmPC and the labelling are updated. The package leaflet and the RMP (version 1.1) are updated in accordance

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

### 5.3.36. Tadalafil - ADCIRCA (CAP) - EMEA/H/C/001021/X/0035/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form associated with a new strength (2 mg/ml oral suspension); 2) extension of indication to paediatric use from 6 months to 17 years based on study 4 (H6D-MC-LVHV [LVHV]): a 24-week placebo-controlled efficacy and safety study with an open-label long-term extension phase. 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 labelling are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template and editorial changes have been implemented. The RMP (version 9.1) is updated in accordance

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

### 5.3.37. Tixagevimab, cilgavimab - EVUSHELD (CAP) - EMEA/H/C/005788/II/0003

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.2, 4.8, 4.9, 5.1 and 5.2 of the SmPC in order to change the posology recommendations in the pre-exposure prophylaxis indication based on study TACKLE (D8851C00001). The package leaflet is updated accordingly. The RMP (version 2) has also been submitted

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

#### 5.3.38. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/X/138

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add a new strength of 3 µg for individuals 6 months to 4 years of age. The RMP (version 5.1) is updated accordingly

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

#### 5.3.39. Treosulfan - TRECONDI (CAP) - EMEA/H/C/004751/II/0013, Orphan

Applicant: medac Gesellschaft für klinische Spezialpräparate mbH

PRAC Rapporteur: Julia Pallos

Scope: Update of section 5.3 of the SmPC in order to update the description of non-clinical information regarding musculoskeletal and connective tissue disorders in form of lymphohistiocytic infiltration in the skeletal muscles and renal and urinary disorders which show up as haematuria. These new determinations are based on results from study LPT 37259. A revised RMP version 1.0 was also submitted

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

#### 5.3.40. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0003

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adult patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic leukaemia (SLL) based on results from: 1) study BGB-3111-304: an ongoing, international, phase 3, open-label, multiple-cohort, randomised study designed to evaluate the efficacy of zanubrutinib versus bendamustine plus rituximab (B+R) in patients with previously untreated CLL/SLL; 2) study BGB-3111-305: an ongoing, international phase 3, open-label, randomised study of zanubrutinib versus ibrutinib with relapsed/refractory (R/R) CLL/SLL. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are being updated. The package leaflet and the RMP (version 1.1) are updated in accordance. In addition, as part of the application the MAH requested a 1-year extension of the market protection

**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. Abrocitinib - CIBINQO (CAP) - PSUSA/00010976/202203

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.2. Apalutamide - ERLEADA (CAP) - PSUSA/00010745/202202

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.3. Axitinib - INLYTA (CAP) - PSUSA/00010022/202201

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.4. Baloxavir marboxil - XOFLUZA (CAP) - PSUSA/00010895/202202

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.5. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/202202

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP



6.1.6. [Bempedoic acid - NILEMDO \(CAP\); bempedoic acid, ezetimibe - NUSTENDI \(CAP\) - PSUSA/00010841/202202](#)

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Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.7. [Bevacizumab - ABEVMY \(CAP\); ALYMSYS \(CAP\); AVASTIN \(CAP\); AYBINTIO \(CAP\); MVASI \(CAP\); ONBEVZI \(CAP\); OYAVAS \(CAP\); ZIRABEV \(CAP\) - PSUSA/00000403/202202](#)

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Applicant: Amgen Technology (Ireland) Unlimited Company (Mvasi), Mabxience Research SL (Alymsys), Mylan IRE Healthcare Limited (Abevmy), Pfizer Europe MA EEIG (Zirabev), Roche Registration GmbH (Avastin), Samsung Bioepis NL B.V. (Aybintio, Onbevzi), STADA Arzneimittel AG (Oyavas)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.8. [Bimekizumab - BIMZELX \(CAP\) - PSUSA/00010953/202202](#)

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Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.9. [Burosumab - CRYSVITA \(CAP\) - PSUSA/00010669/202202](#)

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Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.10. [Ceftazidime, avibactam - ZAVICEFTA \(CAP\) - PSUSA/00010513/202202](#)

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Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.11. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - PSUSA/00010916/202202

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.12. Degarelix - FIRMAGON (CAP) - PSUSA/00000944/202202

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Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.13. Dexamethasone<sup>6</sup> - OZURDEX (CAP) - PSUSA/00000985/202201

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.14. Eptinezumab - VYEPTI (CAP) - PSUSA/00010966/202202

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Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.15. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202202

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Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.16. Esketamine<sup>7</sup> - SPRAVATO (CAP) - PSUSA/00010825/202203

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Applicant: Janssen-Cilag International N.V.

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<sup>6</sup> Centrally authorised product(s) only, indicated in the treatment of uveitis and macular oedema

<sup>7</sup> Centrally authorised product(s) only

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.17. [Evinacumab - EVKEEZA \(CAP\) - PSUSA/00010945/202202](#)

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Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.18. [Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR \(CAP\) - PSUSA/00010352/202202](#)

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Applicant: Holostem Therapie Avanzate s.r.l., ATMP<sup>8</sup>

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CAT and CHMP

#### 6.1.19. [Fedratinib - INREBIC \(CAP\) - PSUSA/00010909/202202](#)

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.20. [Fenofibrate, simvastatin - CHOLIB \(CAP\) - PSUSA/00010096/202202](#)

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Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.21. [Ferric maltol - FERACCRU \(CAP\) - PSUSA/00010476/202202](#)

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Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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<sup>8</sup> Advanced therapy medicinal product

6.1.22. Hepatitis B (rDNA<sup>9</sup>) vaccine (adjuvanted, adsorbed) - FENDRIX (CAP) - PSUSA/00001598/202202

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Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.23. Ibalizumab - TROGARZO (CAP) - PSUSA/00010797/202203

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Applicant: Theratechnologies Europe Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.24. Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202202

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Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.25. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - FLUCELVAX TETRA (CAP) - PSUSA/00010737/202203

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Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.26. Isatuximab - SARCLISA (CAP) - PSUSA/00010851/202203

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Applicant: sanofi-aventis groupe

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.27. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202202

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Applicant: Nabriva Therapeutics Ireland DAC

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<sup>9</sup> Recombinant deoxyribonucleic acid

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.28. Lonapegsomatropin - SKYTROFA (CAP) - PSUSA/00010969/202202 (with RMP)

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Applicant: Ascendis Pharma Endocrinology Division A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.29. Nitisinone - ORFADIN (CAP) - PSUSA/00002169/202202

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Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.30. Pegfilgrastim - CEGFILA (CAP); FULPHILA (CAP); GRASUSTEK (CAP); NEULASTA (CAP); NYVEPRIA (CAP); PELGRAZ (CAP); PELMEG (CAP); ZIEXTENZO (CAP) - PSUSA/00002326/202201

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Applicant: Accord Healthcare S.L.U. (Pelgraz), Amgen Europe B.V. (Neulasta), Jutta Pharma GmbH (Grasustek), Mundipharma Corporation (Ireland) Limited (Cegfila, Pelmeg), Pfizer Europe MA EEIG (Nyvepria), Sandoz GmbH (Ziextenzo), Viatrix Limited (Fulphila)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.31. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58<sup>10</sup>) - EMEA/H/W/002300/PSUV/0062

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUR procedure

**Action:** For adoption of recommendation to CHMP

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<sup>10</sup> 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).

#### 6.1.32. Pralsetinib - GAVRETO (CAP) - PSUSA/00010961/202203

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.33. Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202202

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Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.34. Ribociclib - KISQALI (CAP) - PSUSA/00010633/202203

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.35. Ropeginterferon alfa-2b - BESREMI (CAP) - PSUSA/00010756/202202

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Applicant: AOP Orphan Pharmaceuticals GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.36. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/202202

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.37. Somapacitan - SOGROYA (CAP) - PSUSA/00010920/202202

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.38. Sotrovimab - XEVUDY (CAP) - PSUSA/00010973/202202

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.39. Telotristat - XERMELO (CAP) - PSUSA/00010639/202202

Applicant: SERB S.A.S.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.40. Tezacaftor, ivacaftor - SYMKEVI (CAP) - PSUSA/00010730/202202

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.41. Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/202202

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.42. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/202202

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.43. [Ulipristal acetate<sup>11</sup> - ESMYA \(CAP\) - PSUSA/00009325/202202](#)

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.44. [Upadacitinib - RINVOQ \(CAP\) - PSUSA/00010823/202202](#)

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.45. [Vosoritide - VOXZOGO \(CAP\) - PSUSA/00010952/202202](#)

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Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

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. [Anidulafungin - ECALTA \(CAP\); NAP - PSUSA/00000215/202201](#)

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Applicant: Pfizer Europe MA EEIG (Ecalta), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.2.2. [Dexrazoxane - SAVENE \(CAP\); NAP - PSUSA/00001001/202202](#)

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Applicant: Clinigen Healthcare B.V. (Savene), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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<sup>11</sup> Indication(s) for the treatment of moderate to severe symptoms of uterine fibroids only



### 6.2.3. Influenza vaccine (surface antigen, inactivated, adjuvanted) - FLUAD TETRA (CAP); NAP - PSUSA/00010300/202203

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Applicant: Seqirus Netherlands B.V. (Fluad Tetra), various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.2.4. Orlistat - ALLI (CAP); XENICAL (CAP); NAP - PSUSA/00002220/202202

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Applicant: GlaxoSmithKline Dungarvan Ltd (Alli), CHEPLAPHARM Arzneimittel GmbH (Xenical), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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

### 6.3.1. Acetylsalicylic acid (NAP) - PSUSA/00000039/202202

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Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.2. Alverine (NAP) – PSUSA/00000124/202202

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Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.3. Alverine, simeticone (NAP) - PSUSA/00000125/202202

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Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.4. Amlodipine, atorvastatin (NAP) – PSUSA/00000177/202201

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Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.5. Carbomers (NAP) - PSUSA/00000557/202201

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Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.6. Carboplatin (NAP) - PSUSA/00000559/202201

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Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.7. Cromoglicic acid (NAP) - PSUSA/00000883/202202

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Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.8. Dorzolamide (NAP) - PSUSA/00003168/202202

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Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.9. Gabapentin (NAP) - PSUSA/00001499/202202

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.10. Glipizide (NAP) - PSUSA/00001535/202201

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.11. Hydroxyethyl starch (HES) (NAP) - PSUSA/00001694/202203

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.12. Influenza vaccine<sup>12</sup> (split virion, inactivated) (NAP) - PSUSA/00010298/202203

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.13. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/202203

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.14. Interferon gamma (NAP) - PSUSA/00001760/202201

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

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<sup>12</sup> Non-centrally authorised product(s) only

#### 6.3.15. Ketoprofen<sup>13</sup> (NAP) - PSUSA/00001809/202201

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.16. Ketoprofen<sup>14</sup> (NAP) - PSUSA/00009205/202201

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.17. Levothyroxine (NAP) - PSUSA/00001860/202201

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Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.18. Lisdexamfetamine (NAP) - PSUSA/00010289/202202

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.19. Loratadine (NAP) - PSUSA/00001907/202202

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Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.20. Loratadine, pseudoephedrine (NAP) - PSUSA/00001908/202202

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Applicant(s): various

PRAC Lead: Jean-Michel Dogné

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<sup>13</sup> All formulations except topical

<sup>14</sup> For topical use only

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.21. Lorazepam (NAP) - PSUSA/00001909/202201

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.22. Mesalazine (NAP) - PSUSA/00001990/202202

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.23. Mesterolone (NAP) - PSUSA/00010551/202201

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.24. Moxonidine (NAP) - PSUSA/00002095/202201

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.25. Zanamivir (NAP) - PSUSA/00003141/202201

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

## 6.4. Follow-up to PSUR/PSUSA procedures

### 6.4.1. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/LEG 008.1

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to LEG 008 [cumulative review of cases of colitis, diarrhoea, alopecia/alopecia aerate and appendicitis, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010662/202103) adopted in November 2021] as per the request for supplementary information (RSI) adopted in July 2022

**Action:** For adoption of advice to CHMP

## 6.5. Variation procedure(s) resulting from PSUSA evaluation

### 6.5.1. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0022

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Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on pericarditis and myocarditis and to add pericarditis and myocarditis to the list of adverse drug reactions (ADRs) with frequency not known following the outcome of MEA/014.4 (5<sup>th</sup> monthly summary safety report) based on PRAC assessment on pericarditis and myocarditis concluded in August 2022. The package leaflet is updated accordingly

**Action:** For adoption of PRAC Assessment Report

### 6.5.2. Elasmolan - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0077

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Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of section 4.8 of the SmPC to include acute and delayed urticaria as an adverse reaction, with the frequency 'rare', as requested by the PRAC in the 13th Safety Summary Report (EMEA/H/C/005791/MEA/011.12) concluded in June 2022. The package leaflet is updated accordingly

**Action:** For adoption of PRAC Assessment Report

## 6.6. Expedited summary safety reviews<sup>15</sup>

### 6.6.1. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 009

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Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Justification letter submitted by the MAH for not submitting a monthly summary safety report (letter covering reporting period of 24 June 2022 to 31 July 2022) for (COVID-19 vaccine (inactivated, adjuvanted) Valneva during the coronavirus disease (COVID-19) pandemic

**Action:** For adoption of advice to CHMP

### 6.6.2. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 009.1

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Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Justification letter submitted by the MAH for not submitting the second summary monthly safety report (SSR) (letter covering reporting period of 01 August 2022 to 31 August 2022)] for (COVID-19 vaccine (inactivated, adjuvanted) Valneva during the coronavirus disease (COVID-19) pandemic

**Action:** For adoption of advice to CHMP

### 6.6.3. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.6

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Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Seventh expedited summary safety report (SSR) for Nuvaxovid (COVID-19 vaccine (recombinant, adjuvanted)) during the coronavirus disease (COVID-19) pandemic

**Action:** For adoption of PRAC Assessment Report

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<sup>15</sup> Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

## 7. Post-authorisation safety studies (PASS)

### 7.1. Protocols of PASS imposed in the marketing authorisation(s)<sup>16</sup>

#### 7.1.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSA/S/0089

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Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial amendment to an agreed protocol for a non-interventional PASS to investigate the risk of mortality in multiple sclerosis patients treated with Lemtrada (alemtuzumab) relative to comparable multiple sclerosis patients using other disease modifying therapies: a cohort study

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

#### 7.1.2. Ciltacabtagene autoleucl – CARVYKTI (CAP) - EMEA/H/C/PSP/S/0100

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Applicant: Janssen-Cilag International NV, ATMP<sup>17</sup>

PRAC Rapporteur: Jo Robays

Scope: Protocol for study 68284528MMY4004: an observational PASS to evaluate the safety of multiple myeloma patients treated with ciltacabtagene autoleucl

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

#### 7.1.3. Ciltacabtagene autoleucl - CARVYKTI (CAP) - EMEA/H/C/PSP/S/0101

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Applicant: Janssen-Cilag International NV, ATMP<sup>18</sup>

PRAC Rapporteur: Jo Robays

Scope: Protocol for study 68284528MMY4009: an observational PASS to evaluate the safety of multiple myeloma patients treated with ciltacabtagene autoleucl

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

#### 7.1.4. Pomalidomide – IMNOVID (CAP) - EMEA/H/C/PSA/S/0090

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Substantial amendment to a non-interventional post authorisation registry of patients treated with pomalidomide for relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy

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<sup>16</sup> In accordance with Article 107n of Directive 2001/83/EC

<sup>17</sup> Advanced therapy medicinal product

<sup>18</sup> Advanced therapy medicinal product



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

#### 7.1.5. Teduglutide – REVESTIVE (CAP) - EMEA/H/C/PSA/S/0086

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Substantial amendment (version 8.0) to a protocol previously agreed in June 2022 (PSA/S/0082.1) for study TED-R13-002: a prospective, multicentre registry for patients with short bowel syndrome]

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

#### 7.1.6. Valproate<sup>19</sup> (NAP) - EMEA/H/N/PSP/J/0075.8

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0075.7 [submission of the third interim report for drug utilisation study (DUS) extension to assess the effectiveness of the risk minimisation measures and to further characterise the prescribing patterns for valproate and related substances, in Europe, using databases, in Germany, France, Netherlands, Spain, Sweden and United Kingdom, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate and related substances, completed in February 2018 (EMEA/H/A-31/1454)]. The MAH also provided an updated protocol (version 9.0), in response to the request included in the assessment report evaluating the second interim report, as well as to describe for which country data are expected to be available in the third and fourth interim report

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

#### 7.1.7. Valproate<sup>20</sup> (NAP) - EMEA/H/N/PSA/J/0091

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: Substantial amendment (protocol version 7.0, including amendment 3.0, dated 11 July 2022) to an agreed protocol for a non-interventional retrospective longitudinal study, conducted in the United Kingdom and France to evaluate and identify the best practices for switching of valproate and related substances in clinical practice [Valse study (VALNAC09344)], as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate and related substances, completed in February 2018 (EMEA/H/A-31/1454)]

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

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<sup>19</sup> Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium

<sup>20</sup> Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium

## 7.2. Protocols of PASS non-imposed in the marketing authorisation(s)<sup>21</sup>

### 7.2.1. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/MEA 035.4

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Amendment to a previously agreed protocol for study 20180204 (listed as category 3 study in the RMP): an observational registry study to evaluate the use and safety of cinacalcet among paediatric patients with secondary hyperparathyroidism

**Action:** For adoption of advice to CHMP

### 7.2.2. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 002.3

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Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Amendment to a previously agreed protocol for study MS 700568-0002 (CLARION) (listed as category 3 study in the RMP): a prospective, observational cohort study evaluating the safety profile, in terms of incidence of adverse events of special interest, in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine

**Action:** For adoption of advice to CHMP

### 7.2.3. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 006

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Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Updated protocol for study 2019nCoV-404: US post-authorisation safety study to evaluate the pooled of risk of selected adverse events of special interest (AESI) within specified time periods after vaccination with Nuvaxovid using a claim and/or electronic healthcare record (her) database

**Action:** For adoption of advice to CHMP

### 7.2.4. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092.4

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 092.3 [amendment to a previously agreed protocol for study 20190404 (listed as a category 3 study in the RMP): a retrospective cohort study to assess the use of erythropoiesis stimulating agents (ESAs) in subjects receiving myelosuppressive chemotherapy in Europe] as per the request for supplementary information (RSI) adopted

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<sup>21</sup> 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

in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.5. [Diroximel fumarate - VUMERITY \(CAP\) - EMEA/H/C/005437/MEA 002.1](#)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002 [protocol for study SE-VUM-12146 (listed as category 3 study in the RMP): an observational study utilising data from 'big data' multiple sclerosis registries to evaluate the long-term safety of Vumerity (diroximel fumarate) and Tecfidera (dimethyl fumarate)] as per RSI (request for supplementary information) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.6. [Dulaglutide - TRULICITY \(CAP\) - EMEA/H/C/002825/MEA 006.4](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Amendment to a previously agreed protocol for study H9X-MC-B013 (listed as category 3 study in the RMP): a non-interventional retrospective study to estimate the incidence rates of events of interest among type 2 diabetes mellitus (T2DM) patients treated with dulaglutide compared to other glucagon-like peptide 1 (GLP-1) receptor agonists in order to better characterise the safety profile of dulaglutide in terms of acute pancreatitis, pancreatic and thyroid malignancies

**Action:** For adoption of advice to CHMP

#### 7.2.7. [Empagliflozin - JARDIANCE \(CAP\) - EMEA/H/C/002677/MEA 004.6](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 004.5 [fifth monitoring interim report for study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.8. [Empagliflozin, metformin - SYNJARDY \(CAP\) - EMEA/H/C/003770/MEA 006.8](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 006.7 [fifth monitoring interim report for study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to

empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.9. Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.8

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Maia Uusküla

Scope: Substantial amendment to a protocol previously agreed in September 2017 (MEA 002.6) for study NCEPPEUPASS15741 (listed as a category 3 study in the RMP): assessment of the clinical practice regarding concomitant use of fenofibrate and simvastatin both as free and fixed combination: a European PASS

**Action:** For adoption of advice to CHMP

#### 7.2.10. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 016.1

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 016 [protocol for study GLPG0634-CL-413: a non-interventional, PASS of filgotinib in patients with moderately to severely active ulcerative colitis (a European multi registry-based study)] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.11. Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/MEA 005

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Protocol for study F3Z-MC-B030: a post-approval safety surveillance programme to assess blood glucose data and characterise the frequency of severe hypoglycaemia in patients using a compatible software application for Tempo Pen of Abasaglar/Humalog and to contextualise findings using an appropriate comparator populations [final study report: December 2023]

**Action:** For adoption of advice to CHMP

#### 7.2.12. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/MEA 035

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Mari Thorn

Scope: Protocol for study F3Z-MC-B030: a post-approval safety surveillance programme to assess blood glucose data and characterise the frequency of severe hypoglycaemia in patients using a compatible software application for Tempo Pen of Abasaglar/Humalog and

to contextualise findings using an appropriate comparator populations [final study report: December 2023]

**Action:** For adoption of advice to CHMP

#### 7.2.13. Insulin lispro - LYUMJEV (CAP) - EMEA/H/C/005037/MEA 004

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Mari Thorn

Scope: Protocol for study F3Z-MC-B030: a post-approval safety surveillance programme to assess blood glucose data and characterise the frequency of severe hypoglycaemia in patients using a compatible software application for Tempo Pen of Abasaglar/Humalog and to contextualise findings using an appropriate comparator populations [final study report: December 2023]

**Action:** For adoption of advice to CHMP

#### 7.2.14. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 003.1

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 003 [protocol for study A4250-019 (listed as a category 3 study in the RMP): registry-based safety study in order to collect safety data on hepatotoxicity, diarrhoea, fat-soluble vitamins and fat-soluble nutrients in patients treated with odevixibat] as per request for supplementary information (RSI) adopted in April 2022

**Action:** For adoption of advice to CHMP

#### 7.2.15. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 002.2

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 002.1 [protocol for study OMB157G2407 (listed as category 3 study in the RMP): pregnancy outcomes intensive monitoring (PRIM) to evaluate pregnancy and infant outcomes in patients taking Kesimpta (ofatumumab)] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.16. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 004

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Protocol for a non-interventional study OMB157G2406: Kesimpta long-term retrospective safety study utilizing real-world data from existing multiple sclerosis registries and databases from multiple countries. The primary objective is to estimate the event rates of malignancy and serious infections following ofatumumab treatment in patients with MS.

The secondary objective is to compare the incidence of each serious safety event between ofatumumab exposed patients with RMS and patients with RMS exposed to other approved disease modifying therapies (DMTs)

**Action:** For adoption of advice to CHMP

#### 7.2.17. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.4

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Amendment to a previously agreed protocol for study 165-504: a global, multicenter study to assess maternal, fetal and infant outcomes of exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding

**Action:** For adoption of advice to CHMP

#### 7.2.18. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 003

Applicant: Biohaven Pharmaceutical Ireland DAC

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of protocol for study BHV3000-408: a PASS of rimegepant in patients with migraine and a history of cardiovascular diseases together with a statistical analysis plan (SAP)

**Action:** For adoption of advice to CHMP

#### 7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 018.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 018 [protocol for study A3921407: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the German Biologics in Paediatric Rheumatology Registry (BIKER) and within the Juvenile Arthritis Methotrexate/Biologics long-term Observation (JuMBO) biological register (from X/0024/G)] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.20. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 019.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 019 [protocol for study A3921408: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the Swedish juvenile idiopathic arthritis (JIA) clinical registry (from X/0024/G)] as per the request for supplementary

information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.21. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 020.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 010 [protocol for study A3921409: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the UK juvenile idiopathic arthritis (JIA) biologics register (from X/0024/G)] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

#### 7.2.22. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.5

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to a previously agreed protocol for study C4591012 to assess the occurrence of safety events of interest, including severe or atypical COVID-10 in real-world use of COVID-19 mRNA vaccine

**Action:** For adoption of advice to CHMP

#### 7.2.23. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Amendment for a protocol previously agreed in March 2022 [MEA 037.1] for study C4591009: a non-interventional PASS in US to assess the occurrence of safety events of interest, including myocarditis and pericarditis (from variation II/0059 finalised in October 2021)]

**Action:** For adoption of advice to CHMP

#### 7.2.24. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 053.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 053 [protocol for study CNTO1275PSO4005: a Nordic database initiative for exposure to ustekinumab - a review and analysis of major adverse cardiovascular events (MACE) from the Swedish and Danish national registry systems] as per the request for supplementary information (RSI) adopted in April 2022

**Action:** For adoption of advice to CHMP

#### 7.2.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 054.1

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's Response to MEA 054 [protocol for study CNTO1275PSO4007: an observational longitudinal PASS of Stelara (ustekinumab) in the treatment of psoriasis and psoriatic arthritis - analysis of major adverse cardiovascular events (MACE) using Swedish national health registers] as per the request for supplementary information (RSI adopted in April 2022

**Action:** For adoption of advice to CHMP

### 7.3. Results of PASS imposed in the marketing authorisation(s)<sup>22</sup>

#### 7.3.1. Aprotinin (NAP) - EMEA/H/N/PSR/S/0030

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Applicant: Nordic Group BV

PRAC Rapporteur: Jean-Michel Dogné

Scope: Results of a Nordic aprotinin patient registry to record utilisation information on patients at cardiac surgery centres

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

#### 7.3.2. Lumacaftor, ivacaftor – ORKAMBI (CAP) - EMEA/H/C/PSR/S/0039

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Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Results of an observational study to evaluate the utilisation patterns and long-term effects of lumacaftor and ivacaftor combination therapy in patients with cystic fibrosis

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

### 7.4. Results of PASS non-imposed in the marketing authorisation(s)<sup>23</sup>

#### 7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0090

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from non-interventional study AGLU06909/LTS13930: a prospective safety sub-registry to assess anaphylaxis and severe allergic reactions, and severe cutaneous and systemic immune complex mediated reactions with alglucosidase alfa

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<sup>22</sup> In accordance with Article 107p-q of Directive 2001/83/EC

<sup>23</sup> 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



treatment (Pompe registry report 2020 (in fulfillment of MEA024.15 and MEA025.15))

**Action:** For adoption of PRAC Assessment Report

#### 7.4.2. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0072

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study ALIROC07997 (listed as a category 3 study in the RMP): PASS using healthcare databases to monitor the safety of alirocumab in HIV patients. The RMP version 7.0 has also been submitted

**Action:** For adoption of PRAC Assessment Report

#### 7.4.3. Hepatitis B surface antigen - HEPLISAV B (CAP) - EMEA/H/C/005063/II/0015

Applicant: Dynavax GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study HBV-26 (listed as a category 3 study in the RMP): a post-marketing observational surveillance study to evaluate the incidence of new-onset immune-mediated diseases, herpes zoster, and anaphylaxis in recipients of Heplisav B (hepatitis B surface antigen) with recipients of another hepatitis B vaccine. The RMP (version 1.3) is updated accordingly

**Action:** For adoption of PRAC Assessment Report

#### 7.4.4. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0041, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study NSMM-5001 (INSIGHT) (listed as a Specific Obligation in the Annex II of the Product Information. This is a global, prospective, non-interventional, observational study of presentation, treatment patterns, and outcomes in multiple myeloma patients. The Annex II and the RMP (submitted version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

**Action:** For adoption of PRAC Assessment Report

#### 7.4.5. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0054

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study NB-542 (listed as a category 3 study in the RMP): a cross-sectional survey aimed to evaluate the effectiveness of the Mysimba (naltrexone hydrochloride/bupropion hydrochloride) physician prescribing checklist (PPC)

among physicians in the EU. The RMP (version 12.6) is updated accordingly

**Action:** For adoption of PRAC Assessment Report

#### **7.4.6. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/II/0049**

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Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report for study 241501 (listed as a category 2 study in the RMP in order to fulfil SOB/001.4): a prospective and retrospective, non-interventional post-authorisation safety study (PASS) to evaluate the safety and effectiveness of Obizur in real-life practice. The RMP version 6.0 has also been submitted

**Action:** For adoption of PRAC Assessment Report

#### **7.4.7. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0073**

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Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study MLN0002\_401 (listed as a category 3 study in the RMP in order to fulfil MEA/001.2): an international observational prospective cohort study comparing vedolizumab to other biologic agents in patients with ulcerative colitis or Crohn's disease. The RMP version 8.0 has also been submitted

**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. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/MEA 001.6**

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Applicant: Almirall S.A

PRAC Rapporteur: Mari Thorn

Scope: Fourth annual interim results for study M-41008-40 (listed as a category 3 study in the RMP): an observational PASS in European psoriasis registers to evaluate the long-term safety of Skilarence (dimethyl fumarate) used for the treatment of patients with moderate to severe psoriasis

**Action:** For adoption of advice to CHMP

#### **7.5.2. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.7**

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Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Eighth annual report (reporting period: 14 February 2021 to 12 February 2022) for the multicentre, multinational, observational Morquio A registry study (MARS): a voluntary

observational registry study to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population and to evaluate the long-term effectiveness and safety of Vimizim (elosulfase alfa) [final clinical study report (CSR) expected by March 2025]

**Action:** For adoption of advice to CHMP

#### 7.5.3. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 002

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Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Progress report for study ZX008-1503: an open-label extension trial to assess the long-term safety of ZX008 (fenfluramine hydrochloride) oral solution as an adjunctive therapy in children and young adults with Dravet syndrome

**Action:** For adoption of advice to CHMP

#### 7.5.4. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 002.1

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jo Robays

Scope: Second annual report for study ACE-536-LTFU-001: a study to evaluate the long-term safety, including thromboembolic events (TEEs) and progression to acute myeloid leukaemia (AML) and/or other malignancies/pre malignancies of luspatercept in patients who have participated in company-sponsored luspatercept clinical trials

**Action:** For adoption of advice to CHMP

#### 7.5.5. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/MEA 009

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: First interim report for study M11-001 (listed as category 3 study in the RMP): an observational, non-interventional multi-center, multi-national study of patients with atypical hemolytic-uremic syndrome (aHUS registry) together with a statistical analysis plan (SAP)

**Action:** For adoption of advice to CHMP

#### 7.5.6. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.5

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Applicant: sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 005.4 [1] eighth annual progress report for pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project, 2) fifth annual progress report for OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide)] as per request for supplementary information (RSI) adopted in June 2022

**Action:** For adoption of advice to CHMP

#### 7.5.7. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 024

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: First interim report for study A3921347 (listed as category 3 study in the RMP): a prospective non-interventional active surveillance study in the US, to quantify the incidence of key safety events of interest in patients with moderate-to-severe ulcerative colitis patients treated with tofacitinib and other systemic therapies in the clinical practice (real world) setting [following variation II/0038, the 2 non-interventional US studies (A3921347 & A3921348) were combined into the A3921347 protocol to allow for the consolidation of resources by using the same US database and vendor]

**Action:** For adoption of advice to CHMP

#### 7.5.8. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010.4

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Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591012: clinical study to assess the occurrence of safety events of interest, including severe or atypical COVID-19 in real-world use of COVID-19 mRNA vaccine

**Action:** For adoption of advice to CHMP

#### 7.5.9. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 026.4

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

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

**Action:** For adoption of advice to CHMP

#### 7.5.10. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 027.4

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

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

**Action:** For adoption of advice to CHMP

## 7.6. Others

### 7.6.1. Avatrombopag - DOPTelet (CAP) - EMEA/H/C/004722/MEA 003.2

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Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 003.1 [feasibility assessment for a study to further characterise the long-term safety profile of avatrombopag in patients with primary chronic immune thrombocytopenia in European patient registers and electronic healthcare databases as requested in the conclusions of variation II/0004/G finalised in December 2020] as per the request for supplementary information (RSI) adopted May 2022

**Action:** For adoption of advice to CHMP

### 7.6.2. Azathioprine - JAYEMPI (CAP) - EMEA/H/C/005055/MEA 001

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Applicant: Nova Laboratories Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Monitoring of medication error reports specifically due to 'conversion of patients from tablet to liquid formulation and two dosing syringes' annually and submitted as post authorisation measure (PAM outside the context of azathioprine PSUR) (from initial opinion/MA)

**Action:** For adoption of advice to CHMP

### 7.6.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 008

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Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Proposal to replace the existing PASS to assess the safety of Vaxzevria (coronavirus (COVID-19) vaccine (ChAdOx1-S[recombinant])) in patients receiving immunosuppressant medication or with primary immunodeficiency with systematic literature review for studies evaluating adverse events of AZD1222 in patients taking immunosuppressant medications and/or with primary immunodeficiency

**Action:** For adoption of advice to CHMP

### 7.6.4. Radium (Ra<sup>223</sup>) - XOFIGO (CAP) - EMEA/H/C/002653/ANX 013.2

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Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Request for deletion of ANX 013.1 post-approval commitment (study 20511): an open-label, multicentre, non-randomized Phase 1 study that has been requested by the European Commission as a result of the referral procedure (EMEA/H/A-20/1459/C/002653/0028) to further characterize the correlation between the extent of the

disease, the dose and the distribution of radium-223 in bone metastases versus sites of impaired bone health versus normal bone structure

**Action:** For adoption of advice to CHMP

#### **7.6.5. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 002.5**

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Revised statistical analysis plan (SAP) for study P16-751: pregnancy exposures and outcomes in psoriasis patients treated with risankizumab: a cohort study utilising large healthcare databases with mother-baby linkage in the United States

**Action:** For adoption of advice to CHMP

#### **7.6.6. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 032.2**

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: MAH's response to MEA 032.1 [submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding] as per the request for supplementary information (RSI) adopted in March 2022

**Action:** For adoption of advice to CHMP

#### **7.6.7. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 024.2**

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 032.1 [submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding] as per the request for supplementary information (RSI) adopted in March 2022

**Action:** For adoption of advice to CHMP

#### **7.6.8. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 024.4**

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

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

**Action:** For adoption of advice to CHMP

## 7.7. New Scientific Advice

None

## 7.8. Ongoing Scientific Advice

None

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

None

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

## 8.1. Annual reassessments of the marketing authorisation

### 8.1.1. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/S/0046 (without RMP)

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Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.1.2. Ebola vaccine (rDNA<sup>24</sup>, replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/S/0015 (without RMP)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual reassessment of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.1.3. Ebola vaccine (rDNA<sup>25</sup>, replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/S/0012 (without RMP)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual reassessment of the marketing authorisation

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<sup>24</sup> Ribosomal deoxyribonucleic acid

<sup>25</sup> Ribosomal deoxyribonucleic acid

**Action:** For adoption of advice to CHMP

#### 8.1.4. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/S/0008 (without RMP)

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

**Action:** For adoption of advice to CHMP

## 8.2. **Conditional renewals of the marketing authorisation**

#### 8.2.1. (1R,2S,5S)-N-((1S)-1-Cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/R/0023 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.2.2. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/R/0031 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.2.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/R/0079 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Conditional renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.2.4. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/R/0018 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation



**Action:** For adoption of advice to CHMP

### 8.3. Renewals of the marketing authorisation

#### 8.3.1. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - RIARIFY (CAP) - EMEA/H/C/004836/R/0022 (with RMP)

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.2. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRYDONIS (CAP) - EMEA/H/C/004702/R/0025 (with RMP)

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.3. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/R/0057 (without RMP)

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.4. Infliximab - ZEESLY (CAP) - EMEA/H/C/004647/R/0025 (without RMP)

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Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.5. Insulin glargine - SEMGLEE (CAP) - EMEA/H/C/004280/R/0040 (without RMP)

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Applicant: Viatris Limited

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.3.6. Sodium zirconium cyclosilicate - LOKELMA (CAP) - EMEA/H/C/004029/R/0027 (without RMP)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.3.7. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/R/0029 (without RMP)

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

## 9. Product related pharmacovigilance inspections

### 9.1. List of planned pharmacovigilance inspections

None

### 9.2. Ongoing or concluded pharmacovigilance inspections

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

### 9.3. Others

None

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

### 10.1. Safety related variations of the marketing authorisation

None

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

None

### 10.3. Other requests

None

### 10.4. Scientific Advice

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

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

### 11.1. Safety related variations of the marketing authorisation

#### 11.1.1. Bismuth subcitrate potassium, metronidazole, tetracycline (NAP) - DE/H/2467/001/II/052

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Applicant: various

PRAC Lead: Martin Huber

Scope: PRAC consultation on a type II variation (DE/H/2467/001/II/052) for Pylera (bismuth subcitrate/metronidazole/tetracycline) on the product information warning for patients with Cockayne syndrome, on request of Germany

**Action:** For adoption of advice to Member States

### 11.2. Other requests

None

## 12. Organisational, regulatory and methodological matters

### 12.1. Mandate and organisation of the PRAC

#### 12.1.1. PRAC membership

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**Action:** For information

#### 12.1.2. Vote by proxy

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None

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

None

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

None

### **12.4. Cooperation within the EU regulatory network**

#### **12.4.1. Coronavirus (COVID-19) pandemic - update**

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**Action:** For discussion

#### **12.4.2. PRAC and CMDh strategic review and learning meeting (SRLM) under the Czech Presidency of the European Union (EU) Council – Prague, 17 – 19 October 2022 - agenda**

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PRAC lead: Eva Jirsová, Jana Lukačičinová

**Action:** For discussion

### **12.5. Cooperation with International Regulators**

None

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

None

### **12.7. PRAC work plan**

None

### **12.8. Planning and reporting**

#### **12.8.1. Marketing authorisation applications (MAA) forecast for 2022 – planning update dated Q3 2022**

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**Action:** For discussion

### **12.9. Pharmacovigilance audits and inspections**

#### **12.9.1. Pharmacovigilance systems and their quality systems**

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None

### 12.9.2. Pharmacovigilance inspections

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None

### 12.9.3. Pharmacovigilance audits

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None

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

### 12.10.1. Periodic safety update reports

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None

### 12.10.2. Granularity and Periodicity Advisory Group (GPAG)

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PRAC lead: Menno van der Elst, Maia Uusküla

**Action:** For discussion

### 12.10.3. PSURs repository

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None

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

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**Action:** For adoption

## 12.11. Signal management

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

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PRAC lead: Menno van der Elst

**Action:** For discussion

## 12.12. Adverse drug reactions reporting and additional reporting

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

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None

#### 12.12.2. Additional monitoring

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None

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

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**Action:** For adoption

### 12.13. EudraVigilance database

#### 12.13.1. Activities related to the confirmation of full functionality

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None

### 12.14. Risk management plans and effectiveness of risk minimisations

#### 12.14.1. Risk management systems

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None

#### 12.14.2. Tools, educational materials and effectiveness measurement of risk minimisations

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None

### 12.15. Post-authorisation safety studies (PASS)

#### 12.15.1. Post-authorisation Safety Studies – imposed PASS

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None

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

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None

#### 12.15.3. International Conference on Harmonisation (ICH) E19 - A selective approach to safety data collection in specific late-stage pre-approval or post-approval clinical trials

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**Action:** For discussion

## 12.16. Community procedures

### 12.16.1. Referral procedures for safety reasons

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None

## 12.17. Renewals, conditional renewals, annual reassessments

None

## 12.18. Risk communication and transparency

### 12.18.1. Public participation in pharmacovigilance

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None

### 12.18.2. Safety communication

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None

## 12.19. Continuous pharmacovigilance

### 12.19.1. Incident management

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None

## 12.20. Impact of pharmacovigilance activities

### 12.20.1. Impact of EU label changes on post-referral prescribing trends and risk of long-term/persistent symptoms associated with gadolinium based contrast agents (GBCA) exposure

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**Action:** For adoption

## 12.21. Others

### 12.21.1. Data analysis and real world interrogation network (DARWIN EU) – introduction of the coordination centre and next steps for real-world evidence (RWE)

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**Action:** For discussion

### 12.21.2. Launch of EMA coordinated CHMP/PRAC requested GVP inspections in IRIS

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**Action:** For discussion

## **13. Any other business**

Next meeting on: 24-27 October 2022



## 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](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/](http://www.ema.europa.eu/)